DNA METHYLATION ANALYSIS OF PAEDIATRIC LOW-GRADE ASTROCYTOMAS IDENTIFIES A TUMOUR-SPECIFIC SIGNATURE AT A SET OF ENHANCERS

Sheer, D; Jeyapalan, J; Doctor, GT; Jones, TA; Alberman, SN; Tep, A; Haria, CM; Schwalbe, EC; Clifford, SC; Tatevossian, RG; Qaddoumi, I; Ellison, DW

47th CONGRESS OF THE INTERNATIONAL SOCIETY OF PAEDIATRIC ONCOLOGY (SIOP)

CAPE TOWN, SOUTH AFRICA OCTOBER 8–11, 2015 SIOP ABSTRACTS

ABSTRACT CONTENTS:

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SIOP ABSTRACTS

SIOP Award Session

O-001

PRE-ENUCLEATION CHEMOTHERAPY IN ADVANCED INTRAOCULAR RETINOBLASTOMA IN CENTRAL AMERICA. LONG TERM FOLLOW-UP: AHOPCA II

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Background/Objectives: A significant percentage of patients in Central America present with buphthalmos, carrying a high risk of globe rupture and orbital contamination. In 2007, the protocol AHOPCA II introduced a study of chemotherapy before enucleation in children with buphthalmos and for families who refused enucleation at diagnosis. This is the final report.
Design/Methods: Patients with advanced intraocular disease were considered standard-risk and underwent enucleation. Those with diffuse invasion of choroid, post-laminar optic nerve, or anterior chamber invasion received 4-6 cycles of adjuvant chemotherapy (vincristine 1.5 mg/m^2 and, carboplatin 500 mg/m^2 day 1, and etoposide 100 mg/m^2 days 1-3). Patients with buphthalmos or perceived to be at risk for refusal or abandonment were considered high risk and given 2-3 cycles of chemotherapy before scheduled enucleation and adjuvant chemotherapy to complete 6 cycles regardless of pathology. All cases were discussed via online meetings.
Results: From 2007 to 2014, 396 patients were enrolled on AHOPCA II; 239 had IRSS stage I (174 unilateral). There were no refusals; 143 had upfront enucleation, 95 had pre-enucleation chemotherapy, and 1 is pending enucleation. Of 95 high-risk group, 8 abandoned, 20 had relapse/progression (13 bilateral), 6 had toxic deaths and 61 are alive at first event. Of high risk patients, OS for 56 with unilateral disease was 80±0.06 at 7 years. For patients with buphthalmos OS was 77%±0.07. The estimated 7-year OS (abandonment sensitive) for all IRSS 1 was 90±0.03 and 79±0.04 for standard-risk and high-risk patients, respectively (p=0.007).
Conclusion: AHOPCA was able to address advanced intraocular disease with an innovative approach. Histopathology at the time of enucleation can define risk. In eyes with buphthalmos and patients with risk of abandonment, neo-adjuvant chemotherapy is effective, when followed by post-enucleation chemotherapy. This approach saved patients from ocular rupture and intensified therapy; and reduced refusal rate compared to our previous experience.

O-002

OUTCOMES FOR CHILDREN AND ADOLESCENTS WITH HODGKIN LYMPHOMA 2000-2010: A FIRST REPORT BY THE SOUTH AFRICAN CHILDREN'S CANCER STUDY GROUP

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Background/Objectives: A multicentre retrospective study was conducted by the South African Children's Cancer Study Group (SACCSG) to analyse the outcome and prognostic factors of paediatric patients with biopsy-proven Hodgkin lymphoma (HL) in South Africa. HL has excellent survival rates in high income countries, but there is scant data on outcome in South African and African patients. Differing approaches to treatment are used in centres across the country, and the SACCSG has embarked on a programme to audit outcomes in order to harmonise treatment protocols.
Design/Methods: All dedicated paediatric oncology units participated in a retrospective data review. All patients with Hodgkin lymphoma treated between January 2000 and December 2010 were included. Survival analysis was conducted using Kaplan-Meier survival plots. Prognostic factors were generated using the Cox regression model.
Results: Two hundred and ninety five patients were elligible for inclusion. The mean age at presentation was 9.63 years (range 2.9 – 18.8). Fifty five percent of patients presented with Stage III and IV disease. Ten percent of patients were HIV positive. First-line therapy consisted of ABVD in 161 patients, OEPA/OPPA-COPP in 98 and ABVD-ChlVPP in 34 patients. The five year OS was 79% (95% CI 73-84%). OEPA/OPPA-COPP was found to be most myelosuppressive, but patients receiving ABVD-ChlVVP had the highest rate of infections. Treatment with ABVD was associated with higher survival rates ($p = 0.028$) while black race ($p = 0.001$), B symptoms ($p = 0.001$), HIV infection ($p < 0.001$) and under-resourced settings ($p = 0.0278$) were associated with a poorer prognosis.
Conclusion: Overall survival rates are encouraging for a middle income country, although economic disparities continue to impact negatively on outcomes. These results will form the basis for national protocol development and will be used to lobby for more equitable allocation of resources for paediatric cancer care.

O-003

PREDICTION OF PROGNOSIS BY PREOPERATIVE CHEMOTHERAPY RESPONSE IN HEPATOBLASTOMA PATIENTS TREATED BY JPLT-2 PROTOCOL

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Background/Objectives: The Japanese Study Group for Pediatric Liver Tumor(JPLT)-2 study (1999-2012) was designed to evaluate the efficacy of cisplatin/pirarubicin for hepatoblastoma (HB). We considered HBs in 3 risk categories as follows: standard (tumors involving three or fewer sectors of the liver), intermediate (tumors involving all sectors of the liver or invasion into portal or hepatic vein) and high (tumor with distant metastasis). In this study, we aimed to clarify whether preoperative chemotherapy response represents a prognostic factor for HB.
Design/Methods: In the JPLT-2 study, 385 HB children were eligible for inclusion. Except for primary resected cases, after 2 cycles of preoperative chemotherapy, tumor response evaluation by imaging was classified into CR, PR, NC, PD according to RECIST criteria and cases were defined as responsive if serum AFP levels declined by at least 90% of the highest AFP level.
Results: Among the 385 cases, there were 31 PRETEXT I, 120 II, 145 III, and 89 IV, including 86 metastatic HBs. The 3-year EFS/OS of standard risk HBs were 94/82%, while those of intermediate and high risk HBs were 64/49% and 34/28%, respectively. In the standard risk group except for primary resected cases, EFS/OS (86%/96%) of the CR/PR cases were significantly better than other cases (58%/81%) and EFS/OS (96%/100%) of AFP reduced cases were significantly better than others (53%/84%) ($P < 0.05$). In the intermediate/high risk groups, there were no significant differences in EFS/OS when using these preoperative chemotherapeutic response classifications.
Conclusion: Evaluation of efficacy of preoperative chemotherapy after two cycles is useful for standard risk HB. Therefore, to improve the prognosis and to reduce side effects in this risk group, it may be beneficial for responders to undergo primary tumor resection and for non-responders to reconsider their chemotherapeutic regimen after two cycles. In intermediate/high risk HBs, other response criteria should be adopted for evaluation of treatment efficacy.

O-004

SHORT (STI) AND LONG TERM INFUSION (LTI) OF CH14.18/CHO IMMUNOTHERAPY: TOXICITY PROFILES AND OUTCOMES IN 530 HIGH RISK NEUROBLASTOMA (HR-NBL) PATIENTS IN TWO SIOPEN TRIALS

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Background/Objectives: Design of a tolerable and effective immunotherapy with ch14.18/CHO monoclonal antibody immunotherapy (IT) ± subcutaneous interleukin 2 (scIL2).
Design/Methods: The HR-NBL1/SIOPEN Phase III trial (APN311-302)(EudraCT:2006-001489-17) randomized 406 high risk first-line neuroblastoma patients (HR-pts) in consolidation phase with oral 13-cis-RA (160 mg/m^2,d19-32) to receive 100 mg/m^2 ch14.18/CHO (d8-12) as 5 daily 8-hour short-term infusion (STI) alone (STIA) or combined with 6×10^6IU/m^2 scIL2 (d1-5;8-12) (STIB). In the SIOPEN-Phase II study (APN311-202)(EudraCT:2009-018077-31) 124 relapsed/refractory neuroblastoma pts (VHR-pts) received a 10 day long-term infusion (LTI) of 100 mg/m^2 ch14.18/CHO (d8-17) aiming to reduce the pain profile and scIL2 and 13-cis-RA as outlined above. Both trials planned a total of 5 IT cycles. Median follow-up was 2.1 years (0-4.5) for the STI and 0.8 years (0-3) for the LTI trial.
Results: General tolerance improved with LTI. A Lansky performance status of ≤30% was found in 10% of LTI-pts, 39% STIB-pts and 17% STIA-pts ($p<0.001$). CTC-grade 3&4 allergic reactions were observed in 10% LTI-pts, 20% STIB-pts and 9% STIA-pts (<0.001). Incidence of capillary leak and CTC-grade 3&4 fever was not different between scIL2 containing LTI (9% and 48%) and STIB (9% and 40%) but significantly lower without scIL2 STIA (1% and 14%). Markedly reduced pain and intravenous morphine usage was observed in the LTI setting. The 2-year EFS rates for HR-pts in CR (or VGPR/PR) treated with STIA were 65%±5% (58%±6%) and with STIB 67%±5% (59%±6%) indicating no benefit for scIL2. The 2-year EFS rate in LTI treated VHR-pts was 50%±7%. Early termination of IT occurred in 18% in STIA but in 44% in STIB (36% toxicity-related, 8% progressions) and in 42% in LTI (21% toxicity-related, 21% progressions).
Conclusion: Although disease risk-profiles differed between trials, reduced toxicities were observed with LTI. Ongoing randomised SIOPEN trials will clarify the role of scIL2 with the LTI scheme.

O-005

INTEGRATED GENOMIC ANALYSIS IDENTIFIES SPECIFIC ALTERATIONS AND ACTIVATION OF YAP IN RELAPSED NEUROBLASTOMA

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Background/Objectives: Neuroblastoma is a malignancy of the developing sympathetic nervous system that is often lethal when relapse occurs, but the molecular mechanisms behind this process are poorly defined.
Design/Methods: We used whole-exome sequencing, mRNA expression, arrayCGH and DNA methylation analysis to holistically characterize 16 paired samples from neuroblastoma patients at diagnosis and relapse.
Results: Global allele frequencies at relapse indicated clonal mutation selection during disease progression. Promoter methylation patterns were consistent over disease course and patient-specific. No relapse tumor acquired new mutations in previously identified neuroblastoma driver genes, but MYCN amplification was acquired in one. Inactivating mutations in the putative PTPN14 tumor suppressor and a relapse-specific activity pattern for the PTPN14 target gene, YAP, were identified, and represent the first hint for Hippo/YAP signaling involvement in neuroblastoma relapse. Overexpressing a naturally occurring mutant PTPN14 in a neuroblastoma cell line caused YAP nuclear translocation and enhanced clonogenic survival. Recurrent new mutations in HRAS, KRAS, DOCK8, and genes mediating cell-cell interaction in 13 of 16 relapse tumors also point to disturbances in signaling pathways mediating mesenchymal transition.
Conclusion: Our results suggest a role for Hippo/YAP signaling and possibly mesenchymal transition processes and their modulation by genomically altered upstream signaling in disease recurrence.

O-006

MOLECULAR (RE-)CLASSIFICATION AND GENETIC CHARACTERIZATION OF CNS PRIMITIVE NEUROECTODERMAL TUMORS (CNS-PNET)

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Background/Objectives: Childhood CNS primitive neuro-ectodermal tumors (CNS-PNETs; WHO °IV) are poorly differentiated embryonal tumors with early onset and aggressive clinical behavior. Histological diagnosis can be complicated by morphological heterogeneity and divergent differentiation. Recent studies suggest the existence of molecular subgroups of CNS-PNETs sharing biological characteristics with other childhood CNS tumors.
Design/Methods: We analyzed 254 fresh-frozen or paraffin-embedded CNS-PNET samples using DNA methylation (n=254) and expression (n=76) arrays. (Epi-)genetic profiles of CNS-PNETs were compared to those of >5000 other childhood brain tumors including embryonal, astrocytic, and ependymal entities, and their respective molecular subgroups.
Results: DNA methylation and gene expression profiles showed a clear segregation of pediatric brain tumors by histological entities and molecular subgroups. Interestingly, CNS-PNET profiles showed a significant overlap with various well-defined entities, including AT/RT, ETMR, high-grade glioma, medulloblastoma, and ependymoma, which was validated by the presence of characteristic genetic hallmarks, such as mutations in *SMARCB1, IDH1,* or *H3F3A*; amplification of *19q13.42*; or other established protein markers. Strikingly, a subset (~25%) of CNS-PNETs, which could not be reclassified, segregated into four distinct molecular subgroups, each with its own characteristic pattern of DNA-methylation, copy number aberrations, gene expression, and mutations. We also identified several cases among previously diagnosed glioblastomas, ependymomas or other brain tumors that now classify to one of these true CNS-PNET groups.
Conclusion: The correct classification of CNS-PNETs remains challenging. Based on DNA methylation, many cases can be reliably re-classified, indicating that a significant proportion of CNS-PNETs may comprise a variety of other tumor subtypes. These findings suggest that the use of established and novel subgroup markers is needed in order to assist the histopathological evaluation of these tumors. In addition, we have identified a number of true CNS-PNET subtypes and are currently analyzing them in more detail in order to elucidate the genetics and clinical behavior of these distinct groups.

Free Papers 01: Stem Cell Transplantation

O-007

VIABILITY OF CRYOPRESERVED PERIPHERAL BLOOD STEM CELLS (PBSC) DOES NOT GUARANTEE FUNCTIONAL ACTIVITY: IMPORTANT IMPLICATIONS FOR QUALITY ASSURANCE OF STEM CELL TRANSPLANT PROGRAMMES

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Background/Objectives: Cryopreserved PBSC are used for myeloablative therapy (MAT) rescue in the autologous setting, and occasionally for allografts. Standard PBSC quality assurance (QA) uses CD34+ cell counts and viability using vital dyes. In 2013, concerns were raised at Great Ormond Street Hospital (GOSH) about a series of patients who experienced delayed engraftment after MAT with cryopreserved PBSC.
Design/Methods: Root cause analysis was undertaken including all aspects of the pathway: PBSC mobilisation, apheresis, cryopreservation, reinfusion and count recovery. Data were collected from patient and laboratory records and interviews with staff. When initial investigations failed to identify a cause, a series of experiments were undertaken in which a single PBSC product was divided into three and cryopreserved in parallel using a control-rate freezer (CRF) or passive freezing method (−80°C freezer) at GOSH, and the same passive freezing at another centre. Viability by thaw CD34+/7AAD- flow cytometry and colony assays (CFU-GM) were undertaken.
Results: Eight consecutive patients who received PBSC cryopreserved at GOSH experienced delayed engraftment. Although PBSC viability and cell doses were adequate in all cases, the cryopreservation method was investigated further. Comparison of parallel cryopreservation methods (repeated x4) revealed equivalent and adequate PBSC viability in all experiments. However, although CFU-GM assays demonstrated colonies from the products cryopreserved using passive freezing (both at GOSH and at the other laboratory), products cryopreserved using the CRF did not form any colonies. The CRF device was shown to be operating within manufacturer's specifications.
Conclusion: The cause of the cryopreservation problem at GOSH remains unclear. Nevertheless, this experience has important implications for quality assurance for all transplant programmes, particularly those using cryopreserved products. The failure of thaw CD34+/7AAD- counts, the best routine QA test available, to ensure PBSC function is of great concern and should prompt a reassessment of protocols and QA procedures by all centres.

O-008

PERSISTENCE AND REACTIVATION OF HUMAN ADENOVIRUSES IN THE IMMUNOCOMPROMISED HOST

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Background/Objectives: Primary infections with human adenoviruses (HAdVs) most commonly occur during early childhood and can lead to viral persistence in different tissues. Reactivation in patients with impaired immune surveillance is associated with high morbidity and mortality, particularly in paediatric haematopoietic stem cell transplant (HSCT) recipients. Although invasive HAdV infections are thought to mainly arise from the gastrointestinal (GI) tract, and rising virus levels in serial stool specimens were shown to precede disseminated disease, the specific sites of HAdV persistence and proliferation are not well characterised.
Design/Methods: We have prospectively screened biopsies from 143 immunocompetent children undergoing routine gastrointestinal endoscopy and monitored serial stool specimens from 148 paediatric HSCT recipients for the presence of HAdV by real-time PCR screening. The intracellular location and protein expression of HAdV were determined by in-situ hybridisation and immunohistochemistry.
Results: Persistence of various HAdV species in the GI tract was identified in 31% of the children screened, with the highest prevalence in the terminal ileum. HAdV persistence was identified primarily in lymphoid cells of the lamina propria and immunohistochemistry indicated low virus production. By contrast, transplant recipients with HAdV infection revealed a high concentration of replicating HAdV in intestinal epithelial cells. The frequency of HAdV persistence in the GI tract and the prevalence of HAdV species in immunocompetent children were similar to the rate of reactivation and the prevalence of HAdV species found in HSCT recipients. Detection of intestinal HAdV shedding pre-transplant correlated with high risk of invasive infection.
Conclusion: HAdV persistence in the GI tract is a likely origin of infectious complications in severely immunocompromised children. Intestinal lymphocytes represent a reservoir for HAdV persistence and reactivation, while the intestinal epithelium is the main site of viral proliferation preceding dissemination. The findings have important implications for assessing the risk of life-threatening invasive HAdV infections.

O-009

DAY+100 SURVIVAL ANALYSIS BY PRIOR HEMATOPOIETIC STEM CELL TRANSPLANT TYPE FROM AN ONGOING US STUDY OF DEFIBROTIDE FOR HEPATIC VENO-OCCLUSIVE DISEASE

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Background/Objectives: Hepatic veno-occlusive disease (VOD; or sinusoidal obstruction syndrome) is an unpredictable, life-threatening complication of hematopoietic stem cell transplant (HSCT). Severe VOD (sVOD) is associated with >80% mortality; it is characterized clinically by multi-organ failure (MOF). In the European Union, defibrotide is approved for treatment of sVOD in HSCT. In the United States, defibrotide is available through an ongoing, expanded-access, protocol-directed treatment IND (T-IND) in VOD post-HSCT/chemotherapy. T-IND day+100 survival was analyzed in autologous/allogeneic subgroups.
Design/Methods: Patients received defibrotide 25 mg/kg/day, ≥21 days recommended. Eligibility: Originally, sVOD with MOF (renal/pulmonary) by Baltimore criteria post HSCT; amended to include patients post HSCT/chemotherapy with non-sVOD (without MOF), VOD per modified Seattle criteria, or biopsy-proven VOD.
Results: Of 641 patients post HSCT/chemotherapy enrolled through 2013 receiving defibrotide (median treatment, 21 days), 57% were male; median age was 13y (range 0–69y) with 58% (372/636) ≤16y. Most common underlying diagnoses included acute myelogenous leukemia (27%) and acute lymphocytic leukemia (23%). Most common graft-vs-host disease agents were tacrolimus (41%), cyclosporine (30%), and methotrexate (29%). Of 336 patients with sVOD and HSCT, 54% were male; median

age was 12y (range 0–69y) with 61% (204/333) ≤16y. For 526 patients post HSCT with survival data, 467 received allografts and 56 received autografts (3 grafts unknown); sVOD rates were 54% and 48%, respectively. Day+100 survival post allograft was 50% (95% CI 46–55%) overall, 43% (37–49%) for sVOD, 58% (52–65%) for non-sVOD. Post-autograft survival: 66% (54–79%) overall, 59% (41–78%) for sVOD, 72% (56–89%) for non-sVOD.
Conclusion: In this study, day+100 survival rates in both allograft and autograft sVOD subsets were consistent with prior defibrotide studies. The higher survival rates in the non-sVOD subsets indicate further study is warranted to determine the impact of treatment earlier in the course of VOD. *Support*: Jazz Pharmaceuticals.

O-010

OUTCOME OF SALVAGE CHEMOTHERAPY FOLLOWED BY STEM CELL TRANSPLANTATION IN RELAPSED OR REFRACTORY HODGKIN LYMPHOMA IN CHILDREN- A SINGLE CENTRE EXPERIENCE

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Background/Objectives: Hodgkin Lymphoma (HL) in children is highly curable with overall survival (OS) approaching 70% even in advanced lymphoma. Relapsed and Refractory HL however, has poor outcomes unless managed with aggressive salvage chemotherapy (CT) followed by Stem Cell Transplantation (SCT). Outcomes of children with relapse/ refractory HL managed at a large tertiary center in a developing were analyzed.
Design/Methods: Case records of patients less than 18 years age undergoing SCT for Relapsed or Refractory HL from Jan 2008 to February 2015 were analyzed retrospectively. Patient and disease characteristics, treatment histories and salvage/ SCT strategies used were studied and outcomes analyzed. Progression Free Survival (PFS) and OS were calculated by Kaplan-Meier method and univariate analysis on risk factors was done.
Results: Thirty-five patients underwent transplant at a median age of 13 yrs (5-18 yrs). At diagnosis, 63% had Stage III or IV disease, 66% had B symptoms and 28% had bulky disease. Thirty-four received Adriamycin, Bleomycin, Vinblastine, Dacarbazine (ABVD) as initial chemotherapy followed by 2 or more salvage regimens in 16. Involved Field Radiation Therapy was given in 18 prior to SCT. All except 1 had stage III or IV disease prior to use of salvage therapy. GDP (Gemcitabine, Cisplatin, Steroids) was used as salvage CT pre- SCT in 43% cases followed by Mitoxantrone, Ifosamide, Etoposide in 31%. Thirty-two children underwent autologous SCT with Lomustine, Ara-C, Cyclophosphamide, Etoposide (LACE) conditioning while 2 underwent allogeneic SCT. At time of SCT, 8 were not in complete remission (CR). Two (5.7%) had transplant related mortality (TRM). PFS and OS were 60% and 68% at 4 years. On univariate analysis, CR status pre-SCT significantly impacted outcome (p=0.001).
Conclusion: Salvage CT followed by SCT in Relapse/ Refractory HL has favorable outcome with 2/3rd patients benefitting with low TRM. It is important to achieve CR pre-SCT.

Free Papers 02: Hodgkin & ALCL

O-011

A RISK-ADAPTED, RESPONSE-BASED THERAPEUTIC REGIMEN USING A MODIFIED STANFORD V APPROACH FOR THE TREATMENT OF CHILDREN WITH HIGH RISK HODGKIN LYMPHOMA, AHOPCA LH 2004

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Background/Objectives: Hodgkin Lymphoma (HL) is highly curable with reported event-free survival (EFS) estimates of greater than 90% even in high-risk patients. Unfortunately, EFS of HL in low-income countries is much lower, about 50%. We now report mature five-year results from this previously reported study.
Design/Methods: All newly diagnosed biopsy proven HL patients stages IIB, IIIB and IV, that presented between April 2004 and April 2009 were eligible. Treatment consisted of a modified Stanford V regimen with cyclophosphamide substituting for nitrogen mustard and instead of 35 Gy involved field radiation therapy (IFRT) like in the original regimen only gave 20Gys IFRT to subjects with a complete anatomical response (CR) at the end of chemotherapy and 25 Gy to those with a partial response (PR).
Results: Of 221 patients enrolled in the protocol, 206 were evaluable. Male subjects predominated (79%) with a median age of 10 years (2-19 years). Forty-nine (23%) had stage IIB, 100 (48%) stage IIIB, 4 (2%) stage IVA and 50 (24%) stage IVB HL. Forty-five per cent of patients had nodular sclerosis, 42% mixed cellularity, 5%, lymphocyte predominant, 2% lymphocyte depleted and for 6% histology was not specified. The most important grade 3 and 4 toxicities were hematological (75%) and there were two grade 5 toxicities, one infectious and one pulmonary. EFS (±SE) at 5 years was 55.4 % (± 4.4), considering abandonment of therapy as an event. Abandonment of therapy was 14.6%. Five-year EFS by stage was: stage IIB 79% (± 6%), IIIB 56% (± 7%) and IVB 29% (± 8%).
Conclusion: Our modified Stanford V regimen was well tolerated with acceptable toxicities. It did not require growth factor support and was delivered in an outpatient setting. However, the EFS of patients was less than expected for the group as a whole, (55.4%).

O-012

PEDIATRIC HODGKIN LYMPHOMA TREATMENT WITH CHEMOTHERAPY ALONE: FRENCH-AFRICAN PEDIATRIC ONCOLOGY GROUP (GFAOP) EXPERIENCE

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Background/Objectives: Hodgkin lymphoma (HL) is a common childhood cancer; there is limited information regarding its management in developing countries. Until now, the majority of children and young adults with HL are cured with combined chemotherapy and radiation therapy in high-income countries. Sub-Saharan Africa has the poorest supply of radiotherapy equipment. The aim of this multicentre prospective study was to assess the safety and effectiveness of hybrid protocol COPP/ABV alone for the management of paediatric HL in sub-Saharan Africa.
Design/Methods: Were prospectively registered children/adolescents under 18 years, diagnosed with a histologically confirmed classical HL in seven paediatric oncology centers in sub-Saharan Africa. Initial work-up included physical examination, chest X ray, abdominal ultrasonography, myelogram or bone marrow biopsy. The protocol used was COPP/ABV regimen (Cyclophosphamide, Vincristine, Prednisone, Procarbazine, Adriblastine, Bléomycine, Vinblastine). Number of cycles was between 4 and 8 according to stage and early response, evaluated after two cycles.
Results: Between October 1st, 2006 and November 30th, 2012, 127 children with HL were registered. Mean age was 10 years, with the age group 5-10 years representing 40% of cases. Males represented 3/4 of the patients. There was a majority of advanced stages: 57.2% stages III and 78.6% with B symptoms. Overall the scleronodular form (39%) was the most common, followed by mixed cellularity form (21.3%). 44/90 were « good responders » after 2 courses. COPP/ABV protocol was well tolerated. Overall survival (OS) rate was 82% and event-free survival (EFS) rate 67% with mean follow up of 3 years. The relapses were late with an average of 13 months.
Conclusion: Hybrid protocol COPP/AVB alone is feasible, with less toxicity and gives satisfactory results in African low-income countries.

O-013

OUTCOME OF PEDIATRIC HODGKIN LYMPHOMA TREATED WITH ABVD: A MULTICENTRIC ANALYSIS OF 335 PATIENTS

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Background/Objectives: With advent of ABVD (Adriamycin, bleomycin, vinblastine, dacabazine) as an effective regimen for Hodgkin lymphoma in adult population this regimen has been successfully been used in pediatric population based on the extrapolation of results. However there are very few studies which evaluated its efficacy in pediatric population.
Design/Methods: Between January 2003 and December 2013, 359 patients diagnosed Hodgkin lymphoma received ABVD regimen. Early stage and patients with bulky disease received additional radiotherapy. Data from 3 tertiary cancer centers in India was collected andanalysis was done for freedom from treatment failure (FFTF), overall survival (OS) after obtaining ethical clearance from the institute ethics committee of respective centers.
Results: Of 359 patients 8 patients received treatment other than ABVD and 16 patients were lost to follow up before treatment initiation. Of 335 patients who received ABVD, 151 and 183 were early and advanced stages respectively. Complete remission was

attained in 92.5% of patients. While 11 (3.3%) patients achieved partial remission at the end of treatment, 10 of them achieved complete response on observation and follow up. Median follow up duration of the cohort was 46.5 months. Median freedom from treatment failure (FFTF) and overall survival (OS) was not reached for cohort. FFTF and OS at 5 yr was 89.9%± 0.02 and 96.9%±0.01 respectively. FFTF at 5 yr for early and advanced stages was 96.9±1.5% and 83.4±3 %(logrank,p=0.003) respectively. Total 8 patient died of whom 5 died of progressive disease and 3 had treatment related mortality. On multivariate analysis only more than 3 nodal regions, extranodal disease were significantly associated with inferior outcome. Patients having either of them or both have odds ratio for treatment failure is 4.3 and 19.3 respectively.
Conclusion: Combined modality treatment with ABVD and radiotherapy results in excellent long term outcome in children with Hodgkin lymphoma.

O-014

ANAPLASTIC LARGE CELL LYMPHOMA IN CENTRAL AMERICA: A REPORT FROM THE CENTRAL AMERICAN ASSOCIATION OF PEDIATRIC HEMATOLOGY ONCOLOGY (AHOPCA)

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Background/Objectives: While anaplastic large cell lymphoma (ALCL) is curable in high-income countries (HICs), data from low- and middle-income countries (LMICs) are lacking. We therefore conducted a retrospective study of the Central American Association of Pediatric Hematology Oncology (AHOPCA) experience in treating ALCL.
Design/Methods: We included all patients age <18 years newly diagnosed with ALCL treated between 2000 and 2013 in 7 AHOPCA institutions. Retrospective data were extracted from the Pediatric Oncology Network Database.
Results: 28 patients met inclusion criteria. 22 (79%) had advanced disease (stage III and IV), 4 (14%) were treated on the APO (doxorubicin, prednisone, vincristine) regimen, and 24 (86%) on the European-based treatment regimens. 5-year overall EFS and OS were respectively 69.5% ± 9.1% and 69.0% ± 9.3%. 5-year EFS in patients treated with an APO regimen was 100% ± 0% compared to 65.2% ± 10.0% in patients treated with European-based regimens; the difference was not statistically significant (P=0.24). All 10 events occurred in patients treated on European-based treatment regimens: 2 patients experienced relapse, 6 treatment related mortality (TRM), and 2 abandonment.
Conclusion: Treatment of ALCL in countries with limited resources is feasible with similar outcomes as HIC, though the causes of treatment failure differ. Less intensive regimens may be preferable in order to decrease TRM and improve outcomes. Prospective clinical trials determining the ideal treatment for LMIC children with ALCL are necessary.

Free Papers 03: Glioma

O-015

METASTATIC LOW GRADE GLIOMAS IN CHILDREN: 20 YEAR EXPERIENCE AT ST. JUDE CHILDRENS RESEARCH HOSPITAL

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Background/Objectives: Low-grade gliomas (LGG) are the most common brain tumors during childhood. Long-term survivals are excellent with the current treatments. Dissemination of LGG along the neuroaxis is rare. Robust data regarding true incidence, outcome and best management approaches does not exist. In this study, we describe the longest follow period up of a large cohort with metastatic LGG, at diagnosis and/or at follow up, treated at St Jude Children's Research Hospital.
Design/Methods: Data was retrospectively collected between January 1990, and December 2010. Inclusion criteria were: diagnosis of metastatic LGG, age less than 21 years at diagnosis, MRI of the brain and/or spine at diagnosis and follow up. Demographic, treatment and outcome data was collected and analyzed.
Results: A total of 599 patients with LGG were identified. Thirty-eight patients (6%) had metastatic disease either at diagnosis or at follow up. Most of the tumors were located in the brain (87%), one half had metastatic disease at presentation. Only 3 patients did not have tissue confirmation at diagnosis. The most common diagnosis was pilocytic astrocytoma (55%). Chemotherapy was the most common initial treatment modality. Median number of treatments per patient was 3 (range 1-5). Fifteen patients (40%), died at a median of 6 years from diagnosis (range 0.8 to 15 years). Death occurred due disease progression in all but 1 case. Median survival for the whole group was 6.2 years (range 0.1-16.9). Overall survivals were 80.7 ± 6.6%, 63.0 ± 10.2%, and 50.9 ±16.0% at 5, 10 and 15 years respectively.
Conclusion: This study describes the longest follow up of metastatic LGG in children to date. We showed that this disease is underestimated and entails major morbidity and mortality. Large-scale studies are required to unveil the true incidence, study the molecular characteristics, and determine the best treatment and follow up modalities.

O-016

OUTCOME OF NEUROFIBROMATOSIS TYPE 1 PATIENTS TREATED WITH FIRST LINE VINBLASTINE FOR OPTIC PATHWAY GLIOMAS (OPG): A CANADIAN MULTICENTER STUDY

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Background/Objectives: Vincristine and carboplatin continues to be the first-line chemotherapy for children with NF-1 and OPG in the majority of countries. Vinblastine has shown promising activity in a phase-II study in children with recurrent/refractory low-grade glioma (LGG). The aim of this study was to assess the activity of vinblastine in chemotherapy naïve children, and to assess the toxicity profile.
Design/Methods: Patients <18 years-old with unresectable or progressive LGG were eligible if no previous treatment with chemotherapy or radiation. Vinblastine was administered weekly at a dose of 6 mg/m2 over a period of 70 weeks.
Results: Overall, the study enrolled 54 patients with LGG. A total of 13 patients (24.1%) had NF-1. Patients with NF-1 were younger at diagnosis: median age 3.84 years (range, 1.74-16.36) vs. 7 years in non-NF-1. Tumor location in all NF-1 patients was the optic pathway. Treatment was very well tolerated, however, 5 patients (38%) needed dose reductions. Most common toxicity was hematological: 1 patient with grade 3+ neutropenia (vs. 10 patients non-NF1). There were only 2 episodes of febrile neutropenia, no RBC transfusions and no toxic death. Best response to chemotherapy was assessed centrally by an independent radiologist: 2 PR, 1 MR, 8 SD, and 2 PD, for a response rate of 23.1%. At a median follow-up of 5.37 years (3.45 – 6.57y): Only two NF-1 patients had progression. Five-year progression free survival (PFS) was 85.1±9.7% (vs. 42±7,9% for all non-NF1, p=0.01; and 41.7±14% for non-NF1 with OPG, p=0.01). None of the NF1 patients received radiation (0 vs. 6 non-NF1). No patients died of progression (0 vs. 3 non-NF1).
Conclusion: Weekly vinblastine is well tolerated and can be used in NF-1 children with OPG as first line chemotherapy with good results. The toxicity profile is lower than with other chemotherapies, offering a better quality of life to these patients.

O-017

A CONSENSUS WORKSHOP TO DEVELOP RISK-BASED SELECTION CRITERIA FOR THE NEXT SIOP TRIAL OF "SIGHT-SAVING THERAPY" FOR CHILDREN WITH NF1-ASSOCIATED OPTIC PATHWAY GLIOMA (NF1-OPG)

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Background/Objectives: The natural history of children with NF1-OPG is unpredictable, indications for therapy to save vision, using patient, imaging and visual factors have not been studied in Europe. In order to promote a revised and standardised approach for the next SIOP LGG trial, a multi-disciplinary workshop using a cohort of patients with complete imaging and clinical datasets from SIOP-LGG2004 trial was conducted.
Design/Methods: The workshop involved specialists in neuro-radiology, ophthalmology, NF genetics and neuro-oncology from 8 centres participating in SIOP-LGG2004 trial. Each centre contributed cases of NF1-OPG with complete imaging, visual and clinical datasets. Eighty -three patients were recruited (age at diagnosis: median 4.8 yrs range 1.1-13.1; m:F 37:46, median follow-up 19.2 months range 1.8-121 months). Severe visual impairment/blindness (LogMAR >=1.0) at diagnosis and last follow up, respectively: unilateral 16,21; bilateral 3,7. Anatomical distribution at diagnosis: Dodge Stage A (nerves) 35; Stage B (chiasm) 16; Stage C (nearby structures) 32. Imaging evidence of: response 31: no change:46; progression 6. Analysis of the dataset informed consensus discussion and voting of representative cases for proposed trial criteria for observation, treatment and randomisation, subsequent development of a web-based survey was piloted with workshop participants.
Results: Consensus on imaging and visual classification was achieved, including a schematic for recording patient, visual and imaging details. Criteria for case selection were: age, history of visual decline, presence of severe visual symptoms, unreliable visual assessment, proptosis and post-chiasmatic tumour involvement. A subsequent 19 case web-based questionnaire, supported by a podcast summary of the cohort (http://goo.gl/aTSdaK) was completed by 15 workshop participants. The respondents allocated 8 cases to observation; 8 to immediate treatment and 3 for consideration for randomization.
Conclusion: This workshop has achieved a new consensus on selection criteria using a contemporary trial cohort. We have piloted a web-based questionnaire to assess feasibility of a randomised trial in this disease group.

O-018

CHILDREN WITH BIALLELIC MISMATCH REPAIR DEFICIENCY DEVELOP RAPID ONSET OF ULTRA-HYPERMUTANT TUMORS WHICH ARE RESISTANT TO CURRENT CHEMOTHERAPIES

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Background/Objectives: Biallelic Mismatch Repair Deficiency (bMMRD) is a cancer predisposition syndrome caused by germline mutations in MSH2, MSH6, MLH1, and PMS2. Children with bMMRD develop early onset brain, hematological and gastrointestinal malignancies and rarely reach adulthood. The genomic landscape and response to current therapies of bMMRD cancers are unknown.
Design/Methods: We analyzed 27 cancers and corresponding normal tissues from bMMRD patients using genome, exome sequencing and SNP-arrays. Additionally, we developed a novel functional assay to detect bMMRD and examined sensitivity of bMMRD cells to current chemotherapies.
Results: BMMRD cancer harbored massive numbers of substitution mutations (>100/Mb), greater than all childhood and most adult cancers (>7,000 analyzed). This hypermutation signature is diagnostic for cancers arising from germline bMMRD ($p<10^{-13}$). The functional assay confirmed that out of eight families, all patients with biallelic mutations in MMR genes tested negative for mismatch repair activity. Conversely, nine family members with heterozygous mutations and no cancer phenotype had normal MMR function. Hypermutated bMMRD brain cancers acquired early and conserved somatic mutations in DNA polymerases ε or δ and sequential tumor analysis revealed that brain tumours acquired over 20,000 mutations in less than 6 months during malignant transformation. Importantly, recurrent glioblastomas did not display a higher mutation load than ultra-hypermutant primary tumors with a polymerase mutation. bMMRD cells were resistant to current chemotherapies such as antimetabolites and temozolomide.
Conclusion: Early-onset bMMRD cancers have a unique mechanism of malignant progression through secondary mutations in DNA polymerases and rapid mutation accumulation quickly reaching a threshold. Although bMMRD cancers are resistant to current chemotherapies, the high mutation load and threshold of bMMRD cancers may be it's Achilles' heel, exploitable for diagnosis and therapeutic intervention.

Free Papers 04: Neuroblastoma

O-019

NEUROBLASTOMA IMMUNOTHERAPY TARGETING CSF-1R REVERSES INDUCTION OF SUPPRESSIVE MYELOID CELLS AND CONTROLS AGGRESSIVE TUMOR PROGRESSION

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Background/Objectives: High-risk neuroblastoma is a significant clinical challenge. Despite progress in survival due to intensified multimodal therapy, aggressive metastatic disease induces severe impairments of anti-tumor immunity and has poor clinical outcome. M-CSF (CSF-1) is produced at high levels by neuroblastoma tumors and infiltration of CSF-1R+ myeloid cells is associated with poor clinical survival.
Design/Methods: Human and murine *in vitro* culture models, exploiting CD34+ progenitor cells derived from cord blood, primary human monocytes, and murine bone marrow cells, as well as human and murine neuroblastoma cells, were established to analyze the CSF-1/CSF-1R axis in the induction of tumor-induced immune suppression. Preclinical studies evaluating CSF-1R as therapeutic target were conducted in transgenic TH-MYCN mice.
Results: *In vitro*, neuroblastoma-derived factors hamper myelopoiesis of human CD34+ progenitor cells, and induce suppressive myeloid cells from primary human monocytes and murine bone marrow cells through M-CSF/CSF-1R interaction. In the spontaneous TH-MYCN model resembling aggressive high-risk human neuroblastoma, we observe significant accumulation of myeloid-derived suppressor cells of the granulocytic ($p < 0.01$, grMDSCs, Ly6G+Ly6Clow) and monocytic ($p < 0.0001$, moMDSCs, Ly6GnegLy6Chigh) lineage, as well as F4/80+ macrophages ($p < 0.01$). Sorted from spleens of tumor-bearing mice, Gr1+ cells conduct potent inhibition of T cells through production of indolamine-2,3-dioxygenase (IDO, $p<0.04$) and inducible nitric oxide synthase (iNOS, $p<0.04$). Of note, antagonizing CSF-1R with a selective chemical inhibitor (BLZ945; Novartis) abolishes the induction of human and murine MDSCs and TAMs *in vitro*, and overcomes their induction *in vivo*. Strikingly, treatment in vivo with BLZ945 elicits robust anti-tumor immune responses and efficiently limits progression of established tumors ($p<0.01$) including complete response and eradication of macroscopic neuroblastoma tumors.
Conclusion: Our results demonstrate the essential clinical role of the M-CSF/CSF-1R-axis during the induction of suppressive myeloid cells and suggest the therapeutic potential of targeting this pathway in high-risk neuroblastoma.

O-020

TELOMERASE ACTIVATION BY RECURRENT GENOMIC REARRANGEMENTS IN HIGH-RISK NEUROBLASTOMA

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Background/Objectives: Neuroblastoma shows a broad spectrum of clinical courses, ranging from spontaneous regression to fatal tumor progression. The genetic basis of the various clinical subtypes of the disease has remained largely elusive.
Design/Methods: We performed whole-genome and RNA sequencing of 57 primary neuroblastomas (high-risk, n=40; low-risk, n=17), and targeted sequencing and FISH of an independent cohort of 160 primary neuroblastomas. Six neuroblastoma cell lines representing different genetic subtypes were examined for activity of telomerase and alternative lengthening of telomeres (ALT).
Results: We identified genomic rearrangements affecting chromosome 5p15.22 in a 50 kb region centromeric of the human telomerase reverse transcriptase gene (*TERT*) in 13/57 tumors. The rearrangements occurred only in high-risk neuroblastomas (13/40) in almost mutually exclusive fashion with *MYCN* amplifications and *ATRX* mutations, which are known genetic events in this tumor type. While the structure of the rearrangements varied greatly, they consistently induced massive transcriptional up-regulation of *TERT* and three additional genes located in close proximity to the chromosomal breakpoint. By contrast, *MYCN*-amplified tumors showed only up-regulation of *TERT* itself, suggesting that both *MYCN* amplification and *TERT* rearrangements converge on TERT activation. In the validation cohort, we identified 15 additional tumors with *TERT* rearrangements. In total, *TERT* rearrangements occurred in 13% of primary neuroblastomas and were strongly associated with poor patient outcome (5-year EFS, 0.188±0.098, 5-year OS, 0.429±0.161), independent of the established prognostic markers stage, age and *MYCN* amplification. Supporting a functional role of TERT, both *MYCN*-amplified neuroblastoma cell lines and cell lines bearing *TERT* rearrangements exhibited elevated *TERT* expression and enzymatic telomerase activity, while ALT was detected in cell lines without these aberrations.
Conclusion: Our findings show that remodeling of the genomic context abrogates transcriptional silencing of *TERT* in high-risk neuroblastoma, and places telomerase activation in the center of transformation in a large fraction of these tumors.

O-021

MYCN TRANSCRIPTIONALLY REPRESSES *CD9* TO TRIGGER AN INVASION-METASTASIS CASCADE IN NEUROBLASTOMA

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Background/Objectives: The systemic and resistant nature of neuroblastoma metastasized to distant organs makes it largely incurable with current multimodal treatment. Clinical progression stems mainly from an increasing burden of metastatic colonization. Novel therapeutic perspectives may be won by blocking as yet poorly understood pathways triggering the migration-invasion-metastasis cascade in neuroblastoma.
Design/Methods: The CD9 cell surface glycoprotein was decoded as a major downstream player and direct target of the recently described *GRHL1* tumor suppressor in in-depth transcriptome analyses and ChIP-qRT-PCR. CD9 is known to facilitate carcinoma cell motility and metastasis.
Results: High-level CD9 expression in primary neuroblastomas correlated with patient survival and established markers for favorable disease. Low-level *CD9* expression was an independent risk factor for adverse outcome and predicted poor treatment response in patients with the worst outcome. MYCN and HDAC5 colocalized to the *CD9* promoter and repressed transcription. *CD9* expression was strongly reduced during progressive development of murine tumors in the *TH-MYCN* transgenic mouse model of neuroblastoma compared to expression in ganglia from wildtype mice, further supporting MYCN involvement in *CD9* transcriptional repression in neuroblastoma cells. We detected differential *CD9* methylation in 450K methylation array analyses of primary neuroblastomas, and *CD9* hypermethylation was associated with reduced *CD9* expression, supporting epigenetic regulation. Inducing CD9 expression in a SH-EP cell model inhibited migration and invasion in Boyden chamber assays. Enforced CD9 expression in neuroblastoma cells transplanted onto chicken chorioallantoic membranes strongly reduced metastasis to chicken embryo bone marrow. Combined treatment of neuroblastoma cells with inhibitors for HDACs and DNA methyltransferase induced CD9 expression.
Conclusion: Our results show CD9 is a critical and indirectly druggable mediator of neuroblastoma cell invasion and metastasis.

O-022

COMPREHENSIVE ANALYSIS OF BONE MARROW (BM) INVOLVEMENT AND MINIMAL RESIDUAL DISEASE (MRD) IN NEUROBLASTOMA PATIENTS BY MOLECULAR MARKERS

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Background/Objectives: BM involvement detection in neuroblastoma (NB) is crucial for staging; MRD defines tumor response and could be associated with unfavorable outcome.
Design/Methods: Expression of 4 tumor-associated genes (TAGs): *PHOX2B*, *TH*, *ELAVL4*, *GD2* was analyzed in NB cell lines, in 26 intact BM samples, in discovery (331 BM samples from 57 patients) and validation (311 samples from 55 patients) cohorts. Threshold levels (TLs) of expression were established using ROC-analysis and applied for overall correct prediction (OCP) computation. Criteria of BM positivity were *PHOX2B* expression or tumor cells in BM smears. Event-free (EFS) and overall survival (OS) rates were calculated with median of follow-up 2.45 years.
Results: Neither *PHOX2B* nor *TH* expression was detected in intact BM, expression of *ELAVL4* was revealed in 20, *GD2* – in 15/26 samples. In the discovery cohort 105/107 positive samples had *PHOX2B* expression; 101/107 positive and 5/224 negative samples- *TH*. *ELAVL4* and *GD2* expression was detected in all 107 positive samples and in the majority of negative (209 and 197/224, respectively). OCP values for *TH*, *ELAVL4, GD2* achieved 0.952, 0.828, 0.767 correspondingly, for *PHOX2B*- 0.994. In the validation cohort OCPs were 0.997 for *PHOX2B*, 0.939 for *TH*. Presence of *PHOX2B*/*TH* expression in BM at the time of diagnostics decreased EFS (0.31±0.12vs.0.81±0.06,p<0.01) and OS (0.31±0.13vs.0.87±0.05,p<0.01). Predominance of *PHOX2B* expression over *TH* >1.68 in BM had adverse prognostic significance: EFS 0.00vs.0.56±0.12,p=0.017, OS 0.00vs.0.72±0.11,p=0.006. Persistence of TAGs expression during treatment demonstrated trend to reduced EFS (0.27±0.12vs.0.43±0.19,p=0.08). Positivity of BM for *PHOX2B*/*TH* before stem cells apheresis had strongly negative prognostic impact (EFS 0.00vs.0.35±0.14,p=0.04; OS 0.00vs.0.36±0.15,p=0.03) despite of CD34+ selection.
Conclusion: *PHOX2B* and *TH* are the most appropriate markers for BM involvement and MRD detection. Theirs expression at the time of diagnostics and before PBSC apheresis had strongly adverse prognostic impact. Predominance of *PHOX2B* expression over *TH* can define high risk patients.

O-023

IMPACT OF RESPONSE TO PRIOR THERAPY ON OUTCOME FOR REFRACTORY VS. RELAPSED NEUROBLASTOMA PATIENTS TREATED WITH ^{131}I-METAIODOBENZYLGUANIDINE (^{131}I-MIBG)

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Background/Objectives: ^{131}I-metaiodobenzylguanidine (^{131}I-MIBG) is a targeted radiopharmaceutical with significant activity in high-risk relapsed and chemotherapy-refractory neuroblastoma. The primary aim of this study was to

determine if there are differences in response rates to ^{131}I-MIBG between patients with relapsed and treatment-refractory neuroblastoma.
Design/Methods: This was a retrospective cohort analysis of 218 patients with refractory, persistent, relapsed, or progressive neuroblastoma treated with ^{131}I-MIBG at UCSF between 1996 and 2014. Results were obtained by chart review and database abstraction. Baseline characteristics and response rates between relapsed/progressive and refractory/persistent patients were compared using Fisher exact and Wilcoxon rank sum tests, and differences in OS were compared using the log-rank test. Subanalyses were performed including only patients treated on MIBG monotherapy protocols, and on patients treated on MIBG protocols that did not included myeloablative chemotherapy.
Results: The response rate (complete and partial response) to ^{131}I-MIBG based therapies for all patients was 27%. There was no difference in response rates between relapsed and refractory patients in either univariate or multivariate analysis However, after ^{131}I-MIBG, 24% of relapsed patients had progressive disease compared to only 9% of refractory patients, and 39% of relapsed patients had stable disease compared to 59% of refractory patients ($p = 0.02$). The median follow up for surviving patients was 61 months. Among all patients, the 24-month OS was 47.0% (95% CI 39.9%-53.9%). The 24-month OS for refractory patients was significantly higher at 65.3% (95% CI 51.8%-75.9%), compared to 38.7% (95% CI 30.4%-46.8%) for relapsed patients ($p < 0.001$).
Conclusion: Although there was no significant difference in overall response rates to ^{131}I-MIBG between patients with relapsed and refractory neuroblastoma, more patients with prior relapse developed progressive disease and had a lower 2-year overall survival after ^{131}I-MIBG compared to patients with refractory disease. Our results can be used to guide stratification on future ^{131}I-MIBG clinical trials.

O-024

RELAPSE IN PATIENTS WITH HIGH-RISK NEUROBLASTOMA AFTER TREATMENT WITH 3F8+GM-CSF+CIS-RETINOIC ACID IN FIRST COMPLETE/VERY GOOD PARTIAL REMISSION: PATTERNS, MANAGEMENT AND LONG-TERM OUTCOME

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Background/Objectives: Anti-GD2 immunotherapy is now standard of care for high-risk neuroblastoma (HR-NB). However, prognosis after first relapse post-immunotherapy is deemed dismal; patients are often enrolled on early phase studies without curative intent.
Design/Methods: HR-NB patients relapsing post-3F8+GMCSF+cis-retinoic acid (CRA) in first complete (CR) or very good partial remission (VGPR) (NCT00072358) underwent the following reinduction strategies: (1) Isolated CNS relapse (CNS-R): multimodality therapy including intra-Ommaya radioimmunotherapy (MM-RIT) (J Neurooncol 97:409). (2) Disseminated (D-R) or focal soft-tissue relapse (FS-R): High-dose chemotherapy using active agents as previously described (Cancer 119: 665; Bone Marrow Transplant 48:642; Pediatr Blood Cancer 56: 403; Eur J Cancer 47: 84; Cancer 116: 3054) ±surgery (±IORT)±radiation. (3) Focal bone relapse (FB-R): low-dose chemotherapy (J Clin Oncol 24:5271) ± radiation. Patients achieving second CR/VGPR were retreated with 3F8+GM+CRA (Oncoimmunol In Press 2015) ±anti-GD2/GD3 humoral vaccine (ClinCanRes 20:1375). Progression-free (PFS) and overall survival (OS) analyses were performed (Kaplan-Maier method) and prognostic variables compared (log-rank test).
Results: Of 145 consecutive patients treated with 3F8+GM+CRA in first CR/VGPR, 64 (44%) relapsed (median follow-up 60 months from starting 3F8): 17 CNS-R, 24 D-R, 12 FS-R, 11 FB-R. 39 (61%) achieved second CR. 19 (29%) continued in remission >5 years after relapse. Respective five-year PFS and OS rates (%) for groups CNS-R receiving MM-RIT, D-R, FS-R and FB-R were 77±12 and 68±13, 6±7 and 6±7, 25±13 and 30±7, 54±15 and 62±15. Adverse prognostic factors for survival post-relapse included failure to achieve second CR, D-R as opposed to other relapse patterns, and early (<6mo from starting 3F8) relapse ($p<0.05$ for each), but not *MYCN* amplification ($p=0.4$).
Conclusion: Long-term PFS and OS are possible in HR-NB patients post-relapse if CR/VGPR can be achieved, especially when relapse is focal. Agents with proven anti-NB activity should be considered initially at first relapse rather than purely experimental approaches.

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O-025

A CONSERVATIVE STRATEGY IN INFANTILE FIBROSARCOMA IS POSSIBLE: THE EUROPEAN PEDIATRIC SOFT TISSUE SARCOMA GROUP (EPSSG) EXPERIENCE

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Background/Objectives: Infantile fibrosarcoma (IFS) is a very rare disease occurring in young infants characterized by high local aggressiveness but also an overall favorable survival. To try to reduce the total burden of therapy, the European pediatric Soft Tissue Sarcoma Group (EpSSG) has developed conservative therapeutic recommendations according to initial resectability.
Design/Methods: Between 2005 and 2012, children less than 2 years, with localized IFS were prospectively registered. Initial surgery was suggested only if possible without mutilation. Patients with initial complete (IRS-group I) or incomplete (IRS-group II) resection had no further therapy. Patients with an initial inoperable tumor (IRS-group III) received first-line vincristine-actinomycin-D chemotherapy (VA). Delayed conservative surgery was planned after tumor reduction. Aggressive local therapy (mutilating or external radiotherapy) was discouraged.
Results: A total of 54 infants (median age 1.8 months [0.0-18.7]; 7 % of all Non-rhabdomyosarcoma-soft-tissue-sarcoma), were included in the study, 37% occurred before birth or during the first month of life. ETV6-NTRK3 transcript was present in 73% of all assessed cases. Primary sites were predominantly limbs (55.6%) and trunk (27.8%). At initial surgery, 12 patients were classified as IRS-group I, 8 as IRS-group II, 34 as IRS-group III. VA chemotherapy was delivered to 31 children. An additional drug (alkylating/anthracycline) was necessary for 9 patients. Only 3 survivors need mutilating surgery and 1 radiotherapy. After a median follow-up of 51.5 months, 3-year event free and overall survival were respectively 90.7 (95%CI 79.2-96.0) and 94.4 (95%CI 83.8-98.2).
Conclusion: Conservative strategy is possible in IFS without jeopardizing survival. Mutilating surgery could be avoided in 94%. Alkylating or anthracycline based chemotherapy could be avoided in 65% of patients needing chemotherapy. This study does not support a "wait and see" strategy in this tumor. VA should be regimen of first preference in order to reduce long term effects.

O-026

PEDIATRIC ONCOMINE: A CHILDHOOD CANCER NGS PANEL TO DIRECT DIAGNOSIS AND THERAPY

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Background/Objectives: Chemotherapy of childhood cancer has shown little improvement in outcome over the past several decades. In contrast, adult cancer increasingly employs targeted therapeutics chosen on the basis of an identifiable gene mutation, fusion, or amplification that suggests likely sensitivity to a specific agent. The NCI MATCH (Molecular Analysis for Therapy Choice) program employs a diagnostic panel of such genomic features (Oncomine™) in order to match drug with target in the design of 'precision medicine' clinical trials. Unfortunately, Oncomine™ is designed for use in adult cancer and is ill suited for use in pediatric cancer. Our objective is to develop a pediatric version of Oncomine™, termed Pediatric Oncomine,that is optimized for childhood cancer.
Design/Methods: We have identified 50+ genes in Oncomine™ that match targeted therapeutics for potential use in pediatric cancer. We have also identified diagnostically and prognostically useful gene translocations, as well as copy number variants, useful in the diagnosis of both solid tumors and hematopoietic malignancies. In addition, in order to provide useful dosing guidance for pediatric oncologists we have added a panel of genes like MTHFR, TPMT1, COMT, CYP2B6 UGT1A1, and others. These gene targets have been incorporated into a next generation sequencing panel suitable for use on FFPE tissue developed by the Center for Personalized Medicine at CHLA, which designed the content.
Results: We have adapted a preexisting pan-cancer somatic panel, Oncomine™, for pediatric use by re-utilizing features (largely mutations) relevant to targeted

therapeutics while adding genomic features (largely gene translocations and amplifications) unique to pediatric cancer, as well as a pharmacogenomic module of particular use in pediatric oncology.
Conclusion: A pan-cancer somatic panel designed specifically for use in the diagnosis and management of childhood cancer patients who would benefit from targeted therapy has been created and will be useful in pediatric oncology 'precision medicine' trials.

O-027

TRANSCRIPTOME BASED INDIVIDUALIZED THERAPY OF REFRACTORY PEDIATRIC SARCOMA

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Background/Objectives: Tumor biology in refractory pediatric patients is highly heterogeneous and new approaches addressing resistance are urgently needed. Gene expression profiling may aid in medical decision making in this setting.
Design/Methods: We enrolled patients for whom standard of care and current clinical trials provided no further treatment options in a one arm open label prospective study to assess survival. Tumor samples underwent transcriptome analysis with Affymetrix arrays. We focused on genes with >1.5 fold expression vs. normal tissue, identified as drivers by TARGETgene. Targets ranked between 1-100 were considered for therapy. Drug selection criteria: delivery, no previous use in the patient, citations related to disease, citations related to other cancers, side effects, drug interactions, oral application, approval by German authorities.
Results: During 29 months 22 biopsies were obtained after informed consent from 19 eligible patients at a single institution (TUM) with a mean age of 15.1 years. Diagnosis was sarcoma in 17 (8 Ewing sarcoma, 5 soft tissue sarcoma, 4 osteosarcoma), and embryonal tumor in 2. Targeted therapy was administered in 12, while in 6 no druggable targets could be identified. One patient was noncompliant. Medications assessed: 472. Mean druggable targets per patient: 7. 21 different drugs were recommended with an average of 3 drugs per patient, including PKIs, TKIs, TOP2Is, HDIs, taxanes, nucleoside analogs, arsenic trioxide and ATRA. Therapy was generally well tolerated with no adverse reactions and no side effect-related discontinuation of treatment. In this pilot study survival was at least non-inferior to best medical care.
Conclusion: Targeted therapy is a feasible alternative to best medical care in refractory pediatric cancer. In the majority of patients druggable targets can be identified and therapy typically does not cause side effects. Prospective studies with appropriate sample size to determine potential overall survival benefit are planned within the INFORM consortium.

O-028

CORRELATION OF COPY NUMBER CHANGES AND GENE EXPRESSION IN NEUROFIBROMATOSIS1-ASSOCIATED MALIGNANT PERIPHERAL NERVE SHEATH TUMOURS

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Background/Objectives: Neurofibromatosis type1 (NF1) is a common autosomal dominantly inherited complex neurogenetic disorder and results from the mutational inactivation of the *NF1* gene. Neurofibromin, the *NF1* gene product is a tumour suppressor protein and downregulates Ras. NF1 is characterised by the development of benign and malignant tumours of the peripheral nerve sheath (MPNSTs). Whilst biallelic *NF1* gene inactivation contributes to benign tumour formation, additional cellular changes in gene structure and/or expression are required to induce malignant transformation. Although few molecular profiling studies have been performed on the process of progression of pre-existing plexiform neurofibromas to MPNSTs, the integrated analysis of copy number alterations (CNAs) and gene expression is likely to be key to understanding the molecular mechanisms underlying NF1-MPNST tumorigenesis. In a pilot study, we employed this approach to identify genes differentially expressed between benign and malignant NF1 tumours and then correlated this with copy number alterations.
Design/Methods: The study group comprised nine NF1-associated tumours with biallelic *NF1* genes mutations (comprising four benign plexiform neurofibromas and five high grade MPNSTs from nine unrelated NF1 patient). DNA and RNA were isolated from the same segment of tumour. The same tumour samples were analysed by Affymetrix SNP array 6.0 and Affymetrix Human Exon 1.0 ST array.
Results: *SPP1* (osteopontin) was the most differentially expressed gene (85-fold increase in expression), compared to benign plexiform neurofibromas. Short hairpin RNA (shRNA) knockdown of *SPP1* in NF1-MPNST cells reduced tumour spheroid size, wound healing and invasion in four different MPNST cell lines. Seventy-six genes were found to exhibit concordance between CNA and gene expression level. Pathway analysis of these genes suggested that glutathione metabolism and Wnt signalling may be specifically involved in NF1-MPNST development.
Conclusion: Our study suggests *SPP1* is associated with malignant transformation in NF1-associated MPNSTs and could prove to be an important target for therapeutic intervention.

O-029

BETTER OUTCOME WITH MAINTENANCE THERAPY: PEDIATRIC PATIENTS WITH STAGE IV SOFT TISSUE SARCOMA BENEFIT FROM LONG TERM THERAPY COMPARED TO SCT OR NO FURTHER THERAPY

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Background/Objectives: Despite advances in the treatment of soft tissue sarcoma (STS), the prognosis of patients with metastatic disease remains daunting. While high dose chemotherapy (HDC) and allogeneic stem cell transplantation (aSCT) did not result in a therapeutic breakthrough, maintenance therapy (MT) following a multimodal therapy was shown in the CWS-96 study to be a promising approach and has been recommended therefore for metastatic disease in the CWS 2002 P and CWS-IV-2002 international studies conducted in Germany, Sweden, Swiss, Poland and Austria from 2002-2009. We present a retrospective analysis of patients with metastatic Rhabdomyosarcoma (RMS) and RMS-like STS registered in both studies.
Design/Methods: Multimodal therapy according to protocol included polychemotherapy (Vincristine, Actinomycine D, Ifosfamide, Carboplatin, Etoposide, Epirubicine), surgery and/or radiation, followed by oral MT with a combination of Trofosfamide, Idarubicine, and Etoposide (O/TIE). Many patients however, received other type of consolidation therapy based on individual decision of the treating centers: i.e. HDC, aSCT or the combination of Cyclophosphamide and Vinblastine (Cyc/Vbl).
Results: 176 patients were inlcuded (alveolar RMS n=91, embryonal RMS n=60, RMS-like n=25). The probabilities of overall (pOS) and event free survival (pEFS) were 35%, and 29.9% respectively, with a median follow-up time of 121 weeks (all patients, range 1 – 278). Patients who received intensive chemotherapy only (n=33), or additional allogeneic SCT (n=22) showed a significant lower pOS (18.7% and 15.2%) than patients who received O/TIE (n=81) or Cyc/Vbl (n=26) (pOFS 31% and 54.8% respectively). pOS of all MT patients (n=107) was 38% vs. 17% in all non-MT patients (n=69), p=0,002.
Conclusion: This analysis supports our previous results (CWS-96 IV Study) showing that a MT might improve prognosis in patients with metastatic STS in contrast to HDC, aSCT and to no further therapy. The question what the best MT will be remains open.

O-030

RELAPSE AFTER LOCALIZED RHABDOMYOSARCOMA: EVALUATION OF THE EFFICACY OF SECOND-LINE CHEMOTHERAPY

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Background/Objectives: About one third of patients with rhabdomyosarcoma relapse despite appropriate treatment and experience a poor outcome. Little meaningful improvement in the outcome of this disease has been observed over the last 30 years.

There is no clear international recommendation concerning the use of salvage chemotherapy at relapse. A retrospective multicenter analysis was therefore conducted to analyze the efficacy of various second-line chemotherapy regimens in this setting.
Design/Methods: Forty-nine patients under the age of eighteen, with initially localized rhabdomyosarcoma, who relapsed after first complete remission, treated in 3 SFCE centers (Société Française des Cancers de l'enfant) between 1995 and 2013, were analyzed.
Results: First relapse occurred after a median interval of 22 months and remained localized in 71.4% of cases. All patients received second-line chemotherapy with an overall response to this salvage therapy of 71.7%. Best specific response rates were 86.7% and 85.7% for carboplatin/epirubicin/vincristine-ifosfamide/vincristine/etoposide (CEV/IVE) (13 patients) and vincristine/irinotecan ± temozolomide (VI(T)) (6 patients), respectively. Overall, 40 patients (81.6%) were then eligible for delayed local treatment (surgery and/or radiotherapy) and 30 of them (61.2%) achieved second complete remission. After a median follow-up of 5.4 years since diagnosis of first relapse, 5-year overall survival is 49.4% (95% CI: 34.2-64.6).
Conclusion: Salvage chemotherapy plays a central role in the management of patients with relapsed rhabdomyosarcoma. CEV/IVE and VI(T) regimens can be recommended as neoadjuvant chemotherapy before local treatment for patients with relapsed rhabdomyosarcoma.

Free Papers 06: ALL

O-031

TUMOR SUPPRESSOR GENES IKZF1 AND BTG1 COOPERATE IN ACUTE LYMPHOBLASTIC LEUKEMIA DEVELOPMENT AND GLUCOCORTICOID THERAPY RESISTANCE

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Background/Objectives: *IKZF1* (IKAROS) aberrations have been shown to independently predict poor prognosis in children with BCP-ALL and currently are incorporated in the risk stratification of Dutch pediatric B-cell precursor acute lymphoblastic leukemia (BCP-ALL) patients. Our recent findings show that loss of IKZF1 function has a direct impact on chemotherapy responses by inhibiting glucocorticoid-induced apoptosis in normal and leukemic B-cells. Furthermore, the effect of other genetic aberrations on therapy outcome of *IKZF1*-deleted patients has not been fully addressed. Our analysis has revealed that the event-free survival of *IKZF1*-deleted patients is negatively affected by the co-occurrence of *BTG1* deletions. In addition, *BTG1* deletions appear to occur more frequently in patients with IKZF1 gene alterations (19%) compared to an unselected cohort (9%). We studied the genetic interaction between IKZF1 and BTG1 in leukemia development and glucocorticoid responses using knockout mouse models and human leukemia cell lines.
Design/Methods: *Ikzf1*$^{+/-}$ were crossed onto a *Btg1* knockout background and monitored for spontaneous leukemia development. Additionally, glucocorticoid response was determined in lymphoid cells isolated from compound *Ikzf1*$^{+/-}$;Btg1$^{-/-}$ mice by MTS assay. Additionally, sensitivity towards glucocorticoid-induced apoptosis was determined in human leukemia cell lines displaying loss of IKZF1 and BTG1 function.
Results: We observed a significant acceleration in the onset of T-cell acute lymphoblastic leukemia in *Ikzf1*$^{+/-}$;*Btg1*$^{+/-}$ which was even further enhanced in *Ikzf1*$^{+/-}$;*Btg1*$^{-/-}$ animals. These leukemias were characterized by clonal TCRβ rearrangement and aggressive infiltration into secondary organs. B-cells isolated from *Ikzf1*$^{+/-}$;*Btg1*$^{-/-}$ animals were highly resistant against glucocorticoid-induced apoptosis. Similarly, human leukemia cell lines displaying loss of IKZF1 and BTG1 function showed a glucocorticoid-resistant phenotype that was even stronger than by loss of IKZF1 alone.
Conclusion: Together, our findings establish *BTG1* as a tumor suppressor gene that genetically interacts with *IKZF1* during leukemic transformation and strongly potentiates the IKZF1-mediated glucocorticoid resistance phenotype in normal and leukemic B cells.

O-032

EFFECTS OF ETHNICITY AND SOCIOECONOMIC STATUS ON OUTCOME IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA

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Background/Objectives: Data on the effects of socioeconomic status (SES) and outcome as it relates to race/ethnicity for children with ALL in the United States are limited. Using two large US cancer registries, we investigated the effects of race/ethnicity and community-level SES for children with ALL.
Design/Methods: Patients diagnosed with ALL between 1995-2008 at the age of 1-18 years old were eligible for inclusion. Community level poverty data were calculated for each patient using United States Census data and categorized as a community in which <5%, 5-<20% or 20-100% of households live below the poverty level.
Results: A total of 4,719 patients were included. Race/ethnicity consisted of non-Hispanic White (NHW) (47.6%), Hispanic (H) (43.9%) and non-Hispanic Black (NHB) (8.5%). 5-year overall survival (OS) for NHW, H and NHB patients was 87.7%, 82.9% and 79.2%, respectively (NHW versus H, p<0.001; NHW versus NHB, p=0.008). 5-year OS for patients living in a community with <5% poverty, 5-20% poverty and >20% poverty was 90.5%, 86.3% and 78.4%, respectively (<5% versus 5-20% poverty, p=0.006; <5% versus 20-100% poverty, p<0.001). Patients were categorized into two age groups (1-9 years, 10-18 years) based on the National Cancer Institute's stratification of standard risk and high risk patients. Multivariate analysis of patients 1-9 years of age revealed that race/ethnicity was not independently associated with OS after adjusting for gender, treatment era and socioeconomic status. Patients in communities with >20% poverty experienced worse OS (HR 1.84 [95% CI 1.3-2.6]). For patients age 10-18 years of age, multivariate analysis demonstrated that early treatment era, Hispanic ethnicity and SES were all associated with worse OS. NHB race/ethnicity was not independently associated with worse outcome after adjusting for other factors.
Conclusion: Lower SES has significant adverse effect on OS in children with ALL. Further research into the causes for worse outcome for these patients is warranted.

O-033

ETP ALL IN AIEOP CHILDREN TREATED WITH THE AIEOP-BFM ALL 2009 STUDY

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Background/Objectives: To evaluate the outcome of AIEOP (Italian Association of Pediatric Hematology Oncology) patients with Early T-cell Precursor (ETP) Acute Lymphoblastic Leukemia (ALL) treated in AIEOP-BFM ALL 2009 Study.
Design/Methods: Immunophenotipic criteria for ETP-ALL definition: CD1a and CD8 negative, CD5 weak positive or negative and positive at least one of CD34, CD117, HLADR, CD13, CD33, CD11b, or CD65 antigens. Treatment: BFM protocol I; 4 HDMTX courses (5 g/sqm over 24 hrs) and protocol II in non-high risk (HR) or 3 poly-chemotherapy blocks and protocol III x3 in HR patients; intrathecal therapy ± cranial radiotherapy; maintenance therapy up to 2 years of treatment. Peg-L-Asp is used.
Results: Of the 201 T-ALL eligible patients, 33 (16.4%) had ETP ALL. ETP ALL had lower WBC counts (<20,000/mmc 61% vs 20%, p-value<0.001; median 5600 vs 95200); frequent absence of molecular markers for PCR-MRD (61% vs 5%); more PPR (52% vs 36%), MRD-HR at day+15 (BM blasts ≥10% by FCM, 61% vs 27%), resistance to phase IA (BM blasts ≥5% morphologically, 15% vs 5%), high PCR-MRD ($\geq 10^{-3}$) at day+33 (85% vs 45%) and at day 78 (23% vs 14%) for those with markers (13/33), and HR allocation (76% vs 44%). After a median follow-up of 2.3 years 29/33 patients (88%) are in CCR, including 8/10 after HSCT, with 2 deaths in Induction and 2 after HSCT. 2 yrs EFS in ETP is 85.9%(6.7) vs 79.1%(3.6) in non-ETP T-ALL.
Conclusion: ETP is characterized by poor initial treatment response; phase IB is effective in reducing MRD. Although follow-up and number of patients are limited, these data suggest that ETP and non-ETP ALL patients treated with current BFM stratification and treatment strategy have comparable outcomes, as recently reported for UKALL and COG protocols using Peg-L-Asp. The role of innovative therapies and HSCT in ETP ALL needs to be further investigated.

O-034

INADEQUATE LUNG SHIELDING IN CHILDREN WITH ALL UNDERGOING ALLO-HSCT IS ASSOCIATED WITH INFERIOR SURVIVAL: REPORT FROM THE CHILDREN'S ONCOLOGY GROUP/PEDIATRIC BLOOD AND MARROW TRANSPLANT CONSORTIUM

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Background/Objectives: Lung shielding has not been standardized during total body irradiation (TBI) preparative regimens for hematopoietic stem cell transplantation (HSCT), leading to differences in pulmonary radiation dose. We examined the relationship between lung radiation dose, transplant-related mortality (TRM), relapse-free (RFS) and overall survival (OS) in children undergoing TBI-based HSCT for acute lymphoblastic leukemia (ALL) on COG trial ASCT0431/PBMTC ONC051.
Design/Methods: The lung radiation dose received during TBI (1200 or1320 cGy given bid in 6 or 8 fractions) was analyzed in relation to: total TBI dose, TBI dose per fraction, TBI dose rate, TBI fields, patient position, pulmonary toxicity, acute graft versus host disease (GVHD), veno-occlusive disease (VOD), TRM, donor type, minimal residual disease (MRD) levels, RFS and OS.
Results: Of 143 enrolled, 109 patients had lung doses available for analysis. Patients treated with lateral fields were significantly more likely to receive lung doses ≥ 800cGy ($p < 0.001$). Patients receiving lung dose ≥ 800cGy had higher rates of relapse or TRM ($p = 0.034$), and a trend for higher rates of death ($p = 0.078$). There was no association between lung dose and rates of pulmonary toxicity ($p = 1.000$). In univariate analysis, lung dose ≥ 800cGy, grade IV vs. grade I-III GVHD, VOD, pulmonary toxicity, MRD, higher disease risk group and unmatched donor types were associated with inferior RFS and OS. Multivariate analysis identified lung dose ≥ 800cGy to be significantly associated with inferior RFS (HR 1.9; $p = 0.031$) and OS (HR 2.1; $p = 0.023$) while controlling for risk group and donor type.
Conclusion: This data showed that lung irradiation dose ≥ 800 cGy during TBI was associated with inferior RFS and OS. Understanding the mechanisms underlying these results will require more research, but shielding to reduce the lung dose to 800cGy for TBI regimens administering ≥ 1200cGy is recommended.

O-035

AGGRAVATED BONE DENSITY DECLINE FOLLOWING SYMPTOMATIC OSTEONECROSIS IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Background/Objectives: Osteonecrosis (ON) and decline of bone mineral density (BMD) are serious side effects during and after treatment of childhood acute lymphoblastic leukemia (ALL). It is unknown whether ON and low BMD co-occur in the same patients, and whether these two osteogenic side-effects can mutually influence each other's development.
Design/Methods: BMD and the incidence of symptomatic ON were prospectively assessed in a national cohort of 466 patients with ALL (4-18 years of age) who were treated according to the dexamethasone-based Dutch Child Oncology Group-ALL9 protocol. Bone mineral density of the lumbar spine (BMD_{LS})(n=466) and of the total body (BMD_{TB})(n=106) were measured by dual X-ray absorptiometry. BMD was expressed as age- and gender-matched standard deviation scores.
Results: Thirty patients (6.4%) suffered from symptomatic ON. At baseline, BMD_{LS} and BMD_{TB} did not differ between patients who developed or who did not develop ON. At cessation of treatment, patients with ON had a lower mean BMD_{LS} and BMD_{TB} than patients without ON (respectively, ON+:-2.16 vs. ON-:-1.21, $p<0.01$ and ON+:-1.73 vs. ON-:-0.57, $p<0.01$). Multivariate linear models showed that patients with ON had a steeper BMD_{LS} and BMD_{TB} decline during follow-up than patients without ON (interaction group time, $p<0.01$ and $p<0.01$).
Conclusion: We conclude that BMD status at ALL diagnosis does not seem to influence the occurrence of symptomatic ON. BMD decline occurs from the moment of ON diagnosis, this suggest that the already existing BMD decline during ALL therapy is further aggravated by factors such as restriction of weight bearing activities and destruction of bone architecture due to ON. Therefore ON can be considered as a risk factor for low BMD in children with ALL.

O-036

EFFECTIVE TARGETING OF B-CELL PRECURSOR ACUTE LYMPHOBLASTIC LEUKEMIA BY CD70 DIRECTED IMMUNOTHERAPY

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Background/Objectives: Despite successful treatment of acute lymphoblastic leukemia (ALL), relapse of the disease remains a major problem and is associated with poor prognosis. This emphasizes the need for novel treatment strategies in addition to established chemotherapy without increasing general toxicity. Previously, we identified up-regulated *CD70* transcript levels in a subgroup of B-cell precursor (BCP) ALL associated with poor prognosis and patient outcome. CD70 is involved in T/B cell priming and generation of memory B cells and only expressed on activated immune cells. In this study, we aimed to evaluate CD70 as a therapeutic target for directed immunotherapy.
Design/Methods: CD70 surface expression was analyzed by flowcytometry on patient-derived xenograft samples. Effectivity and mechanisms of anti-CD70 directed immunotherapy on BCP-ALL cells were evaluated *in vitro* and *in vivo* using different xenograft mouse models.
Results: CD70 surface expression was analyzed on all together 28 patient-derived BCP-ALL xenograft samples. Interestingly, CD70 surface expression was found to be higher in leukemias associated with poor outcome compared to ALL with favorable outcome while very low CD70 expression was observed in non-leukemic bone marrow control samples. Taking advantage of increased CD70 expression in BCP-ALL, the efficacy of monoclonal antibody based CD70-directed immunotherapy was evaluated. A marked reduction of leukemia load in peripheral blood, bone marrow and spleens of the animals was detected after transplantation of anti-CD70 treated $CD70^{hi}$ primograft ALL cells onto NOS/SCID mice. This effect could be abrogated by both depletion of NK-cells in NOD/SCID mice and by using NK-cell deficient NSG mice as recipients, indicating that decreased *in vivo* leukemia growth upon anti-CD70 treatment is mediated by NK-cell induced cytotoxicity. In line, antibody-dependent cell-mediated cytotoxicity (ADCC) was observed to mediate the anti-leukemic effect *in vitro*.
Conclusion: Thus, we identified significantly up-regulated CD70 expression in BCP-ALL providing a novel target for directed immunotherapy.

Free Papers 07: Myeloid Leukemia

O-037

NEW ASPECTS OF GENETIC HIGH RISK STRATIFICATION IN PEDIATRIC ACUTE MYELOID LEUKEMIA: A REPORT OF AML-BFM STUDY 2004

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Background/Objectives: Conflicting data on poor risk factors in pediatric acute myeloid leukemia (AML) hamper risk stratification systems. The aim was to evaluate the prognostic impact of specific chromosomal aberrations, especially a complex or monosomal karyotype, in uniformly treated children to improve risk-adapted therapy.
Design/Methods: 707 patients <18 years with de novo AML (WHO criteria, no Down Syndrome, no t(15;17)) were included in Study AML-BFM-2004. In 644 (91%) patients genetic data were conclusive for either cytogenetic, FISH analyses or RT-PCR (initial bone marrow or blood samples). Monosomal karyotype (MK) was defined as ≥2 autosomal monosomies or one autosomal monosomy associated with ≥one structural abnormality, excluding favorable cytogenetics. Complex karyotype (CK) was defined as

≥3 aberrations and ≥one structural aberration, without favorable genetics or mixed lineage leukemia (MLL)-rearrangement.
Results: In addition to several known cytogenetic prognostic factors a trisomy 8 was associated with a reduced probability of 5-year event-free survival (pEFS) (n=16, pEFS 25%, SE 11%, P=0.0089), but not if it was combined with other aberrations (n=48, pEFS 50%; SE 8%, P=0.83). Patients with MK showed a dismal outcome (n=25, pEFS 23%, SE 9%, P=0.0080), even after excluding patients with involvement of chromosome 7 (n=19; pEFS 25%; SE 10%, P=0.0066). Although patients with MK had high complete remission rates (80%), the cumulative incidence of relapse was enhanced (CIR 49%, SE 11%, P=0.05). Multivariate analysis of EFS revealed MK as independent high risk factor (Hazard ratio 2.07, 95% Confidence Interval 1.20 – 3.57, $P_{\chi}{}^{2}$=0.009). In contrast the complex karyotype alone had no prognostic significance (n=47, pEFS 47%, SE 7%, P=0.33) after excluding patients with MK.
Conclusion: We identified the monosomal karyotype and trisomy 8 (without additional cytogenetic aberrations) as potentially poor prognostic factors in pediatric AML, thereby diminishing the impact of the complex karyotype. These results might affect future risk stratification and risk-adapted therapy in childhood AML.

O-038

OPTIMIZING RISK STRATIFICATION OF JUVENILE MYELOMONOCYTIC LEUKEMIA USING NEXT GENERATION SEQUENCING

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Background/Objectives: Juvenile myelomonocytic leukemia (JMML) is an aggressive myeloproliferative neoplasm of childhood, with an event free survival of ~50% after hematopoietic stem cell transplantation (HSCT). Next generation sequencing was performed in a large cohort of patients in order to identify additional genetic alterations in this disease.
Design/Methods: Whole exome sequencing was carried out in 29 patients with germline-tumor pairs including seven patients who also had relapsed samples available for analysis. Targeted, deep sequencing was then carried out in an additional 71 patients. Genome wide DNA methylation and RNA-seq analyses were also performed on samples of particular interest.
Results: Pathogenic mutations from exome sequencing were identified in 16 genes, several of which were only detected in a clonal fashion at relapse. The recurrent mutations involved genes regulating signal transduction, gene splicing, the polycomb repressive complex and transcription. Importantly, the number of somatic alterations present at diagnosis was the major determinant of outcome with patients harboring two or more somatic alterations at diagnosis having a significantly inferior survival compared to those with less than two despite treatment with HSCT. The 10-year event free survival rates for patients with zero to one somatic events at diagnosis was 60.6% ± 6.2% versus 22.7% ± 7.4% for those with two or more (p=0.003). In addition, when modeled in a multivariate analysis, only the number of somatic alterations remained independently prognostic of poor outcome. By focusing on patients with relapsed disease, we also established that the model for disease progression in JMML is surprisingly simplistic, with a linear acquisition of mutations compared to the branching model seen in other cancers.
Conclusion: Patients with JMML harboring two or more somatic alterations at diagnosis have unacceptably poor outcomes with conventional treatment and should be risk stratified to receive tailored treatments based on their genetic profile.

O-039

PHF6 MUTATIONS IN PEDIATRIC ACUTE MYELOID LEUKEMIA

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Background/Objectives: Acute myeloid leukemia (AML) is characterized by the presence of different cytogenetic and molecular aberrations, which may influence prognosis. *PHF6*, a gene located on Xq26.3, is a tumor suppressor mutated in 20% of the T-ALL cases (Van Vlierberghe, 2010). In adult AML mutations of *PHF6* are found in ~3% of the cases, all classified as FAB-M0, M1 and M2 (Van Vlierberghe, 2011). In T-ALL and adult AML mutations were found almost exclusively in male patients, probably due to the sex-chromosome localization of the gene. Studies show that suppression of *PHF6* promotes myeloid tumor cell growth in vivo (Meacham, 2015). Our aim was to investigate the frequency of *PHF6* mutations in patients with pediatric AML.
Design/Methods: We investigated a pediatric AML cohort (n=318), enriched for FAB-M0, M1 and M2 (n=143), for the presence of mutations in the complete encoding region of *PHF6* with direct sequencing. Moreover, we analyzed mRNA expression levels of *PHF6* with quantitative PCR, and analyzed outcome.
Results: We identified 5 cases with a *PHF6* frameshift mutation, and one case harboring a point mutation, predicted as damaging by SIFT/PolyPhen analysis. All mutated cases were classified as FAB-M0, M1 and M2. In contrast to adult AML, 4/6 mutated patients were female, of which 1 female showed –X based on conventional karyotyping and *XIST* expression. The frameshift mutated cases showed significantly lower *PHF6* expression compared to other pediatric AML cases, indicating a loss-of-function. Of the 6 patients with a mutation, one was refractory, and 4 relapsed. Four patients died due to leukemia and two are in CCR. Other genetic aberrations found in these patients were *RUNX1*/*RUNX1T1, NUP98*/*KDM5A*, and mutations in *RAS, WT1, TET2, IDH1, BCORL1* and *ETV6*, none of which were recurrent.
Conclusion: We identified recurrent loss-of-function *PHF6* mutations in pediatric AML, in both male and female patients, exclusively found in FAB-M0, M1 and M2.

O-040

IMPLEMENTATION OF ADAPTED AML TREATMENT IN LIMITED RESOURCES COUNTRY (INDONESIA NATIONAL AML PROTOCOL): INTERIM RESULTS

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Background/Objectives: Childhood acute myeloblastic leukemia (AML) treatment has significantly improved over the past decades. In developing countries the success of treatment was estimated below 10% while in developed countries treatment success has reached 65%. Starting 2011 we developed and used the National Protocol for AML. The aim of this study was to determine the profile of childhood AML in Dr. Sardjito Hospital and evaluate the results of three different AML treatments protocols: ADE (Ara-C, Doxorubycine and Etoposide) versus modification of the Nordic Society of Pediatric Hematology Oncology and Indonesia National AML Protocol.
Design/Methods: The health records of children 0 – 18 years of age, newly diagnosed with AML from March 1999 – February 2015 were retrospectively reviewed. The diagnosis of AML was confirmed based on morphological and histochemical examinations of marrow samples. Survival analysis was performed on patients treated on ADE (ara-C, doxorubicinand etoposide) versus m-NOPHO (6-mercaptopurine, cytarabine, etoposide, anthracycline, methotrexate and L-asparaginase) and National AML protocol (doxorubycine, cytarabine and etoposide plus tripel drugs intrathecal: metothrexate, hydrocortison and Ara-C).
Results: Of 301 patients diagnosed with AML, 217 (72%) patients received chemotherapy: 139 (64%) used ADE or m-Nopho protocol, 66 (30%) with National AML protocol and the rest used other protocol 12 (6%). The OS after 2-years in patients who were treated with National AML protocol was 18.6% whereas in the ADE and m-Nopho protocol group, was 3.9% (p=0.05).
Conclusion: Treatment with National AML protocol had a higher survival compared to the ADE and m-NOPHO protocol. Supportive care including infection control has considerable influence to the success in the treatment of AML.

O-041

IMATINIB PHARMACOKINETICS, ITS GOOD EFFICACY BUT ALARMING TOXICITY IN CHILDREN WITH CHRONIC MYELOID LEUKEMIA IN INDIA

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Background/Objectives: Imatinib has limited data on efficacy and toxicity, which is mostly from mostly Caucasian children. Imatinib's potential risk of chronic toxicity due to inhibition of c-kit and PDGF-R involved in normal organ functions in growing children and its metabolism through cytochrome P450 with significant genetic polymorphism, necessitates evaluation of its pharmacokinetics, efficacy as well as chronic toxicity in large cohorts from all ethnic groups.
Design/Methods: Children with CML in chronic-phase on Imatinib (300 mg/m2) underwent monitoring for plasma trough levels by HPLC, efficacy, and acute as well as chronic toxicity (> 1 year of Imatinib usage) for growth, immunological, cardiac, endocrine, musculoskeletal, pulmonary, ophthalmological and auditory functions.
Results: Ninety six children were evaluated (M: F - 2.2:1; median age- 12 years & median follow-up- 55 months). Of these, 84.3% achieved complete cytogenetic response at 12months and 69% Major Molecular response at 18 months. The event free and

overall survival of group was 84.1% and 93.8% respectively.Common acute toxicities were anemia -100%, neutropenia-81.2% & thrombocytopenia 57.3%, hepatic-83.3%, and skin depigmentation in 80.2%. In chronic toxicity, 60 evaluable children had significant growth deceleration at 12 and 24 months which continued till at least 48 months of follow-up. CPK elevation (65%), hypogammaglobulinemia (8%), moderate restrictive airway dusfunction (7%) were also observed. Imatinib trough levels showed significant variability (mean±SD- 1,375ng/ml±715ng/ml, range 430ng/ml-4,980ng/ml) but were comparable to published data. Children with higher median levels(>1,000ng/ml) had better cytogenetic responses at 1 year but no excess toxicity.
Conclusion: Imatinib has similar pharmacokinetics, and good efficacy but higher acute hematological as well as non-hematological toxicity in Indian children. It causes alarming growth retardation and significant skin depigmentation and also has probable impact on immune, pulmonary and muscular system. A larger multicentric prospective study with serial longitudinal testing is required to assess its impact on all organ systems.

O-042

THE CRM1 NUCLEAR EXPORT RECEPTOR IS CRITICAL FOR THE EXPRESSION OF *HOXA* GENES AND CAN SUBSTITUTE FOR CALM IN *CALM-AF10* LEUKEMOGENESIS

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Background/Objectives: The *CALM-AF10* chromosomal translocation is associated with overexpression of *HOXA* genes, which are effectors of oncogenic transformation that are frequently upregulated in pediatric acute leukemias. We have previously shown that a nuclear export signal within CALM interacts with the CRM1 nuclear export receptor and that the CRM1/CALM-AF10 interaction is essential for leukemia development in mice. The goals of the present work are to investigate the molecular mechanisms by which CRM1 participates in *HOXA* upregulation, and to determine whether CRM1 can substitute for CALM in leukemogenic fusions.
Design/Methods: We measured *Hoxa* transcript levels in murine leukemia cells treated with the CRM1 inhibitor Leptomycin B (LMB). We created artificial retroviral *CRM1* fusion constructs and assessed their leukemogenic potential *in vitro* and *in vivo*.
Results: We found that brief LMB treatment of *CALM-AF10* leukemia cells causes a significant reduction of *Hoxa7*, *Hoxa9* and *Hoxa10* levels. In an *in vitro* murine bone marrow (BM) clonogenic assay, native CRM1 overexpression did not transform, while *CRM1-AF10* fusions resulted in immortalization. To investigate leukemogenic potential *in vivo*, we transplanted mice with retrovirally transduced BM progenitors. *CRM1-AF10* induced myeloid neoplasms with a low penetrance and long latency (7/20 mice developed leukemias between 160-350 days). These primary leukemias were transplantable, causing leukemias with a shorter latency, and leukemia blasts expressed elevated levels of *Hoxa* genes.
Conclusion: Our results demonstrate that CRM1 regulates the expression of *Hoxa* genes in murine leukemia cells, and that CRM1 fusions can drive murine leukemogenesis. Of note, a *CRM1-AF10* fusion gene was recently identified in a T-ALL patient (*BLOOD*, 2014). Novel CRM1 inhibitors are currently being tested in clinical trials. Our data also suggest that the efficacy of these inhibitors could be mediated in part by their ability to block CRM1-dependent transcriptional activation of *HOXA* genes.

Free Papers 08: Non Hodgkins Lymphoma

O-043

BURKITT LYMPHOMA : LONG TERM OUTCOME IN 738 PATIENTS TREATED WITH CYCLOPHOSPHAMIDE-BASED PROTOCOLS IN RURAL CAMEROON FROM 2003 T0 2013

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Background/Objectives: A 50% to 60% one year event free survival was previously reported with Burkitt lymphoma protocols which use 3 doses of weekly cyclophosphamide and intrathecal methotrexate as induction followed by one to three more pulses of cyclophosphamide ± vincristine and IV methotrexate for advanced or non – responsive disease. Rescue treatment for early relapses consisted of 3 weekly pulses of cyclophosphamide + vincristine and full retreatment for relapses beyond one year. Patients were all treated at Banso (BBH), Mbingo (MBH)and Mutengene (BHM) Baptist Hospitals in Cameroon. To record the incidence of early deaths, deaths during treatment, relapses and long term survival in this cohort.
Design/Methods: All patients with complete treatment records were followed - up in hospital, by telephone or home visits to ascertain outcome. The diagnosis was based on clinical presentation, fine needle aspirates, cerebrospinal fluid, bone marrow and abdominal ultrasound examinations.
Results: Median age was 8 (range 3 – 15) years. Forty two deaths (5.7%) occurred during induction, and a total of 120 (16.3%) during the total 3 to 8 week treatment period. Deaths during treatment ranged from 10% at BBH to 26% at MBH, because of lapses in standardized supportive care at MBH. One or more relapses occurred in 219 (29.7%) of all patients, with 53 (24%) long term survivors. Follow – up beyond 12 months of onset of treatment in 405 patients in remission, was achieved in 336 (83%) of patients. Overall survival was 55% after median follow – up of 3.7 yrs (range 2 months to 11.8 yrs).
Conclusion: Long term overall survival of 55% was achieved with low cost, low toxicity, high frequency cyclophosphamide based regimens. Relapses can be successfully treated with a 3 week rescue protocol or full retreatment.
Acknowledgements: BTMAT, Swiss Cancer League, WCC, our nurses.

O-044

CHILDHOOD BURKITT LYMPHOMA IN NORTH AFRICA: THE MATII STUDY OF THE FRENCH-AFRICAN PEDIATRIC ONCOLOGY GROUP (G.F.A.O.P.)

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Background/Objectives: A first prospective multicentre study was performed by GFAOP in 2001-2004 to evaluate the feasibility of modified LMB 89 chemotherapy regimens in Burkitt lymphoma (BL) in Africa. Two schemes were proposed: the MAT (Morocco-Algeria-Tunisia) and the GFA2001. North African units except Rabat used the MAT protocol and the other units the less intensive GFA 2001 protocol (without doxorubicin). Overall survival (OS) was 61% with better results with the MAT regimen (74%) (Harif, BPC, 2008).In order to improve outcome of patients with BL in North African GFAOP units, it was decided to extend the MAT protocol to the four North African units for the second study, including Rabat.
Design/Methods: All patients with BL were prospectively registered in a common database in Casablanca. They were stratified in 3 risk groups (A, B, C), and treated with polychemotherapy of progressive intensity.
Results: From 04/2005 to 05/2014, 431 patients were evaluable: sex ratio 2.5/1 Median age was 51/2 years. There were: 18 stages I (4%), 65 stages II (15%), 266 stages III (62%), 67 stages IV (19%) and 15 Burkitt leukaemia, corresponding to 13 patients in group A, 338 in group B and 80 in group C. Any grade III-IV toxicity was observed in 702/2225 courses (31%). Sixty one pts died of toxicity (14%). Fifty three patients relapsed (12%). The event free and OS were respectively 83% and 91% in group A, 71% and 74% in group B, 29% and 32% in group C. OS was 68% for all patients, but increased for stage III patients from 63% in 2005-2008 period to 80% in 2008-2014 period.
Conclusion: Except in group C, a high cure rate was achieved in BL in North Africa with the LMB-based MATII protocol. Improvement in supportive care and increased experience of healthcare teams contributed to the better outcome in the second period.

O-045

A MULTICENTER STUDY FOR TREATMENT OF CHILDREN WITH BURKITT LYMPHOMA IN SUB SAHARAN PAEDIATRIC UNITS. A STUDY OF THE "GROUPE FRANCO AFRICAIN D'ONCOLOGIE PÉDIATRIQUE" (GFAOP)

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Background/Objectives: To evaluate the results of an intense chemotherapy for the treatment of Burkitt lymphoma (BL) in sub-Saharan paediatric units (PU).
Design/Methods: Following 2 previous GFAOP protocols (Harif, PBC 2008; Traore, PBC 2011), 6 PU started in April 2009 a common protocol based on a modified LMB regimen. Treatment starts with a prephase with cyclophosphamide, followed by 2

induction COPM courses (cyclophosphamide-Vincristine-high dose (HD) Methotrexate(HDMTX)) and 2 consolidation CYM courses (cytarabine-HDMTX). HDMTX, associated with intrathecal MTX, is given at the dose of 3g/m^2. Recommendation was to initiate the following course when neutrophil count >500 in ascending phase. We focus the analysis on stage III which represent 80% of all patients. In April 2014, there were 231evaluable cases (sex ratio 2/1). Median age: 7.5 y (12 m-17.5 y). 95% pts had an abdominal tumour and 51% of them had also a facial tumour.
Results: 104 patients are alive in CR1 (94 after protocol treatment and 10 despite early treatment stop), 5 in CR2 and 14 in unknown status. 72 died: 22 (9%) from toxicity during protocol treatment and the others from lymphoma progression or toxicity of 2nd line treatment. In total, 36 (15%) were lost to FU, 8 of them in CR.Overall survival (OS) is 61% (53-68) at 12m (median FU: 9m). Among the 196 pts who achieved induction, OS was significantly better: 73% (61-83) versus 55% (42-67), (p=0.02) when the delay between treatment start and COPM2 start was < or > 34 days.
Conclusion: A prospective multicentre study for treatment of BL is feasible in sub-Saharan Africa. Dose intensity during first weeks of treatment is an important prognostic factor. Although improvements still have to be done, results are encouraging with increase of cure rate and lower percentage of patients lost to FU compared to previous studies.

O-046

CLINICAL SPECTRUM OF LYMPHOMA IN CHILDREN AND ADOLESCENTS IN CENTRAL MALAWI

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Background/Objectives: While Burkitt lymphoma (BL) is the most common pediatric lymphoma in sub-Saharan Africa, Hodgkin lymphoma (HL) and other non-Hodgkin lymphomas (NHL) occur. Diagnosing lymphomas presenting without classical jaw masses is challenging given limitations in radiology and pathology. We describe presentations and outcomes for diverse pediatric lymphomas in central Malawi.
Design/Methods: We retrospectively characterized 121 children with lymphoma from 12/2011 – 6/2013. Diagnosis was pathologically confirmed in 50 patients and clinical in the remainder. Chemotherapy regimens were: stage I/II BL, INCTR 03-06; stage III/IV BL and other NHL, CHOP; HL, ABV-PC.
Results: Median age was 8.4 years (2.1-16.8). Seventy-eight (64%) were male. Clinical sites of presentation were: abdominal mass 50%, jaw mass 35%, peripheral lymphadenopathy (LAD) 34%, cranial nerve palsy and/or lower extremity weakness (CNS+) 17%, peri-orbital mass 13%, mediastinal mass 12%, and severe cytopenias 9%. Diagnoses included: BL 64%, HL 18%, lymphoblastic lymphoma (LBL) 12%, diffuse large B-cell lymphoma (DLBCL) 5%. HL commonly presented with long-standing LAD (21/22). The majority of LBL presented with mediastinal mass (12/15). Murphy NHL stage distribution was: 27% stage I/II, 44% stage III, 29% stage IV. HIV testing was routinely performed; 4 were HIV-infected (3 BL, 1 DLBCL). Chemotherapy was completed in 65%, while 16% were lost to follow-up. At last evaluation, 31% were in complete remission (CR) after median follow-up of 18 months (range 3-31). Four children with CNS+ BL were in CR after 18-31 months. Sustained CR rates were: LBL 0% (0/15), HL 23% (5/22), DLBCL 17% (1/6), and BL 40% (31/78).
Conclusion: Stage I/II BL accounted for only 21.5% of pediatric lymphomas. The majority of lymphomas (>70%) presented with advanced stage III/IV disease, and abdominal primary sites were most common. Outcomes were poor for LBL, DLBCL, and HL. Treatment paradigms accounting for pediatric lymphoma diversity in our setting are urgently needed to improve survival.

O-047

RELAPSES OR REFRACTORY FORMS OF LYMPHOBLASTIC LYMPHOMAS IN CHILDREN: RESULTS AND ANALYSIS OF 23 PATIENTS IN THE EORTC 58951 AND LMT96 PROTOCOLS

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Background/Objectives: The treatment of children with T-cell (T-LBL) and precursor B- (pB-LBL) lymphoblastic lymphomas has improved during the last few decades. However, the patients who relapse or the refractory patients still have poor prognosis.
Design/Methods: We report the characteristics and evolution of T-LBL and pB-LBL relapses in two multicentric prospective studies, LMT 96 and EORTC 58951.
Results: From 1997 to 2008, 194 patients were included in these studies (157 T-LBL and 37 pB-LBL); and 23 patients underwent relapse or progression (18 T-LBL and 5 pB-LBL). The median age was 7.7 years [range 1.4; 16.3]. The survival rate at 8 years was 8.7% (21 deaths). The median duration from diagnosis to relapse was 9 months [range 1; 69], and 11 months [range 1; 45] for T-LBL and pB-LBL respectively. Twenty-two patients received a second line treatment (VANDA) but remission was achieved in 7 patients only. In ten patients, intensification with hematopoietic stem cell transplantation (HSCT) was performed and 4 of them had a second relapse. The two living patients had T-LBL, experienced relapses at 15 and 69 months after diagnosis, and received a HSCT as consolidation. Relapse during the intensive phase and second line treatment without HSCT were identified as risk factors for bad prognosis (p=0.01). Statistic of immuno-genetic parameters could not be obtained.
Conclusion: Results of the second line treatment, including intensive chemotherapy and HSCT, are still disappointing in controlling refractory forms. The early identification of these aggressive forms is mandatory to improve the prognosis with early intensification in first remission. Valid prognostic parameters, such as prognostic biological features are needed with multicentric international cooperation for collecting information on these rare diagnoses.

O-048

TARGETING THE PI3K/AKT/MTOR PATHWAY IMPROVES CHEMORESPONSIVENESS IN CELL LINE MODELS OF CHEMOTHERAPY SENSITIVE AND RESISTANT BURKITT LYMPHOMA

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Background/Objectives: Relapsed/refractory Burkitt lymphoma (BL) has a dismal prognosis with <20% survival, stressing the need for development of novel therapeutic approaches. Recently published data implicated PI3K in Burkitt lymphomagenesis. Chemotherapy-resistant Raji BL cell lines (Raji-2R and Raji-4RH) developed in our laboratory exhibit increased basal PI3K/Akt/mTOR pathway activation, suggesting a possible role of PI3K/Akt/mTOR in chemoresistance.
Design/Methods: The efficacy of targeting the PI3K/Akt/mTOR pathway was investigated in BL Raji, Raji-2R, Raji-4RH, Daudi and Ramos cells. Cell viability, cell cycle progression, and induction of apoptosis were evaluated following exposure to PI3K/Akt/mTOR pathway inhibitors alone and in combination with chemotherapy.
Results: *In vitro* exposure to inhibitors of PI3K (idelalisib), Akt (MK2206) or mTORc1/2 (INK128) resulted in dose- and time-dependent decreases in viability by AlamarBlu assay. BL cells were most sensitive to the mTORc1/2 inhibitor with IC50s in the low nM range. Exposed Raji cells exhibited G1 cell cycle arrest, while G2/M arrest was observed in Raji-2R and Raji-4RH cells. The combination of MK2206 and either doxorubicin or dexamethasone resulted in synergistic decreases in viability in all cell lines tested including both sensitive and resistant cells, by Chou-Talalay method. In Raji and Ramos, MK2206 and doxorubicin in combination resulted in a higher degree of PARP cleavage compared to single agents. No PARP cleavage was noted in Raji-2R and Raji-4RH cells, likely related to impaired apoptotic potential previously reported in these cells. Analysis of phosphoproteomics and gene expression profiling identified B-cell receptor (BCR) activation while miR array and qRT-PCR identified increased expression of Akt activating miR 17 as potential mechanisms of Akt activation in the chemoresistant cells.
Conclusion: Our data suggests constitutive activation of the PI3K/Akt/mTOR pathway, through activation of the BCR pathway and/or over-expression of miR17, is associated with development of resistance in BL cell lines, and inhibition of PI3K/Akt/mTOR can sensitize BL cells to chemotherapeutic agents.

Free Papers 09: New Drugs & Experimental Therapeutics

O-049

PHASE I STUDY OF CABAZITAXEL IN PEDIATRIC PATIENTS WITH RELAPSED OR REFRACTORY SOLID TUMORS: A POETIC GROUP STUDY

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Background/Objectives: *Purpose*: To determine the dose limiting toxicity (DLT) and maximum tolerated dose (MTD) of cabazitaxel in pediatric patients with relapsed or refractory solid tumors including brain tumors. *Background*: Cabazitaxel is a novel taxane with increased activity against other taxane resistant tumors in vitro; with demonstrated penetration through the blood brain barrier, making it a potential therapy for brain tumors. A phase I study was conducted through the Pediatric Oncology Experimental Therapeutics Investigators' Consortium (POETIC) to determine the MTD of cabazitaxel. This study also characterized the safety, tolerability and pharmacokinetic (PK) profile of cabazitaxel.
Design/Methods: Patients with refractory or recurrent solid tumors were enrolled in a standard 3+3 design. The DLT period encompassed the first cycle. The starting dose of cabazitaxel was 20 mg/m^2, which was 80% of the MTD in adult studies. Cabazitaxel was administered IV once every 3 weeks. PK studies were performed during the first cycle and tumor assessment every 9 weeks. Patients could remain on study drug if they had no evidence of progressive disease or unacceptable toxicity.
Results: 26 patients were enrolled at 8 POETIC institutions with 3 screen failures. 19 patients had brain tumors and 4 had solid tumors. 6 of 23 patients had stable disease or partial response for > 3 treatment cycles. Common adverse events were fatigue, diarrhea, nausea and vomiting, febrile neutropenia and hypersensitivity reactions. A total of 3 DLTs (febrile neutropenia) were reported, and after previous dose level expansion, the MTD was determined to be 30 mg/m^2. Slightly higher plasma clearance compared to adult trials was observed.
Conclusion: Cabazitaxel was generally well tolerated in this phase I study and the MTD in children is 30 mg/m^2, which is higher than the adult MTD but with a slightly higher plasma clearance of cabazitaxel. A phase II trial in brain tumors is ongoing.

O-050

ENROLLMENT IN AN EARLY PHASE CLINICAL TRIAL IN PEDIATRIC ONCOLOGY: FACTORS THAT INFLUENCE DOCTORS' PROPOSAL AND PARENTS' DECISION

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Background/Objectives: Since 2007, the Pediatric Regulation was launched in Europe to facilitate access to new medicines for children. Little research has focused on early-phase trials' availability in Pediatric Oncology and reasons for failure to enroll. In this study, we aimed to explore accessibility of early-phase trials for children in palliative phase, and to identify reasons for non-proposal to enroll, parents' refusal or failure of inclusion.
Design/Methods: We conducted a retrospective chart review at Curie Institute for all patients less than 18 years at diagnosis, whose cancer progressed despite known effective treatments between July 2010 and December 2013. Data were recorded anonymously.
Results: This study involved 100 patients (in the same period, the median number of new patients yearly cared for cancer in our Department was 249 [220-265]). Fifty-two experienced at least one early-phase trial's proposal. Despite proposal, 20 parents refused the inclusion, preferring a conventional treatment (n=5/18 reported reasons, data not available in 2 cases), or due to quality of life priority and fear of constraints (n=13/18). Fourteen inclusions failed despite parents' approval, due to rapid deterioration (n=6), non-inclusion criteria (n=6), and unavailability of the trial a posteriori (n=2). No enrollment's proposition was done for 48 patients: no early-phase trial available during the palliative phase (n=5), non-inclusion criteria (n=26), other physical factors (n=5), medical choice for a conventional treatment (n=5), trial's constraints (n=4), psychological factors (n=2), and follow-up in another hospital (n=1).
Conclusion: Availability of early-phase trials has recently increased, thanks to the Pediatric Regulation. Decision not to propose early-phase trials to children is multifactorial, in line with the complexity of palliative care. Better selection of timing to propose, opening less constraining early-phase trials, limiting waiting lists, and improving parents' and children's information may facilitate children's access to new medicines.

O-051

TARGETING ACUTE LYMPHOBLASTIC LEUKEMIA WITH TRANSGENIC MondoA-SPECIFIC ALLORESTRICTED T-CELLS

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Objectives: Oncogene addiction provides ideal targets for immunotherapy. We previously assessed MondoA (also known as MLXIP, MAX like protein X interacting protein) as a metabolic stress sensor, required for leukemogenesis (*Wernicke et al. 2012*). MondoA dimerizes with MLX within the MYC interactome, promotes longevity in C. elegans (*Johnson et al. 2014*) and regulates cancer cell metabolic reprogramming (*Carroll et al. 2015*). MondoA induces stemness, proliferation and B cell receptor signaling pathway in common ALL (cALL, *Wernicke et al. 2012*). Here we report on the role of MondoA in malignancy of cALL *in vivo* and targetability by allorestricted T cell receptor (TCR) transgenic T cells (ATRs).
Design/Methods: NALM6, 697 and Reh cALL lines were lentivirally transduced with MondoA short hairpin RNA (shRNA) and tested in our xenotransplantation model (*Richter et al. 2009*). MondoA specific T cells were generated by priming of donor HLAA0201 negative (A2-) T-cells with A2+ dendritic cells bearing MondoA peptides, multimer-based sorting and subcloning of A2-CD8+ T-cells. Specificity and functionality of T cell clones were tested by ELISpot interferon g (IFg) and granzyme B assays with leukemia lines (A2+, A2-). Transgenic ATRs were generated by infection of lymphocytes with retroviral vector system containing TCR construct.
Results: We found MondoA to be overexpressed in both ALL and AML. MondoA knock down (kd) in cALL cell lines reduced the transcript by 80%. Importantly, *in vivo* MondoA maintained 90-99% of CD10+ leukemic blasts in blood, marrow and spleen. Spleen size and weight normalized by MondoA kd. Our transgenic MondoA specific ATRs successfully recognized and killed A2+ MondoA expressing cALL cell lines. Peptide dependent and independent off target alloreactivity was low compared to reactivity against NALM-6 cALL.
Conclusion: These findings demonstrate that MondoA maintains leukemic burden and malignancy of cALL *in vivo*. Moreover, we identified MondoA as a promising target for immunotherapy of cALL.

O-052

PHASE II PROSPECTIVE, OPEN LABEL STUDY OF EVEROLIMUS IN CHILDREN AND ADOLESCENTS WITH RECURRENT OR REFRACTORY OSTEOSARCOMA, RHABDOMYOSARCOMA AND OTHER SOFT TISSUE SARCOMA

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Background/Objectives: Everolimus is an oral inhibitor of the mammalian target of rapamyn (mTOR). Inhibition of mTOR has been shown to inhibit sarcoma cells in vitro and also inhibit the growth of xenografs of rhabdomyosarcoma and osteosarcoma cell lines in vivo. Mestastic soft-tissue sarcoma and bone sarcomas are typically associates with limited therapeutic options and poor outcomes.
Design/Methods: There were enrolled 17 patients, whom 11 were osteosarcomas and 6 rhabdomyosarcoma, median age of 13 years (range of 4 - 21 years), 14 boys and three girls. Everolimus was given at 5 mg/m^2/ day until progression, which each cycle was defined as 30 days of treatment and after 2 cycles responses were evaluated. All patients were previously heavly treated with a median of three (1 to 6) chemotherapy regimens with three or four drugs.
Results: There were administered 42 cycles in which partial response was reached in two patients (one osteosarcoma and one rhabdomyosarcoma) that lasted for 5 and 11 months respectively, stable disease in other one patient for 4 months and progression in 14 patients. There were adverse events related to everolimus in five patients in which only one patient had grade 3 toxicity. Despite 14 from 17 had disease progression, everolimus therapy was well tolerated with little severe toxicity.
Conclusion: Based on these results, everolimus is safe and well tolerated and displayed some clinical activity. Further studies will be necessary to evaluate efficacy of everolimus as adjuvant therapy in a cohort of pediatric patients enrolled at diagnosis.

O-053

VINCRISTINE, IRINOTECAN AND TEMOZOLOMIDE TREATMENT FOR RECURRENT/PROGRESSIVE PEDIATRIC SOLID TUMORS

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Background/Objectives: The combination of irinotecan and temozolomide has shown activity against manyrecurrent/progressivepediatric solid tumors. We evaluated our experience with vincristine, irinotecan and temozolomide (VIT) given to children with recurrent/progressive solid tumors.
Design/Methods: We retrospectively evaluated 30 patients treated with a combination of vincristine 1.5 mg/m^2/1st day; temozolomide 150 mg/m^2 orally on days 1-5; irinotecan intravenously 50 mg/m^2 on days 1-5, every 21 days. Cefixime prophylaxis was used to reduce irinotecan associated diarrhea in all patients.
Results: A total of 123 courses of VIT were given to 30 patients (27 progressive/3 relapse) with a median of 3 courses per patient. The diagnosis were Ewing sarcoma (13), rhabdomyosarcoma (8), neuroblastom (7) and Wilms tumor (1), osteosarcoma (1). All patients received VIT at second or further relapses. Median time from diagnosis to recurrent/progressive time when VIT was initiated, was 21.8 months (5-63 months). We observed 1 complete (Ewing sarcoma-8 months +), 2 partial responses (1 neuroblastoma 4 mo.+, 1 Ewing sarcoma 4 mo.+) and 9 stable disease in our patients. Median duration of stable disease for all patients was 2 months (1-8mo.). In Ewing sarcoma patients, median duration of stable disease was 6 months (3-8mo.). Radiotherapy was used in 11 patients as local therapy. The main adverse effect of the VIT combination was diarrhea.
Conclusion: In this heavily pretreated cohort, VIT was tolerated and had some effect in recurrent/progressive solid tumors. It may have more effect if used at first relapse.

O-054

PHASE I STUDY OF NON-PEGYLATED LIPOSOMAL DOXORUBICIN IN CHILDREN WITH RECURRENT/REFRACTORY HIGH GRADE GLIOMA

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Background/Objectives: To determine the maximum tolerated dose and pharmacokinetics (PK) of non pegylated liposomal doxorubicin (Myocet®), in children with recurrent or refractory high grade gliomas.
Design/Methods: Children previously treated with surgery, radiotherapy and chemotherapy were eligible. Cohort of at least 3 patients each received escalating doses of Myocet® starting at 60 mg/m^2, administered IV over 1 hour, at 3-week intervals for a maximum of 6 courses. If no dose-limiting toxicity occurred, dosages were escalated to 75 mg/m^2 corresponding to the adult recommended dose. Periodic blood samples were collected and plasma DXR concentrations were quantified to characterize the PK.
Results: Between October 2010 and January 2013, 13 patients aged 6-17 years entered the study. Patients received 1 to 6 courses (median 2) corresponding to 60 to 360 mg/m^2 cumulative doses (median 120 mg/m^2). In total, 27 courses were administered, at the 60 mg/m^2 dosage level in 7 patients without dose-limiting toxicity (DLT), and at 75 mg/m^2 in 6 patients who experienced 2 DLT (grade 4 neutropenia). The most common grade 3 to 4 toxicities reported were neutropenia and thrombocytopenia. No cardiac toxicity occurred. No response was observed, however, 2 patients in stable disease after 4 and 6 courses and who received additional chemotherapy and surgery are alive in PR and CR at 45 and 46 months from the start of Myocet®.60% of the circulating DXR was encapsulated. Median estimates of PK values of T1/2 (h), Cl (L/h/m^2), and V_{ss} (L), were respectively: 32.9, 33.7, and 527 for free DXR; 34.8, 15, and 24.8 for total DXR.
Conclusion: The recommended dose of Myocet® administered every 3 weeks to pediatric patients was 60 mg/m^2. The efficacy of Myocet® on paediatric patients with high grade glioma remains to be determined and should be studied in paediatric Phase II trials.

Free Papers 10: Paediatric Oncology & Global Health

O-055

REFLECTIVE PRACTICE AND GLOBAL LEADERSHIP IN PEDIATRIC HEMATOLOGY/ONCOLOGY: A MODEL FOR "ON THE JOB" TRAINING

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Background/Objectives: TXCH Global HOPE operates projects in sub-Saharan Africa (SSA). Placement in leadership positions in such settings can present significant challenges beyond the scope of pre-service orientation. We adapted our evidence-based Reflective Practice & Leadership Seminar (RP&L) methods[1] to provide "on the job", ongoing leadership mentoring and training for team members in SSA. [1] Frugé, E., Mahoney, D.H., Poplack, D.G. & Horowitz, M.E. Leadership: "They Never Taught Me This in Medical School". *JPHO*, 2010, 32, No. 4, 304-308.
Design/Methods: A one-hour, bi-monthly teleconference seminar was conducted with the Botswana and Angola teams of TXCH Global HOPE. In the Global RP&L method, team members present current challenges and seasoned faculty guide the discussion through a disciplined, step-wise analysis including a "diagnosis" of the situation and a plan for strategic action – the leadership dimension of the African team member's role.
Results: Topics covered in the seminar included the challenges of bringing new staff members onto the team, negotiating care delivered by an ancillary in-country service, petitioning for resources within the context of a larger local organization, negotiating for the change of medical personnel provided through a separate institution, and negotiating change within an external institution that directly affects program function. Self-report post-seminar questionnaires indicated participants strongly agreed (5 on 1-5 scale) with the following statements: the seminar improved their ability to 1) analyze complicated clinical service situations 2) navigate inter-institutional politics, and 3) effectively build cross-service relationships to improve patient care.
Conclusion: This Global Leadership Seminar has demonstrated success in helping our SSA program teams improve leadership capacity and negotiate change effectively. This Seminar is a novel and effective strategy to mentor international medical leaders in the global setting. As our next phase, we plan to include local leaders in future seminars. Finally, this novel model has proven to be cost-effective.

O-056

CAPACITY BUILDING THROUGH TWINNING IN PAEDIATRIC ONCOLOGY: CANADA AND THE CARIBBEAN AS A MODEL FOR SUCCESS

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Background/Objectives: In 2013, the SickKids Center for Global Child Health at the Hospital for Sick Children (SickKids), Toronto, Canada launched a 5-year, not-for-profit initiative with Caribbean countries to build capacity for care of children with cancer and blood disorders. Formalized through a Memorandum of Understanding with the University of the West Indies (UWI) and with respective Ministries of Health, the SickKids-Caribbean Initiative (SCI) has partnered with in 6 Caribbean countries: The Bahamas, Barbados, Jamaica, St. Lucia, St. Vincent and the Grenadines and Trinidad and Tobago.
Design/Methods: Support from Caribbean and SickKids physician and nursing leaders in the aforementioned territories has helped facilitate formally contracted agreements with academic, hospital and government agencies in the Caribbean, and with the SickKids Division of Haematology/Oncology. Funding secured by SickKids Foundation is used to finance local SCI activities, through contracts between SickKids and Caribbean hospital administrations. Key paediatric oncology deliverables include: (1) establishing a hospital-based database; (2) conducting case consultations with additional diagnostic studies as needed; (3) enhancing diagnostic services; and (4) finalizing a nursing curriculum with UWI School of Nursing.
Results: Integral to the success of SCI, communication is maintained through a standardized network of telemedicine facilities, installed or upgraded by SCI in all participating countries. All of the above elements have been key to building the

foundation of SCI with relationships at the university, hospital and government levels, in collaboration with a strong donor-base, support from Canadian Embassies in the Caribbean and the Caribbean Diaspora in Toronto.
Conclusion: SCI has achieved its goals for the first phase of this ambitious project establishing the formal links between six countries and SickKids. This will now pave the way for the second phase of the project to assure that SCI can contribute to improving diagnosis and management of children with cancer and blood disorders in the partner Caribbean countries.

O-057

ERICC (ELECTRONIC REGISTRY IN CHILDHOOD CANCER)

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Background/Objectives: The burden of paediatric cancer is rising, but few population-based registries exist in Low & Middle Income Countries (LMIC), hence there is limited understanding of baseline statistics or the scale of the problem. Collecting data on incidence, mortality and survival is crucial for service planning, demonstrating progress and making a robust case for support to funders and local policy makers. Many treatment centres in LMIC have neither the facilities available nor sufficient capacity of trained staff to be able to plan for reliable electronic data collection.
Design/Methods: World Child Cancer (WCC) supports 8 twinning partnerships around the globe and has come to understand the need for a freely available, uncomplicated and offline electronic patient registry which can be wholly owned by local teams. Through GlaxoSmithKline's 'PULSE' skills-based volunteering programme, a member of the company's medical department with experience in data management and programming joined WCC for 6 months with the purpose of developing such a registry. A consultation period was undertaken with healthcare professionals and data collection experts on site at WCC's partner hospital in Bangladesh, and with WCC's medical trustees, to obtain advice on the essential fields required for storing paediatric oncology data. The patient registry was then designed and programmed in Microsoft Excel with Visual Basic.
Results: The system was tested at WCC's partner hospitals in Ghana, by trained and experienced local database managers. A training manual was also developed to support the use of the system. Both are available free of cost for any interested LMIC paediatric oncology centre.
Conclusion: A simple, reliable and safe database system has been created and introduced to a number of local paediatric oncology teams. Each database is owned and controlled by local teams and will permit them to log and analyse patient data systematically.

O-058

ROLE OF TRADITIONAL MEDICINE IN BURKITT LYMPHOMA DIAGNOSIS AND MANAGEMENT IN CAMEROON - NECESSITY FOR COLLABORATION

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Background/Objectives: Childhood cancers constitute an important public health concern in Cameroon. Burkitt Lymphoma (BL) is the most common childhood malignancy. There are four centres in the country where children with Burkitt lymphoma are treated, with reported cure rates between 50 and 60%. Traditional medicine is a choice of many Cameroonians for health care. The scope of knowledge and practice of traditional healers is undefined, and often entraps children with malignancies. This study looks at the diagnosis, methods and costs of treatment, and parent's attitudes in relation to traditional medicine in the setting of BL.
Design/Methods: The study involves Children diagnosed with BL in Banso Baptist Hospital and Mbingo Baptist Hospital in the Northwest region, and Baptist Hospital Mutengene in the Southwest region. A questionnaire was used to interview parents on the use of traditional medicine in their child's disease. Patients diagnosed between 2010 and 2014 were analysed.
Results: 117 parents were interviewed. 56% were male and 44% female. The modal age group was 6-10. 46.15%(54) had visited a traditional healer. Common diagnosis provided by the traditional healers include: liver problem, abscess, witch craft, poison, hernia, side pain, spleen, mushroom in the belly, toothache, mumps. Methods of management include: massage, cuts, concoctions, and incantations. The charge for these services include domestic animals, farm tools, and cash ranging from 200FCFA (0.4USD) to over 100,000FCFA (200USD). The choice of traditional medicine was based on failure of earlier attempts in a hospital, recommendation of relatives, and belief that some diseases can only be treated by traditional medicine.
Conclusion: Traditional healers are significantly involved in BL management in Cameroon. There is widespread ignorance about BL amongst traditional healers, resulting in non-referral, and thus delay in diagnosis and management. Collaboration with traditional healers could reduce late diagnosis and improve cure rates of BL.

Free Papers 11: Liver Tumours

O-059

IMPACT OF PRIMARY SURGERY IN PEDIATRIC HEPATOCELLULAR CARCINOMA

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Background/Objectives: Complete tumor resection is essential for prognosis in pediatric hepatocellular carcinoma (HCC). Aim of the following analysis was to evaluate the impact of agressive primary surgery on survival in HCC in our study and in comparison with other HCC series.
Design/Methods: From 1999 to 2008 60 pediatric patients with HCC were registered in the German Cooperative Liver Tumor Study HB99, a prospective, single arm study from the German Society of Pediatric Oncology and Hematology (GPOH). Initial complete tumor resection, if somehow feasible, was aim for all patients. Histology of tumor specimens was zentrally reviewed. After resection patients received two courses of adjuvant chemotherapy with Carboplatin and Etoposid (CARBO/VP16). In case of unresectable tumorsize neoadjuvant high dosage chemotherapy with CARBO/VP16 was supplied.
Results: Data from 43 patients could be analyzed. 5-year OS (Kaplan-Meier) was 53% (95%-CI 52.7 – 90.7) and EFS was 43% (95%-CI 40.9 – 76.6). OS was significantly influenced by younger age at diagnosis, multifocality, metastasis, PRETXT-stadium and portal vein invasion. In 25 patients (58%), mainly PRETEXT II + III-tumors, primary surgery was performed. 19/25 (76%) survived with no evidence of disease (NED), 6 died of disease. 17/18 patients with unresectable HCC received neoadjuvant chemotherapy. One patient died before any treatment was started. In 11/17 (65%) partial response to chemotherapy was observed resulting in tumor shrinkage and secondary resection. In 9/17 cases (53%) complete tumor resection was achieved. However, only 4 patients with neoadjuvant chemotherapy and secondary complete resection survived with NED. Compared to other pediatric HCC series OS and primary resection rate is superior in our study, although patients and tumor characteristics are similar except for a higher percentage of underlying liver disease in other series.
Conclusion: Primary surgery remains the cornerstone of treatment in pediatric HCC. Further prognostic factors such as underlying liver diesease should be analyzed in larger trials.

O-060

CLINICAL CHARACTERISTICS AND OUTCOME OF MULTIMODALITY TREATMENT ON HEPATOBLASTOMA IN A MULTI-CENTER PROTOCOL: A REPORT FROM THE CHINA SOCIETY OF PEDIATRIC ONCOLOGY

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Background/Objectives: Wuhan Protocol is the first national protocol in China for children with hepatoblastoma (HB). The study retrospectively analyzed the clinical outcome of those patients treated by *Wuhan protocol* and assessed the feasibility and effectiveness of this protocol, in order to provide the basis for further optimization of treatment.
Design/Methods: A total of 127 patients with HB in 11 hospitals during Jan 2006 to Dec 2013 were enrolled in this cohort. Data about demographic characteristics, clinical manifestations, PRETEXT stage, COG stage, pathology subtype, serum AFP, chemotherapy regimen, surgical options and complications were analyzed. All statistical data were evaluated by SPSS version 19.0. Survival curves were estimated according to Kaplan Meier.
Results: There were 90 boys and 37 girls, the male to female ratio was 2.4:1, and the median age at diagnosis was 16.0 (1.3-132.0) months. The 6-year overall survival (OS) rate and event-free survival (EFS) rate were (85.3±3.3)% and (72.1±4.1)% respectively. The univariate analysis of HB showed that the patients younger than three years old ($P = 0.038$), PRETEXT I/II stage ($P = 0.001$), complete surgical resection($P = 0.000$), no metastases at diagnosis ($P = 0.000$) and delayed surgery after neoadjuvant

chemotherapy ($P = 0.000$) had better prognosis. The multivariate analysis revealed that metastases at diagnosis (HR 2.804, 95%CI 1.076-7.309, $P = 0.035$) and PRETEXT IV stage (HR 2.640,95%CI 1.141-6.107,$P = 0.023$) could be regarded as independent poor prognostic factors.
Conclusion: Neoadjuvant chemotherapy could improve the complete surgical resection rate effectively. The primary results of multi-center showed that *Wuhan Protocol* is feasible and efficacious in China, but it still should be further optimized from surgery indications and based on risk-stratification chemotherapy.

O-061

LIVER TRANSPLANTATION (LT) FOR HEPATOCELLULAR CARCINOMA IN CHILDHOOD AND ADOLESCENCE: THE BRUSSELS EXPERIENCE

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Background/Objectives: Hepatoblastoma (HB) and hepatocellular carcinoma (HCC) are the most common hepatic malignancies in children. The role of LT in children with HCC is still a matter of debate. The aim of this study was to review our experience with total hepatectomy and liver transplantation as treatment for HCC in children.
Design/Methods: Medical records of patients who underwent LT for unresectable primary HCC between July 1993 and October 2014 in our pediatric program were retrospectively reviewed; follow-up ranged from 6 to 183 months.
Results: During the study period, 50 children were transplanted for a liver malignancy, including 35 HB (70%) and 11 HCC (22%). An underlying liver disease was present in 10/11 patients. On pre-transplant assessment only 3 patients were within the Milan criteria. Only 2 patients received systemic chemotherapy before LT. A living donor LT was used in 8/11 patients. The actuarial disease-free survival rates at one and five year was 90% and 79%. Two patients showed HCC recurrence (pulmonary). One patient died of recurrent HCC.
Conclusion: Liver transplantation for unresectable HCC can be curative with optimal long-term survival rate. There is no argument, either biological or based on evidence, that the selection of pediatric candidates for transplantation should be based on the same criteria as in adult patients (Milan criteria). The use of living donor LT for this indication provides an optimal timing, avoiding HCC dissemination before a cadaveric organ becomes available. The role of neo-adjuvant approaches, including trans-arterial chemo-embolization, is still unclear in pediatric HCC.

O-062

INTEGRATED EXOME ANALYSIS IN CHILDHOOD HEPATOBLASTOMA: BIOLOGICAL APPROACH FOR MOLECULAR TARGETING

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Background/Objectives: Hepatobastoma (HB) is more than 80% of childhood hepatic malignant tumors. The outcome of the HB cases mainly depends on the biological characteristics and disease staging, but the candidate genes correlated with HB progression have not been identified. Sequence capture enrichment strategies and massively parallel next generation sequencing (NGS) were used for such gene discovery.
Design/Methods: Out of approximately 400 HBL case treated according to the JPLT (Japanese Study group for Pediatric Liver Tumor)-2 protocol, 49 cases whose non-treated tumor and normal samples were available were analyzed by a method for whole-exome sequencing using the Illumina DNA-sequencing platform. In these cases, 10 had lung metastatic cases and 13 of the remaining 39 cases had vascular invasion or multifocal lesions at admission. Consequently, 14 cases had a relapse and 10 cases died of disease.
Results: Among these 49 HBL cases, mutations and deletions compared the corresponding normal sample were 67 and 887 (median 302) and 324 genes including CNNB1 exon 3 was nominated as more than 10 cases had mutations. Among them, MUC related genes including MUC4, MUC 6, and MUC12 had mutations in more than 40 cases. The pathway analysis revealed Wnt signal genes including AXIN1 and FAP genes as well as CNNB1, α-fetoprotein (AFP) production correlated genes, and some imprinting genes were frequently mutated. Among the cases with metastatic lesion and/or those derived from the consequently dead, PI3K/Akt/mTOR pathway genes showed mutation and deletion.
Conclusion: Whole-exome sequencing using NGS in hepatoblastoma revealed several candidates mutated or deleted genes for carcinogenesis such as MUC family genes, Wnt signal pathway and AFP production pathway genes. Our NGS research revealed that PI3K/Akt/mTOR inhibitors can be one of the effective molecular targeting therapies in aggressive HB.

Free Papers 12: Rare Tumours

O-063

MICRORNA SIGNATURES IN PEDIATRIC ADRENOCORTICAL TUMORS: IDENTIFICATION OF MICRORNAS AND PREDICTED PATHWAYS INVOLVED IN TUMORIGENESIS AND PROGNOSIS

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Background/Objectives: Abnormal microRNAs expression has been shown to play an important role in development and progression of different human cancer, but data in pediatric adrenocortical tumors (ACTs) are limited. The present study aimed to evaluate the microRNAs signature in samples from pediatric patients with ACTs.
Design/Methods: The global expression of microRNAs was evaluated by Human microRNA Microarray Kit (V3) (Agilent Technologies) in 37 samples of pediatric ACTs and 9 pediatric non-neoplastic adrenal cortices. *In silico* prediction of targets were made using software Ingenuity Pathway Analysis (Qiagen Company). Nine microRNA were validated by qRT-PCR using TaqMan probes and one microRNA was chosen for functional *in vitro* studies.
Results: A significant modulation of the expression was found in 294 microRNAs with a $P \leq 0.05$ (false discovery rate corrected) between ACT and pediatric non-neoplastic tissue. In the validation by qRT-PCR it was observed the up-regulation of miR-17-3p, -145-5p, -146a-5p, -150-5p, -196b-5p, -495-3p and -598-3p; and down-regulation of miR-149-3p in children with ACTs compared to non-neoplastic pediatric adrenal cortices. The miR-196b-5p e miR-149-3p also showed up regulated in patients who had relapsed and had lower event-free survival (EFS). To miR-146a-5p, higher expression was associated with significant higher EFS. After miR-196b-5p inhibition by lentiviral vector (pLV-miR-196b-Locker) in NCI-H295R ACT cell line it was observed an increased number of cells in the clonogenic assay, and increased expression of EGF receptor, but no change the doubling time and viability. *In silico* analyses showed the MAPK, Insulin, ERBB, GNRH and mTOR signaling pathways are mRNA-target to miR-196b-5p.
Conclusion: Our findings suggest a potential role of microRNAs in pediatric ACT development and prognosis, which can contribute to a better understand in the mechanisms of action of miRNAs in this tumor.

O-064

DIFFERENTIATED THYROID CARCINOMA IN CHILDHOOD AND ADOLESCENCE: INDICATIONS FOR CONSERVATIVE SURGERY. AN ITALIAN MULTICENTRIC STUDY ON 260 PATIENTS

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Background/Objectives: In the recent decades the incidence of paediatric differentiated thyroid carcinoma (DTC) increased. DTC in paediatric age is rare and has an excellent prognosis. Nevertheless, the best surgical treatment is unclear, and the debated focuses on radical vs conservative surgery. Total thyroidectomy has a lower rate of recurrence but a higher risk of complications. Our study purposes to draw-up surgical indications to guide the choice of the surgeon between conservative or radical surgery.
Design/Methods: The authors conduced an Italian multicentric retrospective analysis about paediatric patients suffering from DTC between 2000 and 2014. Medullary carcinomas have been excluded. A total of 260 patients underwent surgical treatment: conservative surgery (lobectomy associated to isthumesctomy) has been performed in low risk patients (neoplasm limited to one lobe, no extra-thyroid spread, absence of distant metastasis) with a tumour < 2cm; the other patients have been treated by radical surgery.
Results: Total thyroidectomy has been performed in 236 (90.8%) patients whereas hemithyroidectomy in 24 (9.2%) patients. Post-surgical complications occurred in 55 patients (21.2%): 37 (14.2%) transitory hypocalcaemia, 11 (4.2%) permanent hypocalcaemia, 7 (2.7%) laryngeal nerve injury with vocal cord palsy (5 ipsilateral, 2

bilateral). All post-surgical complications occurred after radical surgery. To date, after a median follow-up of 5.8 years (range 1-14 years) all patients are alive (overall survival 100%); 30 patients (11.5%) had relapse, in average after 1.7 years: 29 after radical surgery and 1 after conservative surgery (it presented lymph nodal metastasis).
Conclusion: The surgical treatment should be personalized and based on an accurate evaluation of the risk to choose the best surgical approach. Small tumours in low-risk paediatric patients should be treated by conservative surgery since it is not associated to a higher risk of recurrence and it decreases the rate of post-surgical complications, permitting a better quality of life.

O-065

EXCELLENT REMISSION RATES WITH LIMITED TOXICITY IN RELAPSED LANGERHAN CELL HISTIOCYTOSIS WITH PULSE DEXAMETHASONE AND LENALIDOMIDE IN CHILDREN

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Background/Objectives: Lenalidomide which has been licensed for use in adults with multiple myeloma and myelodysplastic syndromes is a drug with immunomodulatory potential with antiangiogenic, proapoptotic, and anti-inflammatory activities. We present a series of four children with refractory/ relapsing Langerhan Cell Histiocytosis(LCH) who have achieved durable remission with a lenalidomide based chemotherapeutic regimen with minimal toxicity.
Design/Methods: The study was conducted between June 2012 and December 2014 and the children aged between 31/2 to 51/2 years had a biopsy proven diagnosis of LCH treated with steroids and vinblastine followed by second line therapy with cytarabine and cladribine upon relapse. Consent was obtained from the families after detailed explanation of the potential side effects of lenalidomide including neuropathy and pulse dexamethasone including osteoporosis as per institutional guidelines. The regimen consisted of 6 cycles of pulse dexamethasone and lenalidomide with each cycle being 28 days. Lenalidomide was given continuously for 21 days at a dose of 15 mg / m^2 and dexamethasone at 0.8 mg/kg on days 1,8,15 and 21 of each cycle. The children were monitored carefully for potential neurological side effects, constipation, headache, myalgia and cytopenias during follow up ranging from 1 month to 18 months.
Results: All 4 children managed to complete the regimen without compliance issues as it was outpatient based and well tolerated. One child had a fracture of both bones of forearm after a trivial fall. There were no documented grade IV cytopenias. Three out of four children showed PET negative lesion and one has resolution of lesion on MRI.
Conclusion: Pulse dexamethasone and lenalidomide can be used with good efficacy and safety profile in children with refractory /relapsing disease. The pilot regimen needs to be validated with more number of patients and long term safety studies and is particularly suited for resource poor countries.

O-066

PEDIATRIC ATYPICAL CHOROID PLEXUS PAPILLOMA REDEFINED: INCREASED MITOTIC ACTIVITY IS A PROGNOSTIC MARKER ONLY IN CHILDREN OLDER THAN THREE YEARS

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Background/Objectives: Atypical choroid plexus papilloma (WHO grade II) is characterized by increased mitotic activity and a higher probability of recurrence. Anecdotal evidence suggests that some younger children harboring atypical choroid plexus papillomas experience excellent outcome. We therefore aimed to investigate the prognostic value of increased mitotic activity in pediatric choroid plexus papillomas according to age.
Design/Methods: Clinical details, neuropathological findings and follow-up data of 149 children harboring choroid plexus papillomas were retrieved from the CPT-SIOP registry. The effect of increased mitotic activity (≥2 mitoses per 10 HPF) on progression-free survival and overall survival was examined according to age group (<3 years vs. ≥3 years) using Kaplan-Meyer-Analysis.
Results: Median age at diagnosis of the 77 boys and 72 girls was 18 months. The vast majority of these pediatric choroid plexus papillomas was located supratentorially (119/149, 80%). On neuropathological examination, 73 (49%) of the choroid plexus papillomas displayed increased mitotic activity. Children harboring tumors with increased mitotic activity experienced significantly shorter progression-free survival [108 months (94-121 months) vs. 156 months (148-164 months), mean (95% confidence intervals), P=0.002]. Importantly, the prognostic role of increased mitotic activity was mainly restricted to older children (≥3 years) [67 months (40-94 months) vs. 115 months (105-126 months), P<0.001], but not significant in younger patients (P=0.10). Five year overall survival accounted for 97-100% in all groups.
Conclusion: In choroid plexus papillomas, increased mitotic activity is associated with a higher probability of recurrence. Since the prognostic role of increased mitotic activity is restricted to older children, we suggest that a diagnosis of atypical choroid plexus papilloma according to current WHO criteria should not be made in children younger than 3 years.
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O-067

IS BIOPSY A RISK FACTOR FOR WILMS TUMOUR (WT) LOCAL RECURRENCE IN THE SIOP WT 2001 TRIAL?

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Background/Objectives: The implications of biopsying WT at diagnosis are controversial. Multivariable analysis (MVA) in the UKW3 trial showed that biopsy was not significantly associated with increased risk of local relapse but was limited by the small number of events. To further address this important clinical question, we performed a similar analysis on patients registered in the SIOPWT2001 trial.
Design/Methods: 3,009 patients with unilateral WT (stages I-IV) treated by total nephrectomy after pre-operative chemotherapy were eligible with 392 relapses, including 137 local relapses. 'Local' was defined as relapse within the abdomen except for liver metastases, considered as 'distant' relapse together with other haematogenous routes. Risk factors for recurrence were analyzed by Cox proportional hazard methods.
Results: Biopsy was performed in 970/3,009 (32%) patients (64% cutting needle, 30% fine needle aspiration (FNA), 6% open biopsy). Only open biopsy required treatment as stage III. In MVA that included all factors associated with local recurrence in univariate analysis (age, high-risk histology, abdominal stage III, lymph node involvement (LNI), tumour rupture, tumour volume at diagnosis and after pre-op chemo, any biopsy-FNA of marginal significance), only high-risk histology (hazard ratio, HR=8.9); age≥2years (HR=2.2) and tumour volume after chemo (HR=1.06/100ml) remained significant. The HR for the association with [KP1] biopsy was not significant (1.31;0.76-2.25,p=0.33). In MVA of event-free survival, high-risk histology (HR=8.17), stage IV (HR=2.13), age≥2years (HR=1.6), tumour volume after chemo (HR=1.08/100ml) and LNI (HR=1.41) were significantly associated with adverse EFS, the HR for biopsy was not significant (1.24;0.91-1.71,p=0.18). In MVA of overall survival, high-risk histology (HR=11.1), age>4years (HR=1.8), stage IV (HR=3.6), abdominal stage beyond stage I (HR=2.1) and tumour volume after chemo (HR=1.1/100ml) were associated with excess hazard for death, the HR of 1.33(0.85-2.07) for biopsy was not significant (p=0.21).
Conclusion: This *posthoc* analysis did not show a significant association of biopsy with risk of local recurrence.

O-068

MINIMALLY-INVASIVE SURGERY FOR WILMS TUMOUR: HOW OFTEN WILL IT BE FEASIBLE?

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Background/Objectives: In the process of writing future protocols guidelines, the SIOP-Renal Tumour Study Group has defined criteria, which would allow to perform laparoscopic total nephrectomy (MIS) in Wilms' tumours (WT). We aimed to investigate in what proportion of renal tumours these criteria were present.

Design/Methods: Inclusion criteria: Consecutive WT referred to a single institution. All children received preoperative chemotherapy according to SIOP protocols.
Retrospective blind reviews of preoperative post-chemo CT-scans and pathology reports, to determine the prevalence of the following criteria : tumour volume, invasion of surrounding organs/main vessels, vascular thrombus, extension beyond the ipsilateral edge of the vertebral body.
Results: Among 86 consecutive tumours (79 patients), one or more criteria excluding potential feasibility of MIS were present in 60% of cases. The main reason for ruling out MIS was tumour volume (54%), invasion of renal vessels (19%), extension to surrounding organs (17%), or suspected fragility of the tumour due to preoperative retroperitoneal rupture or intra-tumoral bleeding (10%).Among 34 (40%) tumours potentially eligible for MIS, 21 also met criteria for partial nephrectomy (NSS) (either predisposed syndromic patients n=10, or new SIOP-RTSG criteria for elective NSS in unilateral WT, n=11).Analysing pathology reports of the 24 cases eligible for total nephrectomy by MIS (without SIOP mandatory indication for NSS), 25% had open incomplete microscopic resection after open nephrectomy, 25% had positive lymph nodes and 20% were high-stage histology.
Conclusion: Among a population of 86 consecutive WT, the proportion of tumours potentially amenable to MIS was 40%. After exclusion of tumours eligible for NSS, there remained a subset of 13/86 tumours (15%) with no contra-indication to laparoscopic total nephrectomy. Considering the increased risk of local relapse related to microscopic residue, this finding suggests that these cases should be centrally reviewed and discussed, and the procedures be performed in a limited number of institutions.

O-069

NEPHRON-SPARING SURGERY FOR UNILATERAL UNSCREENED WILMS TUMOUR: HOW OFTEN IS IT FEASIBLE?

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Background/Objectives: In the process of writing future protocols guidelines, the SIOP-Renal Tumour Study Group has defined criteria, which would allow to perform partial nephrectomy (NSS) in Wilms' tumours (WT). We aimed to investigate in what proportion of unscreened renal tumours these criteria were present.
Design/Methods: Inclusion criteria: Consecutive unscreened paediatric WT referred to a single institution. Predisposed syndromic children, and bilateral WT with diffuse nephroblastomatosis were excluded. All children received pre-operative chemotherapy according to SIOP protocols. Retrospective blind reviews of preoperative CT-scans were correlated with postoperative pathology reports, to determine the prevalence of the following criteria: potential for sparing healthy kidney, peripheral location, invasion of calyces, surrounding organs, main vessels, or renal sinus. In eligible cases, 3D-volume rendering analyses calculated tumour and renal parenchyma volumes, preservable parenchyma volume being expressed as percentage of contralateral healthy kidney volume.
Results: Among 75 consecutive patients, one or more criteria excluding potential feasibility of NSS were observed in 85% of cases. The main reason for ruling out NSS was central tumour location (77%), extension to surrounding organs (5.5%), or vascular thrombus (3%).NSS was deemed feasible in 11/75 children (15%), with a volume of potentially preservable parenchyma of 63% [34-113]. Histopathology review of these cases showed evidences of perilobar or intralobar nephrogenic rests in 5/11 specimens (including 2/5 in distant healthy parenchyma), microscopic incomplete resection (n=1), and high risk histology (n=2). Had NSS been performed, secondary total nephrectomy would have been recommended after pathology analysis in at least 3/11 cases.
Conclusion: Among the population of sporadic WT, the proportion of tumours potentially amenable to NSS is 15%. Considering the increased risk of local relapse, this finding suggests that these cases should be centrally reviewed and discussed, and the procedures be performed in a limited number of institutions.

O-070

THE SIOP AFRICA / PODC COLLABORATIVE WILMS TUMOUR PROJECT – BASELINE EVALUATION AND PROGRESS

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Background: The SIOP Africa PODC Collaborative Wilms tumour project comprises eight centres in Ghana, Malawi, Cameroon, Uganda and Ethiopia. The project is implementing SIOP PODC Wilms tumour and supportive care adapted treatment guidelines as a prospective clinical trial. Projected two year event free Wilms tumour survival in Malawi increased from < 30% to 46% after introducing a similar guideline. Baseline Wilms tumour outcome and causes of treatment failure in the other participating centres had not been reported. Methods: A retrospective chart review was performed of patients admitted with Wilms tumour in the three years (2011-2013) preceding the collaborative trial. Patient outcome at the end of treatment was documented for all patients diagnosed in 2011 and 2012. Enrolment to the prospective trial started January 2014.
Results: In the baseline evaluation the mean disease free survival at end of treatment was 39% (69/176) ranging from 11% to 61% between participating centres. Overall two year survival is estimated at 25%. Incomplete treatment (31%) is the most common cause of treatment failure, ranging from 14% to 48%. Twenty six percent of patients died during treatment, ranging from 13% to 37%. In the prospective trial so far 97 children have been included, data of 63 patients have been entered into the central database. Of these 63, 5 patients were misdiagnosed and are excluded. Of the remaining 58 patients with a Wilms tumour 7 (12%) did not complete treatment, 8 (14%) died during treatment, 4 (7%) had progression and / or relapse of disease and 39 (67%) are alive and well, either on or after treatment.
Conclusion: Sharing similar local challenges in this regional collaborative project helps to identify and implement feasible, sustainable and successful strategies. We are working towards our aim to increase survival to 50% with <10% incomplete treatment and <10% treatment related deaths.

O-071

RESULTS OF THE SECOND WILMS TUMOUR STUDY OF THE "FRANCO AFRICAIN ONCOLOGIE PEDIATRIQUE GROUPE" (GFAOP) IN SUB-SAHARAN AFRICA

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Background/Objectives: Following the first Nephroblastoma feasibility study of GFAOP (Moreira PBC 2011), this second trial was run from 2005-2011 in 8 centers in sub-Saharan Africa. The objectives were to evaluate the progress in existing centers and assess the capacity of the new centers to follow the protocol, and observe its effect on the overall survival.
Design/Methods: The study was conducted in 8 centers, 5 of which were new. This prospective single arm study registered all children suspected of having renal tumor, but included in the trial only patients whose diagnosis of standard risk nephroblastoma was assessed. The protocol is identical to the initial GFAOPNEPHRO 01 study, based on the SIOP2001 protocol. Data was collected locally and sent for analyses to Gustave Roussy.
Results: Three hundred and thirteen children were registered, 55 of whom did not fulfill study criteria, 89 were excluded secondarily (31 preoperative deaths, 21 unfavorable histology, 18 abandoned treatment, 11 not Wilms, 08 poor response to initial treatment) leaving a trial study group of 169 (158 localized and 11 metastatic). During the preoperative period 167 (99%) were treated according to protocol. Histological staging is known for 105 children and surgical staging for 153. Histological review was carried out in only 7% of cases. Post-operative treatment was carried out for 146 (86%). None of the 68 patients with stage III (60 localized, 8 metastatic) were irradiated due to absence of radiotherapy. The 3 year post-surgery overall survival is 73% and EFS 55%.
Conclusion: Clearly there remains work for our group and caution must be observed because of the number of deaths in the preoperative phase and the small number of histologically reviewed cases. However our results are encouraging given that no dedicated protocol existed for the treatment of nephroblastoma in 5 of the 8 participating centers prior to this study.

O-072

LONG-TERM FOLLOW-UP OF SOLITARY FUNCTIONING KIDNEY (SFK) IN WILMS TUMOR SURVIVORS

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Background/Objectives: Children with unilateral Wilms tumor (WT) treated with chemotherapy and/or radiotherapy and nephrectomy have excellent survival rates. A solitary functioning kidney (SFK) is associated with renal injury at late follow-up. This study aims to investigate the additional effect of Wilms tumor treatment on renal function compared to children with a SFK for non-oncological reasons.
Design/Methods: A single center retrospective cohort study on renal injury markers of 79 survivors of unilateral WT was performed and compared to a matched group of children with a SFK for non-oncological reasons. Mean age at follow-up was 12.4 years, mean follow-up duration was 9.1 years.
Results: During follow-up, mean estimated glomerular filtration rate (eGFR) and blood pressure z-scores remained stable at an acceptable level. However, in the group of 31 WT patients with a follow-up of 15 years, 23% showed signs of renal injury, defined as high blood pressure, proteinuria, drug use to treat either condition, and/or an eGFR <60 ml*min^{-1}*1.73m^{-2}. This proportion of renal injury was significantly less ($p=0.004$) then the 54% in a group of SFK patients based on non-oncological causes.
Conclusion: Renal injury in survivors of WT occurs comparable to children with SFK for non-oncological reasons but with a lower overall incidence after long-term follow-up. This may be due to absence of information on proteinuria. As with patients with a non-oncological SFK, long-term follow-up is essential to monitor, inform and deliver adequate treatment for survivors of WT.

Free Papers 14: Nollenburg Prize Session Bone Tumours

O-073

THE GENOMIC LANDSCAPE IN OSTEOSARCOMA

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Background/Objectives: Osteosarcoma recurrences come up to 40% in a 5-year period. An explanation of this dismal figure may be that different etiologies are responsible for the underlying chromosomal breakage resulting in mutations in many genes. To develop future targeted treatment strategies it is crucial to have a clear understanding of the molecular complexity of this tumor. Understanding of mutation ordering poses another challenge that has now become possible to tackle using deep next-generation sequencing and machine learning models.
Design/Methods: We used exome sequencing to explore the fine-scale clonal structure and hierarchy of osteosarcoma from 25 patients. We aimed to identify genetic causes underlying chromosomal instability that drives the onset of the disease, explore whether linear or branching models better explain osteosarcoma evolution and single out rare clones with potential roles in therapy resistance and disease recurrence. We analyzed the clonal diversity by building an evolutionary history of each tumor on a fine scale with phylogenetic and advanced statistical models.
Results: We confirmed previous findings of TP53 and RB1 as the main cancer drivers together with RET, MUTYH, NUMA1 and FANCA as novel drivers. The mutations in these genes occur in both somatic as well as in germ-line settings with predicted effects on the stability of proteins that carry out DNA repair and control cell cycle checkpoints. The TP53/FANC-driven susceptibility for DNA damage in osteosarcoma is amplified by parallel evolution of cancer clones carrying mutations in genes which maintain chromosomal segregation and recombination repair (e.g. BRCA1, BRCA2, PALB2, ATM), mismatch repair (MLH1, MSH2), single and double-strand DNA break repair (XRCC1, RAD50), and telomere integrity maintenance (TERT).
Conclusion: The project provides an insight into the complexity of osteosarcoma with the specific aim to model its clonal composition. This knowledge will assist to introduce more individualized treatment approaches in this heterogeneous tumors.

O-074

FUNCTIONAL OUTCOME AND DAILY-LIFE ACTIVITY IN 603 LONG-TERM SURVIVORS OF EWING SARCOMA

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Background/Objectives: Since 1980 patients with Ewing sarcoma have been treated according to consecutive protocols of the German Society of Pediatric Oncology and Hematology (GPOH). Rising survival rates have raised the question of the quality of long-term survivorship. Objective and subjective measurement tools are used to evaluate the actual health status and daily-life activity level as an indicator for restitution of function.
Design/Methods: Long-term outcome of 603 survivors of the CESS81, CESS86, EICESS92, and EURO-E.W.I.N.G.99 trials, diagnosed between 1980 and 2009, was assessed by the Toronto Extremity Salvage Score (TESS), Short-Form Health Survey (SF-36), and Brief Symptom Inventory (BSI) questionnaire scales, and by the StepWatch Activity Monitor (SAM) accelerometer device. A 1:2 non-random peer control group was selected to compare results with healthy individuals. Median age of former patients was 28.7 years, 56% were males. Median observation time was 12.9 years (range 3.7-31.2).
Results: Former patients were less active than the control group, contributing to a mean step count difference of 1,758 steps per day (10,394 vs. 12,152; $p<0.01$), but have reached the recommended level for an active life-style ($>10,000$). Negative prognostic factors were pelvic tumors (9,265; $p<0.01$) and primary metastatic disease (9,322; $p<0.05$). Correlations between self-reported scales and the step measurement were rather low ($r<0.30$). The TESS score (>90), BSI somatization, anxiety and depression scales (raw values <0.50), and the SF-36 (Physical/Mental Component Summary scores=47.9/49.7) showed no major clinical or functional limitations. Around 15% of former patients rated their health status as less good or poor compared to 2% of the controls.
Conclusion: The present study comprised a follow-up period of up to 30 years after the treatment of Ewing sarcoma. Former patients seemed to return to a normal lifestyle with minor limitations. The generally positive outcome is an encouraging finding for patients with this severe disease.
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O-075

ASSOCIATION OF PHARMACOGENETIC VARIANTS WITH EFFICACY AND TOXICITY IN PATIENTS WITH OSTEOSARCOMA

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Background/Objectives: Pharmacogenetics can be used to optimize treatment of patients with osteosarcoma. We have previously identified genetic markers predictive of treatment outcome in genes of cisplatin and doxorubicin metabolic pathways. However, the complex metabolism of the drugs used in osteosarcoma treatment involves a broader range of drug metabolic enzymes and transporters. Therefore we have performed large scale screening of 1,936 genetic variants in 231 genes involved in drug metabolism and transport.
Design/Methods: Germline DNA of 2 cohorts (n=139 and n=177) of patients with osteosarcoma treated with cisplatin and doxorubicin-based chemotherapy was genotyped using the DMET Plus array. Associations between genetic variants and ototoxicity (SIOP grade 1-4) and 5-year Disease Free Survival (DFS) were assessed using logistic regression models and Cox proportional hazards models respectively. Additionally, patients with refractory/progressive disease (primary tumor growth/growth or development of new metastases, up to 3 months post chemotherapy) were compared to control patients (without refractory/progressive disease or recurrence) using logistic regression models, as were patients with recurrent disease (local or distant relapse). As the number of patients available for this analysis was limited, we analyzed the data as 1 cohort.
Results: After standard quality control, 669 markers and 310 patients remained for analysis. Upon meta-analysis, 16 markers were significantly associated ($P < 0.05$) with ototoxicity and 23 variants showed association with 5-year DFS. Furthermore, of 280 eligible patients, 36 experienced progression and 76 recurrence. Twenty-five genetic markers were significantly associated ($P < 0.05$) with refractory/progressive disease. Of these, 18 genetic variants in 13 genes were uniquely associated with refractory/progressive disease and not with recurrent disease or DFS in this cohort.
Conclusion: We have detected significant associations of treatment response and ototoxicity with genes previously unknown to be related to cisplatin and doxorubicin metabolism and transport. Upon validation, these markers are of potential interest for optimizing current therapy for patients with osteosarcoma.

O-076

EWING SARCOMAS EXPRESS IMMUNE-INHIBITORY HLA-G IN THEIR TUMOR MICROENVIRONMENT

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Background/Objectives: Novel therapies are needed to cure disseminated, relapsed or refractory Ewing sarcoma (EwS). Identification of mechanisms by which EwS cells manipulate the immune system may allow to develop strategies that reverse tumor-induced immunosuppression and sensitize tumor cells to lysis by preexisting or therapeutic effector cells. We hypothesized that the non-classical, immune-inhibitory molecule HLA-G may contribute to immune escape of EwS.
Design/Methods: We used flow cytometry to detect HLA-G expression in EwS cell lines, and ELISA to quantify soluble HLA-G isoforms in cell culture supernatants and in serum. To study HLA-G expression within their tumor microenvironment, we analyzed paraffin-embedded pretherapeutic tumor biopsies from 35 EwS patients by immunohistochemistry. For functional experiments addressing the immune-inhibitory properties of HLA-G in EwS, we expressed HLA-G1 in two EwS cell lines by retroviral gene transfer.
Results: Membrane-bound HLA-G1 was not identified in any of 14 EwS cell lines even after interferon-γ stimulation, but one of the cell lines (TC-32) responded to cytokine stimulation by significant upregulation of soluble HLA-G1 and G5 (p=0.004). In 19 EwS patients, serum HLA-G was not increased compared to 15 healthy controls. Moreover, no significant differences in the proportions of naturally occurring HLA-G+ CD4+ or CD8+ suppressor T cells among peripheral blood lymphocytes were found. HLA-G expression was detected in 12 of 35 EwS biopsies (34%), either on the tumor cells (10/35) and/or on infiltrating lymphocytes (7/35). Coincubation of gene-modified, HLA-G-expressing EwS cells with freshly isolated allogeneic NK-cells resulted in suppression of EwS cell lysis in 3 of 6 NK cell donors in a flow cytometry based cytotoxicity assay.
Conclusion: We conclude that local expression of HLA-G within the tumor microenvironment in EwS is a candidate mediator of immune escape and a potential barrier to cellular immunotherapeutics. Strategies that modulate HLA-G expression may be effective to overcome local immune suppression in this cancer.

O-077

TUMOR DIVERSITY: A CHALLENGE OF GENOMIC CANCER THERAPY

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Genomics engendered the promise of targeted therapies. So far, targeted therapies have failed in childhood cancer. They rather prime for resistance. An exception may be the targeting of oncogene addiction. The promise of targeted therapies was provoked by the cancer stem cell model. This model may not represent intratumoral diversity. Pediatric cancer display genomic and particularly, epigenomic plasticity, when under selective pressure, yielding subclones that are non-dominant at one point in time and dominant at another. Employing longitudinal biopsies we observed activation of oncogenic pathways during individualized expression-based targeted therapy in advanced Ewing Sarcoma (ES). Simultaneous targeting of both the EWS/FLI1 dependent catalytic subunit polycomb repressor complex 2 enhancer of zeste homologue 2 (EZH2) as well as reactive oxygen species (ROS) independent pathways yielded loss of EWS/FLI1 target genes expression and up regulation of ROS signaling. Cytotoxic drugs can have specific effects on oncogene signaling. Increase of sensitivity due to repression of oncogene down stream targets widens the therapeutic index; i.e. the sensitivity of the tumor as compared to normal cells. In ES, trabectedin interferes with EWS-FLI1 driven expression of the Werner (WRN) protein in ES cells (Grohar 2014). Since WRN-deficient cells are known to be hypersensitive to irinotecan, we have performed a pilot trial using trabectedin to block EWS-FLI1 activity, and selectively sensitizing ES cells to the DNA damaging effects of irinotecan (Herzog 2015). This molecular precision chemotherapy is capable of controlling, with persistent quality of life, about half of the cases of advanced pediatric sarcomas refractory to any established therapy. The contribution of molecular precision therapy vs. more general cytotoxic effects remains to be elucidated.
In Conclusion: Intratumoral diversity may require strategies of molecular precision chemotherapy with synergistic effects and some collateral damage. Such oncogene addiction directed precision chemotherapy can overcome resistance to selective targeted therapies.

O-078

PHASE II TRIAL DESIGNS IN OSTEOSARCOMA RELAPSES: REVIEW OF PAST EXPERIENCE

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Background/Objectives: Optimal Phase-II design to evaluate new therapies in osteosarcoma is not defined yet. Our objective is to study the consistency between protocols evaluating new anticancer treatments in osteosarcoma in terms of eligibility criteria, response assessment, endpoints, statistical design and reported results.
Design/Methods: Systematic review of clinical trials registered on clinicaltrials.gov, eudrapharm.eu, and French National Cancer Institute website, or referenced in PubMed or ASCO website, between 2003 and 2014. Relevant trials were identified using the following criteria: (osteosarcoma OR bone sarcoma OR sarcoma) AND (phase II) AND (relapsed OR recurrence OR metastatic).
Results: 54 trials were identified, described as Phase-II (n=45), I/II (n=8) and II/III (n=1) evaluating mostly chemotherapy (n=24) and/or targeted therapies (n=21). Results were published for 22 and partially published (abstract) for 4 trials. Sixteen trials included osteosarcoma only. Eligibility criteria greatly varied in terms of disease presentation. Inclusion ages were either children only (n=1), children to adults (n=24), adolescents to adults (n=16) and adults only (n=13). Overall, 34 trials were run in a multicentre setting, including 7 international trials. Only 8 trials were randomised, including 2 with a cross-over at progression. Primary endpoint was tumour response in 34 trials, either response rate at a given timepoint (n=15) or best response (n=19), with various definitions of "success" (complete+partial+/-minor response and stable disease), mainly evaluated with RECIST criteria (n=25). Main endpoint was Progression-Free Survival in 17 trials and Overall Survival in 3, evaluated at various timepoints. In single-arm trials evaluating response rate, the null hypothesis that was tested (when available, n=11) varied from 5% to 25%. In single-arm osteosarcoma trials, the sample size varied from 15 to 50. Reporting has also greatly varied across trials.
Conclusion: No stable historical data can be derived from past efficacy Phase-II trials in osteosarcoma relapses. This pleads in favour of trans-age randomised Phase-II trials.

Free Papers 15: Pharmacology & Clinical Trials Methodology

O-079

THERAPEUTIC DRUG MONITORING APPROACHES TO THE TREATMENT OF PRETERM AND FULL-TERM NEONATES WITH CANCER - A UK EXPERIENCE

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Background/Objectives: Defining chemotherapy dosing regimens for the treatment of neonates with cancer is particularly challenging and commonly not standardized based on any scientific rationale. The Newcastle Cancer Centre Pharmacology Group (NCCPG) provide a national therapeutic drug monitoring (TDM) service to optimize treatment in challenging patient populations. As an example of the potential benefits of this approach, we report on the use of carboplatin TDM in preterm and full-term neonates within the first month of life and use the data generated to provide guidance for future treatment.
Design/Methods: Carboplatin TDM was performed to achieve target drug exposures (AUC values) in nine preterm and full-term neonates diagnosed with retinoblastoma or neuroblastoma. Carboplatin was administered over 3 days of treatment with TDM utilized to target AUC values of 5.2-7.8 mg/ml.min.
Results: AUC values achieved following TDM were within 15% of target values in all but one patient (12/13 treatment courses), with dose modifications up to 215% required to achieve target AUC values, based on initial mg/kg dosing schedules. Carboplatin clearance determined across three consecutive courses of chemotherapy in two patients increased from 3.4-7.1ml/min and 7.2-16.5ml/min, representing >2-fold increases over several weeks of treatment. Complete remission was observed in 8/9 patients, with no renal toxicity reported and only one patient experiencing ototoxicity.
Conclusion: The study highlights the benefits of utilising TDM to achieve cumulative target carboplatin AUC values in preterm and full-term neonates, particularly in view of marked increases in drug clearance observed during the first weeks of life. Reducing the likelihood of sensorineural hearing loss may be particularly important in terms of quality of life in the case of neonates with retinoblastoma, who may also have some degree of visual impairment. This treatment approach may be beneficial for a range of chemotherapeutics, with a view to optimising the balance between clinical response and toxicity.

O-080

GLOBAL PHARMACOGENOMIC DIVERSITY AND ITS IMPLICATIONS FOR CHILDHOOD CANCER TREATMENT

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Background/Objectives: Inter-individual differences in response to medications are known to have a strong genetic component. Pharmacogenomics involves the study of this genetic contribution and aims to improve drug safety and efficacy by predicting optimal treatment regimes on an individual basis. Research has identified several genes that influence response to anticancer agents relevant to the management of paediatric patients with cancer. By leveraging publically available genomic data, the spectrum of genetic variation in such genes can be extensively investigated and can be used to inform the clinical implementation of pharmacogenomic tests.
Design/Methods: Genes included in this study were selected based on relevance to pharmacogenomics and paediatric oncology. Variants in these regions of interest were extracted from the 1000 Genomes Project sequencing data for 2504 samples from 26 global populations. Variants were subsequently annotated using the Ensembl Variant Effect Predictor and analysed in further detail utilising the program, VCFtools and the software environment, R.
Results: A total of 12050 genetic variants were identified in the 62 genes that met inclusion criteria. Pharmacogenomic variation tended to be most similar within continental populations and all samples carried a median of five clinical variants with a high level of scientific evidence. Genetic variants that would severely impair protein function were found in genes associated with adverse drug reactions encountered in paediatric oncology settings, including vincristine-induced peripheral neuropathy, methotrexate-induced mucositis and cisplatin-induced ototoxicity.
Conclusion: The results of the current study have the potential to inform future pharmacogenomic studies and ultimately improve cancer management in paediatric patients. For example, the current data can be incorporated into research conducted by the Canadian Pharmacogenomics Network for Drug Safety, which is conducting several genomic studies of adverse drug reactions in paediatric patients with cancer.

O-081

GENOME-WIDE ASSOCIATION STUDY OF L-ASPARAGINASE-INDUCED PANCREATITIS IN PAEDIATRIC PATIENTS

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Background/Objectives: L-asparaginase is highly effective in the treatment of paediatric acute lymphoblastic leukemia. Unfortunately, this treatment is accompanied with debilitating adverse drug reactions, such as pancreatitis. This severe adverse drug reaction impacts on the quality of life of paediatric patients and is a frequent cause of treatment discontinuation. As treatment dose and formulation have not been able to explain the inter-individual differences that are observed, it seems likely that genetic factors may play an important role in the development of pancreatitis. Therefore, this study aims to identify the genetic variants associated with L-asparaginase-induced pancreatitis.
Design/Methods: A total of 123 patients who have been treated with L-asparaginase were recruited from 13 oncology units across Canada. Extensive demographic and clinical data have been collected for all patients and genotyping of 740,000 genetic variants spread throughout the entire genome has been performed using the Illumina HumanOmniExpress array. Statistical analyses were performed using the Golden Helix SNP and Variation Suite v8 and packages from the programming environment, R.
Results: Investigation of the clinical variables revealed that factors such as gender, treatment dose and formulation were not significantly associated with the development of L-asparaginase-induced panceatitis ($P < 0.05$). Initial genome-wide association analyses did, however, identify nine regions in the genome that are nominally associated with L-asparaginase-induced pancreatitis ($P < 1\times10^{-5}$), including one non-synonymous variant that was predicted to exert a deleterious effect on the gene in which it occurred.
Conclusion: This study has identified a subset of genetic variants that may be involved with the development of L-asparaginase-induced pancreatitis. If these results can be replicated, these data can ultimately be used to design and implement a predictive pharmacogenetic test, which will allow for the tailoring of treatments in order to prevent the occurrence of pancreatitis.

O-082

NOVEL CLINICAL TRIAL DESIGNS IN PAEDIATRIC CANCER: PROBABILITY-BASED INTERPRETATION

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Background/Objectives: It is often considered impossible to undertake randomised controlled trials (RCTs) in children's cancers because of their rarity. This is because, using a conventional approach to sample size calculation (e.g. alpha=5%, power=80%), the numbers needed are not considered feasible. This leads to new therapies being evaluated via single arm studies, which may be biased for many reasons. In order to obtain more reliable evidence on the efficacy of treatments, reconsideration of the conventional approach is needed and novel RCT designs should be implemented.
Design/Methods: Probability-based interpretation involves plotting Bayesian posterior probability distributions, using non-informative priors and observed data. Based on this distribution, the probabilities that one treatment is better than the other, or better by specified amounts, can be calculated. This information can then be taken in conjunction with other relevant data (e.g. toxicity) to come to a clinical judgement as to which arm is better. In the case of two treatment comparisons, the level of evidence needed to conclude that one treatment is preferable may be lower; e.g. in absence of substantial toxicity differences, a probability of 75% that survival is better with one regimen may be sufficient to select that treatment. In the context of rare diseases, a 90% (or lower) chance that adding a new treatment is better may be adequate (cf. 97.5% with conventional two-sided p=0.05).
Results: Probability-based interpretation will be used in several current and planned trials, covering a range of disease areas and treatment stages. Examples of trials include: frontline (EE2012) and relapsed (rEECur) Ewing sarcoma, comparing the standard European and US chemotherapies, and four widely used chemotherapy regimens respectively; relapsed neuroblastoma (BEACON); acute myeloid leukaemia (MyeChild).
Conclusion: The use of probability-based interpretation in RCTs, based on clinically acceptable levels of certainty, will produce unbiased evidence on the comparative efficacy of treatments.

O-083

BIOMEDE TRIAL: A RANDOMISED TRIAL FROM THE INNOVATIVE THERAPIES FOR CHILDREN WITH CANCER (ITCC) CONSORTIUM TO EVALUATE NEW DRUGS IN DIFFUSE INTRINSIC PONTINE GLIOMA (DIPG)

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Background/Objectives: Treatment of children with DIPG remains challenging. Besides radiotherapy, no validated treatment exists, and most children die within two years of diagnosis. Survival rate has not improved over the last three decades despite many clinical trials. More efficient strategies in pediatric oncology new drug development are needed, considering the multiple hurdles that include disease rarity and limited knowledge about tumour biology.
Design/Methods: Following a biopsy-based translational research program, 3 drugs were selected for clinical evaluation: erlotinib, everolimus and dasatinib. EGFR overexpression (~50%) may be predictive of erlotinib efficacy and PTEN-loss (~90%) predictive of everolimus efficacy. We designed a "targeted-driven" randomised trial where dasatinib is compared to erlotinib and/or everolimus according to biomarker profile defined on immunohistochemical analysis of the tumour. The main efficacy endpoint is overall survival.
Results: This innovative academic trial will recruit 250 patients over 4 years in an international setting. Drugs are provided by 3 pharmaceutical companies. A stereotactic biopsy will be performed at diagnosis to define biomarker profile. The 3 treatments will be allocated by randomisation, stratified by biomarker profile, excluding erlotinib if EGFR-negative and everolimus if no PTEN-loss. The analysis will include pairwise comparisons (erlotinib-versus-dasatinib, everolimus-versus-dasatinib, and erlotinib-versus-everolimus, between randomised subsets, with an expected number of 100, 185 and 90 patients for each of these comparisons) and comparison to historical control.This trial is the first stage of a larger rolling evaluation program in DIPG,

allowing for the evaluation of new drugs that would later become available for testing.The initial biopsy and its associated translational research program will also provide genetic information that may be used for further treatment, and will contribute to increase the knowledge on this disease.
Conclusion: This innovative approach of personalised medicine with randomised comparisons should provide useful information on the effect of new drugs in DIPG.

O-084

INVESTIGATING THE HETEROGENEITY OF ALKYLATING AGENTS' EFFICACY AND TOXICITY BETWEEN GENDERS: A META-ANALYSIS OF RANDOMIZED TRIALS COMPARING CYCLOPHOSPHAMIDE AND IFOSFAMIDE (MAIAGE STUDY)

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Background/Objectives: A marginal interaction between gender and type of alkylating agent (cyclophosphamide or ifosfamide) on event-free survival was observed in the randomized controlled trial (RCT) Euro-EWING99-R1 for Ewing sarcoma. To better judge of the reliability of this interaction on efficacy and to investigate this interaction on toxicity, we performed a meta-analysis of RCTs assessing cyclophosphamide *vs*. ifosfamide.
Design/Methods: A systematic review and meta-analysis on individual patient data for any type of cancer were performed. The endpoints were progression-free survival (PFS), overall survival (OS) and maximum grade of acute toxicity. The hazard-ratios (HR) and odds-ratios (OR) [95% confidence interval] of the treatment-by-gender interactions were assessed using multivariable regression models stratified on trial and gender. Heterogeneity of interaction between trials was evaluated using a 3-order interaction term.
Results: Meta-analysis included 1,528 patients from three RCTs, in pediatric and young adult sarcomas: Euro-EWING99-R1 (n=856), EICESS92 (n=155) and IRS-IV (n=517).
With a median follow-up of 6.8 years, 424 failures and 325 deaths, a marginal (p=0.065) overall difference for PFS was observed between the four groups defined by treatment arm and gender. Multivariable analysis tended to identify poorer PFS in males treated with cyclophosphamide *vs*. ifosfamide (HR=1.26 [0.99;1.61] p=0.06), whereas PFS was not significantly different in females receiving cyclophosphamide *vs*. ifosfamide (HR=0.96 [0.70;1.31] p=0.80). However, the treatment-by-gender interaction was not significant (HR=1.31 [0.89;1.95] p=0.17) without heterogeneity between trials (p=0.36). Similar results were observed with OS. Concerning acute toxicity (leuco-neutropenia, infection and renal toxicity), the treatment-by-gender interactions were not significant (OR=0.82 [0.49;1.37] p=0.45, 1.11 [0.72;1.71] p=0.64, 1.70 [0.76;3.83] p=0.20) without heterogeneity between trials. Significantly more severe leuco-neutropenia and infections were observed with cyclophosphamide (OR=1.47 [1.14; 1.88] p=0.003, 1.55 [1.25; 1.93] p< 0.0001) and in females (OR=0.72 [0.56; 0.93] p= 0.013, 0.80 [0.64; 0.99] p= 0.041).
Conclusion: The meta-analysis could not confirm the hypothesis of treatment-by-gender interactions on efficacy or toxicity outcomes.

Free Papers 16: Supportive Care

O-085

RESULTS OF A CCLG RANDOMISED CONTROLLED TRIAL COMPARING BOLUS INJECTION WITH INFUSED AND/OR LINE-LOCKED TEICOPLANIN IN THE TREATMENT OF COAGULASE-NEGATIVE STAPHYLOCOCCAL SEPTICAEMIA

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Background/Objectives: Coagulase-negative staphylococci (CoNS) are the most common cause of septicaemia in children treated for cancer. Teicoplanin is the UK's first line antibiotic in the treatment of Gram positive organisms. After two 12 hour loading doses, it is given on a daily basis, generally by bolus injection. Concern exists, however, that teicoplanin when given by bolus injection, may be limited in sterilising contaminated central venous catheters (CVCs), with biofilm-forming organisms such as CoNS. CCLG SC 1999 01 was a multi-centre RCT that examined the method of administration of teicoplanin in CoNS bacteraemia.
Design/Methods: Following CVC insertion, children (<18y) were randomised to receive teicoplanin by either bolus injection (BI) or a 2 hour infusion and/or line locks (PE-prolonged exposure). For dual lumen CVCs, teicoplanin was given via each lumen on alternate days. Patients received teicoplanin by the randomised route in the subsequent management of suspected CVC-associated CoNS infection. Re-randomisation was performed for each CVC inserted.
Results: 992 CVCs were randomised from 832 patients; 465 - BI and 457 - PE. One hundred and thirty four CVCs became infected (infection rate 16.1%). The success or failure of antibiotic therapy was predefined and recorded. The overall success rate was 107/134 (79.9%) – BI: 51/69 (73.9%), PE 56/65 (86.2%). The success rate for single lumen CVCs was not significantly different between the two arms (p = 0.323). There was, however, a significantly superior success rate for dual lumen CVCs treated with PE teicoplanin: 28/41 (68.3%) for BI against 42/45 (93.3%) for PE (p = 0.003).
Conclusion: This RCT showed a benefit for teicoplanin given by infusion or line-lock in children with dual lumen CVCs treated for CoNS bacteraemia. This may reflect a sub-optimal drug exposure as a result of the alternate day approach to teicoplanin administration when given by bolus injection in children and young people with dual lumen CVCs.

O-086

A MULTI-CYCLE PHASE III STUDY EVALUATING PALONOSETRON VERSUS ONDANSETRON AT PREVENTING CHEMOTHERAPY-INDUCED NAUSEA AND VOMITING IN PEDIATRIC PATIENTS RECEIVING MODERATELY/HIGHLY EMETOGENIC CHEMOTHERAPY

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Background/Objectives: To demonstrate that palonosetron is non-inferior to ondansetron at preventing chemotherapy-induced nausea and vomiting (CINV) in pediatric patients receiving up to four moderately/highly emetogenic chemotherapy (MEC/HEC) cycles.
Design/Methods: Palonosetron doses (10, 20 μg/kg) were evaluated versus ondansetron (3×150 μg/kg). Statistics were used to demonstrate non-inferiority (δ=-15%) for complete response (CR, no emesis/rescue) rates during the acute phase of cycle 1. CR rates during delayed and overall phases, and safety, were assessed.
Results: In 493 patients aged 2.1 months–16.9 years, CR rates (%) in the acute phase (cycle 1) were 59.4, 54.2 and 58.6 in the palonosetron 20 μg/kg, 10 μg/kg and ondansetron groups, with non-inferiority demonstrated for palonosetron 20 μg/kg (97.5% CI [ΔCR] -11.7–12.4; p=0.0022). CR rates (acute phase, cycles 2–4) were 65.6, 81.4 and 64.5 in the palonosetron 20 μg/kg group, 66.7, 44.2 and 47.4 in the 10 μg/kg group, and 59.3, 63.6 and 52.6 in the ondansetron group. CR rates (cycles 1–4) were: in the delayed phase, 38.8, 38.9, 42.4 and 32.3 in the palonosetron 20 μg/kg group, 28.9, 35.8, 30.2 and 31.6 in the 10 μg/kg group, and 28.4, 32.6, 27.3 and 26.3 in the ondansetron group; in the overall phase, 32.7, 35.6, 40.7 and 29.0 in the palonosetron 20 μg/kg group, 23.5, 33.3, 27.9 and 21.1 in the 10 μg/kg group, and 24.1, 29.1, 27.3 and 21.1 in the ondansetron group. Treatment-emergent adverse events (TEAEs [%], cycles 1–4) were fewer in the palonosetron 20 μg/kg group (69.3, 64.4, 55.9, 48.4) versus the 10 μg/kg (80.2, 76.2, 72.1, 75.0) and ondansetron (81.7, 82.6, 68.2, 72.2) groups. All withdrawals/fatal TEAEs were not considered drug-related. Laboratory/electrocardiogram evaluations raised no concerns.
Conclusion: In pediatric patients, palonosetron 20 μg/kg was non-inferior to ondansetron in the acute phase (cycle 1) and numerically superior to ondansetron across all cycles, with no significant safety risks.

O-087

IMPACT OF BEST PRACTICES TO DECREASE CENTRAL LINE ASSOCIATED BLOOD STREAM INFECTIONS (CLABSI) AMONG ONCOLOGY PATIENTS

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Background/Objectives: CLABSI adversely affects clinical outcomes by increasing morbidity, mortality and waste of healthcare resources. Standardized practices for central venous line (CVL) care have been reported to significantly decrease risk of CLABSI. Primary objective was institutional CLABSI rate reduction to < 2.9/1000 line days from historical rate of 5.8/1000 line days within 12 months and to sustain rate reduction.
Design/Methods: Strategies to decrease risk of CLABSI include implementation and long-term compliance with standardized practices for CVL care. These included CVL insertion guidelines and standardized maintenance care bundles. In 2009, to further decrease CLABSI rate and improve clinical outcomes, our institution adopted standardized best practices under the auspices of the NACHRI Hematology-Oncology Transformation Collaborative. Effectiveness of these interventions was analyzed by comparing pre-interventional (2006-2008) CLABSI rate to post-interventional (2009-2014) rate. To implement new practice and measure its outcome, the institutional CLABSI Core-Working Group used "Model for Improvement" by introducing "test-of-change" through *Plan-Do-Study-Act* (PDSA) cycles (listed below). *Root Cause Analyses (RCA)*: RCA performed on all positive blood cultures to identify any "preventable" cause, analyze system failure, study trends and possible associations. *Nurse/Physician Education*: A tailored approach to education was adopted. *CVL maintenance bundles:* During 2009, several elements of standard CVL care bundles were implemented systematically in multiple stages. *Line Audits*: Weekly line audits and "snap audits" were introduced to measure compliance and to ensure appropriate CVL line maintenance techniques. *CVL Cart*: This carried all necessary supplies needed for CVL maintenance care bundle.
Results: During 2010-2014, serial annual institutional CLABSI rate was 3.9, 1.8, 1.0, 1.3 and 1.4 per 1000 line days respectively. CLABSI reduction resulted in preventing (estimated) 88 CLABSIs and 11 deaths with institutional cost saving of approx. $ 3.01 million.
Conclusion: Systematic introduction of best practices and CVL insertion and standardized maintenance bundles results in significant reduction in CLABSI rate and corresponding morbidity and mortality.

O-088

RISK-SCORING IN PEDIATRIC FEBRILE NEUTROPENIA: EXPERIENCE FROM A SINGLE CENTRE IN INDIA

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Background/Objectives: Risk-prediction models for pediatric febrile neutropenia enable early discharge/outpatient management for 'low-risk' patients. This reduces cost and nosocomial infections, while improving quality of life. We formulated and prospectively assessed a simple risk-scoring model, and compared its performance to 6 previously published decision-rules.
Design/Methods: A prospective study (n=320) identified predictor-variables at admission for a predefined set of complications. Logistic-regression models were used to formulate a risk-score. Scoring was performed as follows: under-nutrition (2), duration from last chemotherapy ≤7-days (2), clinical focus of infection (2), absolute neutrophil count ≤100/μL (2) and C-reactive protein >60 mg/L (5). A total score <7 identified episodes as 'low-risk'. The model's performance was assessed and compared with the published rules on a prospective cohort.
Results: Complication(s) were documented in 109/414 (26.3%) episodes. Two-hundred and eight (50.2%) episodes were classified as 'low-risk.' Accuracy of prediction was 78.5%. Hosmer-Lemeshow test demonstrated adequate calibration (p=0.26). Nagelkerke's R^2 was 34.4%. Discriminatory-performance was comparable for the derivation (c-statistic=0.86; 95% CI 0.82-0.9) and validation-sets (0.81; 95% CI 0.76-0.85). Logistic recalibration using a novel predictor variable identified in the validation-set (albumin <2.5 g/dL) failed to better the c-statistic (0.81; 95% CI 0.76-0.85). Sensitivity was 86.24% (95% CI 78.32-92.08) and negative predictive value was 92.79% (95% CI 88.38-95.91). Odds-ratio for a 'high-risk' episode to develop complications was 10.8 (95% CI 5.97-19.53). Comparing with published rules, the highest c-statistic was 0.69 for a score predicting sepsis. C-statistic for a homogenized outcome (including complications, mortality, sepsis, pneumonia) for the index rule (0.79) was better than the other predictive models (best c-statistic=0.68).
Conclusion: Risk-stratification models validated in developed nations are not applicable in developing countries. Predictors for complications in this setting include under-nutrition and focus of infection. The impressive performance of the index model, incorporating relevant and easily assessable variables, warrants its validation in centres across developing economies.

O-089

SYSTEMATIC REVIEW OF REDUCTIONS IN THERAPY FOR CHILDREN WITH LOW RISK FEBRILE NEUTROPENIA

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Background/Objectives: Reductions in therapy for children with febrile neutropenia at low risk of complications may provide benefits to both patients and the health service. Previous systematic reviews concluded outpatient and oral antibiotic regimens were effective, but did not address the clinical heterogeneity of the studies. We further explored the safety of these regimens and the effect of timing of discharge.
Design/Methods: Multiple electronic databases, conference abstracts and reference lists were searched. Prominent authors were contacted. Randomised controlled trials (RCT) and prospective observational cohorts examining the location of therapy and/or the route of administration of antibiotics in patients with febrile neutropenia, younger than 18 years old, were included. Studies were screened, appraised and data extracted by one researcher and independently checked by a second. Data were combined in a meta-analysis using a random effects model. Heterogeneity was examined using Chi-squared tests, I^2 and by visual inspection of forest plots. Registration: PROSPERO (CRD42014005817).
Results: Thirty-seven studies (including 3205 episodes of febrile neutropenia) were included in the review, including 13 RCTs and 24 observational cohorts. Two deaths occurred in children receiving inpatient intravenous therapy. Two intensive care admissions occurred in children receiving outpatient oral antibiotics. In the included RCTs, the odds ratio for treatment failure with outpatient treatment was 0.98 (confidence interval (CI) 0.44-2.19, I^2=0%) and with oral treatment was 1.05 (CI 0.74-1.48, I^2=0%). When considering all prospective data, the estimated risk of failure using outpatient therapy was 8.57% (CI 8.54-8.61%, I^2=85.4%) and using oral antibiotics was 8.1% (CI 8.1-8.2%, I^2=85.9%). The rate of failure for patients receiving reduced therapy after 48 hours was lower than these estimates, and for patients treated entirely with reduced therapies the rate of failure was higher.
Conclusion: Reductions in therapy for specified groups are safe with low rates of treatment failure.

O-090

PERIPHERALLY INSERTED CENTRAL CATHETERS ARE SIGNIFICANTLY ASSOCIATED WITH SYMPTOMATIC VENOUS THROMBOTIC EVENTS IN PEDIATRIC ONCOLOGY PATIENTS: A POPULATION-BASED STUDY FROM MARITIMES, CANADA

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Background/Objectives: The care of pediatric oncology patients (PCPs) has been supported by central venous catheters (CVCs); although with a risk of symptomatic venous thrombotic events (sVTE). There are limited data addressing the association of type of CVC and sVTE in childhood cancer patients. We describe the association of type of CVC with sVTE in PCPs.
Design/Methods: We abstracted data from the case records of all PCPs from the Maritime provinces managed by the IWK Health Center in Halifax. Patients were <20 years of age and cared for between January 2000 to December 2014. Data were combined from: (i) pediatric oncology hospital database, (ii) Provincial Cancer in Young People database, (iii) Electronic medical records, (iv) Pharmacy database (v) IWK central line database and (v) Hospital Health records. All subjects had signs or symptoms of VTE, radiologically proven VTE and were treated with anticoagulants. The CVCs were categorized by method of insertion and included peripherally insertion central catheters (PICC), totally implanted devices (TID), tunneled lines (TL), and others. Type of first CVC was analyzed.
Results: Forty (5.4%) of the 731 PCPs had sVTE. Among the 459 patients with TID, 67 patients with TL, and 110 patients with other types of CVCs, 25 (5.4%), 4 (6%) and 2 (1.8%) developed sVTE respectively. In comparison, 9 (15.5%) of the 58 patients who received PICC line developed sVTE (p=0.001). Presence of PICC line increased odds of sVTE 4.4 (95% confidence interval: 2.0-9.8) times as compared to other types of CVC. The mean time to sVTE in patients with PICC versus other types of CVC was 59.5±40 days (median=17 days) and 335.7±120 days (median=257 days) respectively (p=0.001).
Conclusion: This pediatric population based study provides evidence that PICC lines are associated with sVTE and confirms adult patient observations in PCPs. This underscores the need for judicious use of PICC lines.

Free Papers 17: Epidemiology

O-091

CARDIOVASCULAR MEDICATION IN PATIENTS DIAGNOSED WITH CANCER AT EARLY AGE IN FINLAND: A NATIONWIDE REGISTRY LINKAGE STUDY

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Background/Objectives: Advanced therapies of childhood and young adulthood (YA) cancer have led to excellent survival results nowadays. Nevertheless, this growing group of surviving cancer patients faces elevated risks for possibly life-threatening morbidities, especially cardiovascular complications.
Design/Methods: Our nationwide registry linkage study investigated the purchase of cardiovascular medication in early onset cancer patients (N=8,197) diagnosed with cancer below the age of 35 years between 1993 and 2004 and in healthy siblings (born between 1958 and 2004) (N=29,974). Purchase data on cardiovascular medication from 1993 to 2011 were extracted from the national drug purchase registry. Regarding the purchase of cardiovascular medication, cumulative incidences and hazard ratios (HR) were analyzed after early onset cancer compared to healthy siblings.
Results: Cumulative incidences for purchasing cardiovascular medications prevailed after both YA and childhood cancer. A markedly increasing trend over time was visible for all investigated medication groups, especially for the purchase of any cardiovascular or specifically cardiac medication.HRs for purchasing cardiovascular medication were elevated especially after childhood, but also after YA cancer compared to siblings. The highest HR stood out for purchasing anticoagulants after childhood cancer (HR 19.8, 95%CI 8.5-45.9), however, with very low purchase numbers among siblings. The next highest HRs were found for any cardiovascular (HR 7.2, 95% CI 5.1-10.1) and cardiac medication (HR 4.8, 95% CI 3.3-6.9) after childhood cancer. Regarding YA cancer patients, the respective increased values were HR 2.5 (2.0-3.2) for anticoagulants, HR 1.7 (1,5-1,9) for any cardiovascular, and HR 1,5 (1,3-1,7) for cardiac medication.
Conclusion: Using a new alternative registry linkage approach, our study demonstrated higher purchases of cardiovascular medication after cancer at young age, reflecting elevated cardiovascular morbidity. This knowledge postulates the need for implementation of long-term cardiovascular control guidelines for this patient group at risk to prevent, detect and adequately treat cardiovascular late effects.

O-092

MATERNAL RESIDENTIAL PROXIMITY TO ROADWAYS DURING PREGNANCY AND CHILDHOOD CENTRAL NERVOUS SYSTEM TUMORS: A POPULATION-BASED ASSESSMENT IN TEXAS, 2003-2009

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Background/Objectives: Due to increasing concerns over the impact of traffic-related air pollution on childhood cancers, we evaluated residential proximity to major roadways and risk for developing a childhood central nervous system (CNS) tumor in Texas.
Design/Methods: We obtained information on all children diagnosed with a CNS tumor at <5 years of age and born in Texas (USA) during the period of 2003-2009 (n=315) from the Texas Cancer Registry. A random sample of birth certificate controls was frequency matched to cases (5:1) on birth year (n=1,575). Based on the maternal residence at the time of the child's birth, we assessed exposures to traffic-related air pollution using residential proximity to major roadways derived from Geographic Information System (GIS) applications. Logistic regression was used to generate odds ratios (OR) and 95% confidence intervals (CI) adjusted for the child's sex and year of birth, maternal education and race/ethnicity, and area-level poverty. We evaluated CNS tumors as a group and by histologic type (e.g., ependymoma, primitive neuroectodermal tumor [PNET]).
Results: Maternal residential proximity to major roadways during pregnancy was statistically significantly associated with CNS tumor risk in offspring. Specifically, risk increased by 30% for every kilometer [km] closer to a major roadway (OR [95% CI]: 1.3 [1.0-1.7]). Moreover, mothers who lived in areas of high roadway density (>1.5-km length of major road segments within a 500-m residential radius) were 1.5-times more likely (95% CI: 1.1-2.1) and 4.2-times more likely (95% CI: 1.2-14.9) to have offspring with any CNS tumor and ependymomas, respectively, when compared mothers in low density areas.
Conclusion: In this large population-based assessment, we found that mothers who live close to major roadways or who live in areas of high roadway density were more likely to have offspring who develop a CNS tumor, particularly an ependymoma.

O-093

NO SOCIOECONOMIC VARIATION IN SURVIVAL FROM SOFT TISSUE SARCOMAS OF CHILDREN AND YOUNG ADULTS IN NORTHERN ENGLAND

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Background/Objectives: Although survival from soft tissue sarcoma (STS) in children has improved, about 30% die within 5-years of diagnosis. This study investigates the association between socio-economic status (SES), using paternal occupation at birth, and survival from STS in children, teenagers and young adults (TYA).
Design/Methods: All cases of STS in children and TYA (0-14 & 15-24 years) diagnosed 1968–2008 were extracted from a population-based specialist registry in Northern England. Paternal occupational social class at the time of the child's birth was obtained and classified into 3 categories: class I/II (professional/managerial), class IIIN/M (skilled non-manual/skilled manual) and class IV/V (semiskilled/unskilled). Kaplan-Meier methods were used to calculate survival and Cox regression used to investigate associations between survival and SES, site of tumour, stage and age at diagnosis.
Results: There were 425 cases of STS; 216 (50.8%) children and 209 (49.2%) TYA, 231 (54.4%) males and 194 (45.7%) females, 158(37.2%) rhabdomyosarcoma and 267(62.8%) non-rhabdomyosarcoma, 135 (31.8%) had tumours in the head and neck, 107 (25.2%) in the trunk, with 97(22.8%) in the extremities. Social class was category I/II for 78 (18.4%) cases, IIIN/M for 197 (46.4%), IV/V for 108 (25.4%) and missing for 42(9.9%). Five-year survival for all cases significantly improved from 37.2% (1968-1977) to 74.8% (1998-2008). Survival was worse for rhabdomyosarcomas versus non-rhabdomyosarcomas (hazard ratio (HR)=2.39, 95%CI 1.71-3.35; $P < 0.001$), for tumour site trunk versus head and neck (HR=2.71, 95% CI 1.86-3.93; $P < 0.001$), for TYA versus children (HR=1.45, 95% CI 1.04-2.00; $P = 0.03$) and for males versus females (HR=1.50 95% CI 1.11-2.03, $P = 0.008$). However, SES was not significantly associated with survival from STS (HR=1.12, 95% CI 0.74-1.69 and HR=1.32, 95% CI 0.85-2.06 for class IIIN/M and IV/V respectively versus class I/II).
Conclusion: This study has shown that site of disease, age and sex, but not SES, are important predictive factors for survival from STS in children and TYA.

O-094

CONSENSUS-BASED PRINCIPLES AND CLASSIFICATION SYSTEMS FOR COLLECTING PAEDIATRIC CANCER STAGE IN POPULATION-BASED CANCER REGISTRIES

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Background/Objectives: Population-based cancer registries (PBCRs) generate estimates of incidence and survival that are essential for cancer surveillance, research, and developing cancer control strategies. Though cancer stage data allow for meaningful assessments of the effectiveness of prevention and early diagnosis campaigns, as well as changes in cancer incidence and outcomes, stage is not collected by most PBCRs. The principal method of staging adult cancers is the tumor, node, metastasis (TNM) classification. The collection of paediatric cancer stage however is more complicated however because it is defined by malignancy-specific parameters and multiple classifications from different research groups have evolved overtime. Thus collection of paediatric stage data represents a significant challenge for PBCRs.
Design/Methods: We assembled key experts and stakeholders (oncologists, cancer registrars, epidemiologists) and utilized a modified-Delphi approach to establish principles guiding paediatric cancer stage collection. Using these principles, recommendations were made on which staging systems should be adopted by PBCRs for the major childhood cancers, including adaptations for low-income countries.

Results: 28 panelists representing multiple stakeholder groups, 17 countries and 6 continents ultimately participated in the Delphi questionnaires and the face-to-face meeting. 12 principles guiding the collection of paediatric stage were identified in 4 categories: rationale for collection, relationship to adult cancer staging, specificities of paediatric staging systems, and adaptation to resource-limited settings. Using these recommendations, staging systems for collection by population-based cancer registries for 18 major childhood malignancies were endorsed, with different tiered systems recommended for different resource settings.
Conclusion: Wide adoption of these recommendations among cancer registries will facilitate international comparative studies of incidence and outcome. We recommend that the tiered, paediatric-specific staging systems endorsed in this paper be adopted for paediatric cases by cancer registries in both LMICs and HICs.

O-095

CHILDHOOD CANCER MORTALITY IN INDIA: DIRECT ESTIMATES BASED ON A NATIONALLY REPRESENTATIVE SURVEY OF CHILDHOOD DEATHS

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Background/Objectives: Though the majority of children with cancer live in low- and middle-income countries (LMICs), estimates of LMIC mortality rates attributable to childhood cancer are few and reliant upon non-representative cancer registries.
Design/Methods: We examined childhood cancer deaths (one month-14 years) in the ongoing Million Death Study (MDS), a representative study of over 27,000 paediatric deaths in India that uses enhanced verbal autopsies. All cases potentially due to childhood cancer were identified. Two paediatric specialists (one in oncology, the other in infectious disease) independently reviewed and categorized cases as definite, probable, possible, or unlikely cancer. Definite and probable cases were assembled and used to estimate national and regional mortality rates attributable to childhood malignancies. Data on symptoms, duration of symptoms, and healthcare seeking behaviour were abstracted from verbal autopsy closed ended questions and caregiver narratives.
Results: Of 700 cases meeting inclusion criteria, 189 were ultimately classified as definite or possible cancer. The kappa statistic of agreement between reviewers was 0·75 (95% confidence interval [CI] 0·71-0·78). Based on these deaths, we estimated that in 2010, 13,726 deaths due to childhood cancer occurred in India, leading to a mortality rate of 3·7 per 100,000 live births per year (95%CI 2·3-5·0), which exceeds prior estimates provided by Indian population-based cancer registries. Disparities between MDS estimates and registry estimates were widest among children in Northeast India, and those with brain tumours. A preponderance of male deaths was seen (male:female ratio 1·6:1). 158 (83·4%) of cohort patients experienced symptom durations of greater than one month.
Conclusion: The burden of childhood cancer mortality in India is substantially higher than previous estimates based on registries. National childhood cancer strategies are warranted in order to improve outcomes for Indian children with cancer.

O-096

OUTCOME DISPARITIES IN 11,410 MEXICAN CHILDREN WITH CANCER: FUNDAMENTAL KNOWLEDGE TO DIRECT PUBLIC HEALTH POLICY

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Background/Objectives: *Childhood cancer is a public health issue in Mexico, being the leading cause of death between ages five and 14. Mortality rates have remained suboptimal for over 25 years. Understanding outcome disparities is essential to create newer health policies to improve the outlook for these children. Describe how clinical, epidemiological and social factors, affect survival in Mexican children with cancer.*

Design/Methods: We evaluated patients registered at the National Childhood Cancer Database between June 2008 and February 2015. Cox proportional hazards model was used to estimate adjusted hazard ratios (HR) for death by clinical and social variables. Cases were grouped according to International Classification of Childhood Cancer (ICCC-3). Significance was set at < 0.05.
Results: From 18,721 registries, 11,410 patients could be enrolled into the model, with 4,177 deaths observed. Five year overall survival was 51.8%. In the Cox model ($p<0.0001$), HR (95% C.I.) for clinical features: Female / male 1.07 (1.01-1.14), every year of age 1.03 (1.02-1.03), every increasing stage 1.46 (1.41-1.52).By type of cancer (leukemia as reference): Lymphomas 0.42 (0.37-0.47), CNS 2.98 (2.51-3.54), neuroblastoma 1.39 (1.16-1.67), renal 0.60 (0.49-0.72), hepatic 1.35 (1.09-1.67) and germ cell tumors 0.31 (0.22-0.43). HR for social context: Treatment in foreign state / own state 1.11 (1.01-1.22), treatment at State Healthcare / Ministry of Health 4.28 (2.22-8.26), education index 0.47 (0.240-0.93), and financial income index 0.56 (0.36-0.84). Other health care institutions, retinoblastoma, sarcomas, carcinomas and other tumors were not statistically significant.
Conclusion: This is the first national study ever made to correlate social and clinical variables with survival for Mexican children with cancer. Adjusted hazard ratios enabled us to estimate the effect of social variables. Age, type of cancer and stage, point of care and geographic location, education and income, significantly affect the prognosis and outcome of childhood cancer. It is time for health policy rethinking and adjustment.

Free Papers 18: Late Effects

O-097

THE INFLUENCE OF CO-MEDICATION ON PLATINUM-RELATED OTOTOXICITY IN LONG-TERM SURVIVORS OF CHILDHOOD CANCER: AN OBSERVATIONAL DCOG STUDY

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Background/Objectives: Platinum administration may lead to hearing impairment or even deafness. Data on the prevalence of hearing impairment after platinum administration in very long-term childhood cancer survivors (CCS) are scarce and the role of co-medication is uncertain. The aim is to identify non-genetic risk factors for ototoxicity, including co-medication, in a multi-center cohort of very long-term CCS treated with platinum-based chemotherapy.
Design/Methods: We analyzed clinical and audiological data after a median follow-up time of 10.2 years [2.0-32.1 years] of all non-cranial irradiated CCS, treated with platinum agents between 1981 and 2013 in 2 of the 7 pediatric oncology centers in the Netherlands. Median age at diagnosis was 3.8 years [0.1-18.9 years]. Hearing function was measured by pure tone audiometry. Severe hearing impairment was defined according to Münster (≥grade 2b) as well as Brock (≥grade 2) classification.
Results: In total, 252 patients received platinum-based chemotherapy, of which 137 were treated with cisplatin alone (median dose: 400 mg/m^2), 75 with carboplatin alone (median dose: 1600 mg/m^2), and 40 with both cisplatin (median dose: 327 mg/m^2) and carboplatin (median dose: 1590 mg/m^2). Overall, the prevalence of hearing impairment was 29.8% (Brock ≥grade 2), respectively 30.5% (Münster ≥grade 2b). Severe hearing impairment was shown in 49/137 (Münster) / 47/137 (Brock) cisplatin-treated patients, in 8/75 (Münster) / 7/75 (Brock) carboplatin-treated patients, and in 20/40 (Münster) / 21/40 (Brock) patients treated with both agents. In univariate analysis, exposure to cisplatin, higher cumulative doses of cisplatin, and exposure to furosemide and vancomycin were associated with hearing impairment. This study is now being further extended to complete the national cohort to determine the role of co-medication on platinum-related ototoxicity.
Conclusion: About one third of the CCS who received platinum-based chemotherapy had severe hearing impairment. Co-medication (furosemide and vancomycin) was associated with platinum-related ototoxicity in long-term survivors of childhood cancer.

O-098

TREATMENT-INDUCED HEARING LOSS AND ADULT SOCIAL OUTCOMES IN SURVIVORS OF CHILDHOOD CNS AND NON-CNS SOLID TUMORS: RESULTS FROM THE ST. JUDE LIFETIME COHORT STUDY

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Background/Objectives: Survivors of childhood cancer treated with platinum-based chemotherapy and/or cranial radiation are at high risk of treatment-induced hearing

loss. The effects of hearing loss on social attainment in adult survivors of childhood cancer have not been well elucidated.
Design/Methods: Three hundred twenty two adult survivors of pediatric central nervous system (CNS; n=152, mean[SD] age at evaluation=26.9[5.5] years, time since diagnosis=18.4[5.4] years) and non-CNS solid tumors (n=170, mean[SD] age at evaluation=31.1[7.3] years, time since diagnosis=22.0[6.1] years) treated with potentially ototoxic cancer therapy completed audiologic evaluations and questionnaires assessing perception of social functioning and attainment (i.e. independent living, marriage, employment). Audiograms were assigned a grade based on the Chang Ototoxicity Grading Scale. Serious hearing loss was dichotomized as no or yes (Chang grade ≤2a *vs.* ≥2b). All analyses were stratified by tumor type (i.e. CNS vs. non-CNS). Multivariable logistic regression models, adjusted for age, sex, and IQ impairment (for CNS models only), were conducted to examine associations between serious hearing loss and social outcomes. Adjusted odds ratios (OR) and 95% confidence intervals (CI) are reported.
Results: Serious hearing loss (hearing levels requiring a hearing aid or deafness), was prevalent in 38% of CNS and 41% of non-CNS tumor survivors. Serious hearing loss was associated with increased risk of perceived negative impact on social functioning for both CNS (OR=1.84, 95% CI, 0.79-4.30) and non-CNS (OR=2.11, 95% CI, 1.07-4.16) tumor survivors. Among non-CNS tumor survivors, serious hearing loss was associated with 2-fold increased risk of non-independent living (OR=2.31, 95% CI, 1.17-4.57), unemployment (OR=1.91, 95% CI, 0.99-3.71) and history of never being married (OR=2.07, 95% CI, 0.98-4.37).
Conclusion: A substantive proportion of adult survivors of childhood cancer treated with potentially ototoxic therapy had serious hearing loss. Treatment-induced hearing loss was associated with reduced social attainment, both perceived and actual, in this large study sample.

O-099

DIFFERENTIAL PROMOTER METHYLATION IN OXIDATIVE STRESS GENES ASSOCIATED WITH OTOTOXICITY AMONG CHILDHOOD CANCER SURVIVORS

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Background/Objectives: There is growing evidence that platinum-based chemotherapeutic agents may up-regulate genes involved in mitochondrial superoxide detoxification leading to cochlear oxidative stress and ultimately ototoxicity. Based on this, we hypothesize that epigenetic mechanisms leading to differential expression of these genes may play a role in treatment-related ototoxicity. Therefore, we evaluated the role of methylation profiles within six mitochondrial superoxide metabolism genes on ototoxicity susceptibility among childhood survivors of medulloblastoma.
Design/Methods: Peripheral blood samples were collected from 63 childhood survivors of medulloblastoma at Texas Children's Cancer Center between 2005 and 2010, with a mean time since diagnosis of 5.2 years. Patients requiring hearing aids ≥1 year following primary therapy were assigned a diagnosis of ototoxicity. DNA methylation profiles were obtained using the Illumina HumanMethylation450 BeadChip array. We assessed probes in promoter-associated CpG sites within the following genes: *SOD2*, *GPX4*, *GSR*, *PRDX3*, *TXN2*, and *TXNRD2*. Ototoxicity-associated differential methylation at these probes was assessed using linear regression adjusting for age, gender, cranial radiotherapy, amifostine, cisplatin dose, and cellular composition. The false discovery rate (FDR) was used to account for multiple comparisons.
Results: Among the 54 probes included in the final analysis, two were associated with ototoxicity (FDR q<0.1): *GPX4* (cg18061485; q=0.079) and *GSR* (cg07077080; q=0.044). Relative to ototoxic cases (n=23), the mean beta methylation values were 12.6% and 7.8% higher in control patients (n=40) for cg18061485 and cg07077080, respectively.
Conclusion: As DNA methylation at CpG sites in promoter regions is associated with decreased gene expression, our results are consistent with evidence that up-regulation of genes involved in mitochondrial superoxide detoxification is associated with ototoxicity. Our study provides preliminary evidence that epigenetic mechanisms may play a role in treatment-related ototoxicity. This information may potentially inform improved risk stratification and chemoprotective strategies for hearing loss among those undergoing therapy for childhood medulloblastoma.

O-100

VALIDATION OF A BRIEF COMPUTERIZED BATTERY FOR NEUROCOGNITIVE FUNCTIONING IN CHILDHOOD CANCER SURVIVORS

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Background/Objectives: Many childhood cancer survivors develop neurocognitive impairment impacting education and psychosocial functioning. Consensus guidelines recommend assessment of at-risk patients, but conventional assessment is time-consuming, costly and requires specialized expertise. Computerized neurocognitive batteries are potential alternatives requiring further study. We evaluated feasibility and validity of the 20-minute Cogstate® computerized battery.
Methods: In this cross-sectional study, childhood cancer survivors, diagnosed at ≤21 years and ≥2 years since diagnosis, completed Cogstate® plus conventional neuropsychological measures at two U.S. cancer centers (8/9/2012-5/14/2014). Standardized Connecticut academic achievement test scores were obtained from schools. We measured 1) administration feasibility 2) convergent validity (associations with conventional measures), 3) concurrent validity (ability to differentiate between groups with known cognitive risk-factors) and 4) predictive validity (associations with academic achievement).
Results: Participants (N=111) were a mean age of 8.0 ±5.1 (range 0.2-18.3) years at diagnosis and 16.7±7.6 (range 8.1-53.9) years at evaluation, 63% male, previously diagnosed with leukemia (52%), lymphoma (14%), brain tumors (20%), and other tumors (14%). Participation and completion rates were 96% and 94%, respectively. Spearman's correlations revealed associations between Cogstate ® and conventional measures for attention ($p < 0.01$), executive functioning ($p < 0.01$), and self/parent report of executive functioning ($p = 0.01$). Linear regression confirmed expected associations between younger age at diagnosis and worse Cogstate® performance in executive functioning (r^2=−1.01, $p < 0.01$) and processing speed (r^2=−0.02, $p < 0.01$); and brain tumor diagnosis (r^2=0.05, $p < 0.01$) and worse Cogstate® performance in processing speed (r^2=−0.02, $p < 0.01$), attention (r^2=0.10, $p < 0.01$), and working memory (r^2=0.05, $p < 0.01$). T-tests revealed differences between survivors above and below Connecticut-defined reading goals on Cogstate's® processing speed ($p = <0.01$) and working memory ($p < 0.01$) tasks, and between those above and below math goals on Cogstate's® executive functioning task ($p = 0.04$).
Conclusion: Results suggest Cogstate® is a feasible, valid method to identify patients at risk for neurocognitive difficulties, potentially useful for clinical and research assessments.

O-101

EFFECT OF SEIZURE MORBIDITY ON NEUROCOGNITIVE OUTCOME, QUALITY OF LIFE, AND SOCIAL ATTAINMENT IN ADULT SURVIVORS OF CHILDHOOD CENTRAL NERVOUS SYSTEM (CNS) AND NON-CNS CANCERS

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Background/Objectives: Adult survivors of childhood cancer are at risk for seizures and reduced functional outcomes. The direct impact of seizures on function in cancer survivors has not been well explored.
Design/Methods: We examined seizure characteristics among 2,022 childhood cancer survivors (48.3% female; median [range] age=31.5[18.4-65.9] years; time since diagnosis=23.6[10.4-51.1] years). Frequency and persistence of seizures and anti-epileptic medications following cancer diagnosis were abstracted from medical records, and reviewed by board-certified neurologists. Survivors completed neurocognitive testing and surveys to assess health-related quality of life (HRQOL) and social attainment. Neurocognitive performance was converted to z-scores (M=0, SD=1.0) based on population norms. Multiple logistical regression and Poisson regression models with robust variance were used to examine associations between seizure characteristics and functional outcomes, stratified by tumor group (i.e. CNS vs. Non-CNS) and adjusted for age, gender, and prior cancer therapy (CNS: cranial radiation [CRT]; Non-CNS: CRT, intrathecal and high-dose intravenous methotrexate).
Results: Seizures were identified in 232 (11.5%) survivors, and were most frequent among survivors of CNS tumor (29.9%) and leukemia (12.6%) compared to lymphoma (4.1%) and solid tumor (4.5%). In multivariable models, seizures were associated with poorer performance on cognitive flexibility (CNS tumor effect size [ES]=-0.74, p=0.02; non-CNS tumor ES=-0.68, p<0.001), fluency (non-CNS tumor ES=-0.37, p<0.001) and short-term memory (CNS tumor ES=-0.63, p=0.001; non-CNS tumor ES=-0.46, p<0.001). Similar effects were observed for attention and processing speed, though seizures were generally not associated with HRQOL. Seizures were associated with less than full time employment for survivors of CNS (ES=1.09, p=0.03) and non-CNS (ES=1.11, p=0.001) tumors. Seizures persisted in 84/232 (36.2%) survivors within the last year of long-term follow-up. Among seizure characteristics, seizure resolution was the most common predictor of poor outcome.

Conclusion: Seizures in cancer survivors impact neurocognitive outcome and employment, independent of prior cancer therapy. Optimal clinical management by achieving seizure control may improve neuro-cognitive function.

O-102

CARDIOVASCULAR CONTRIBUTIONS TO NEUROCOGNITIVE OUTCOMES IN ADULT SURVIVORS OFCHILDHOOD CANCER

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Background/Objectives: Long-term survivors of childhood cancer treated with cranial radiation (CRT) or antimetabolites are at risk for neurocognitive dysfunction. Many also develop cardiovascular complications, though the impact of cardiovascular health on neurocognitive function is not well understood.
Design/Methods: Adult survivors of childhood cancer (n=1,479; 47% female; median[range] age 31.0[18-61] years; median time since diagnosis 24.6[11-49] years) were recruited from the St. Jude Lifetime Cohort Study. Survivors completed comprehensive medical assessments and neurocognitive testing for attention, memory, processing speed and executive function. Survivors with history of neurologic/neurodevelopmental conditions unrelated to cancer diagnosis or treatment were excluded. Multivariable logistic regression was used to examine relative risk (RR, 95% confidence interval [CI]) for neurocognitive impairment, defined as age-adjusted standard scores $<10^{th}$ percentile of population norms. Predictors included current smoking status, abdominal obesity, and the presence of or treatment for hypertension, impaired fasting cholesterol, and impaired fasting glucose, controlling for demographic and neurotoxic treatment variables.
Results: Survivors demonstrated high frequency of hypertension (48.8%), dyslipidemia (64.0%), obesity (67.8%), impaired fasting glucose (32.7%) and current smoking (23.6%). High frequency of neurocognitive impairment was identified in attention (27.6%), memory (28.6%), processing speed (32.4%) and executive function (43.3%). In multivariable models controlling for treatment exposures (CRT dose, cumulative intrathecal methotrexate, cumulative high-dose methotrexate, cumulative high-dose cytarabine and corticosteroids), gender, race, and current age, obesity was associated with risk of attention problems (RR=1.38, CI 1.14-1.67) and slow processing speed (RR=1.37, CI 1.14-1.63). Current smoking was associated with impaired attention (RR=1.50, CI 1.25-1.79), memory (RR=1.49, CI 1.25-1.78), processing speed (RR=1.40, CI 1.19-1.65) and executive function (RR=1.31, CI 1.16-1.49), while hypertension, dyslipidemia, and impaired fasting glucose were not significantly associated with neurocognitive outcomes.
Conclusion: Long-term survivors of childhood cancer are at increased risk for neurocognitive impairment, which may be influenced by risk factors typically associated with poor cardiovascular health.

Free Papers 19: Brain

O-103

MOLECULAR CLASSIFICATION OF EPENDYMAL TUMORS IDENTIFIES TWO PEDIATRIC SUBTYPES WITH POOR PROGNOSIS

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Background/Objectives: Accurate histopathological grading is challenging for ependymal tumors resulting in poor inter-observer reproducibility. In addition, suitable prognostic markers for reliable risk stratification are lacking. We therefore aimed to establish a uniform molecular classification of all ependymal tumors that adequately reflects the full biological, clinical and histopathological heterogeneity across the major anatomical CNS compartments, age groups, and grades.
Design/Methods: Genome-wide DNA methylation profiles for 500 ependymal tumors were generated using the Illumina 450k methylation array followed by unsupervised hierarchical clustering for subgroup identification. Copy-number aberrations, gene expression patterns and signaling pathways as well clinical data were analyzed to validate and further characterize identified molecular subgroups.
Results: Nine distinct molecular subgroups of ependymal tumors across all age groups, three in each anatomical compartment of the CNS, spine (SP), posterior fossa (PF), and supratentorial (ST), were identified. We found that these molecular subgroups are genetically, epigenetically, transcriptionally, demographically, and clinically distinct. One of the subgroups within each compartment was enriched with grade I subependymomas (SP-SE, PF-SE, ST-SE). Previously described molecular subtypes of hindbrain ependymomas (EPN), Group A and B, could be confirmed (PF-EPN-A, PF-EPN-B). Two supratentorial subgroups were characterized by prototypic fusion genes involving *RELA* (ST-EPN-RELA) and *YAP1* (ST-EPN-YAP1), respectively. Molecular subtypes of the spinal cord showed a good concordance with the histopathological diagnoses myxopapillary ependymoma (SP-MPE) und grade II ependymoma (SP-EPN). Analysis of clinical and demographical data revealed that the vast majority of high-risk patients (mostly children) were restricted to just two of the nine molecular subgroups, PF-EPN-A and ST-EPN-RELA.
Conclusion: The described analyses can be performed from minute amounts of DNA extracted from archived material and are therefore ideally suited for routine clinical application. Regarding clinical associations, the molecular classification proposed herein outperforms the current histopathological classification and thus might serve as a basis for the next WHO classification of CNS tumors.

O-104

HYPOFRACTIONATED RADIOTHERAPY (RT) BOOST FOR CHILDREN WITH EPENDYMOMA AND A MEASURABLE RESIDUE AFTER SURGERY: THE ITALIAN ASSOCIATION OF PEDIATRIC HEMATOLOGY AND ONCOLOGY (AIEOP) EXPERIENCE

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Background/Objectives: To evaluate feasibility and clinical results of a RT boost for children with Ependymoma and measurable residual disease after first line or second look surgery.
Design/Methods: The second AIEOP protocol for childhood ependymoma opened in 2003. After centralized pathological review, children were stratified to receive: 1) 3D conformal RT, 59.4 Gy/33 fractions, to the tumor bed if completely resected and grade II; 2) same RT followed by four cycles of VEC chemotherapy if completely resected and anaplastic; 3) VECx4, second look surgery, local RT as in 1) followed by an hypofractionated (8 Gy/2 fractions) boost to the residue if still measurable.
Results: 143 children entered the study (median follow-up 60 months). In 24 children out of 46 with residue, second look wasn't feasible or incomplete and thus received VEC and 59.4 Gy to the tumor bed plus 8 Gy to the residue. Fifteen/24 children are alive without progression at a median of 51 months (range 11-120 months) from diagnosis, five/6 died of local progression, three died after distant relapse. No iatrogenic death or major toxicity occurred: 4 children developed radiation related MRI changes regressing with steroids within 8 months. In the 46 children with residual disease, 3 and 5 years PFS was 64% and 55%, and OS 80% and 68% respectively. Three and 5-year survival free from local relapse was 71% and 64% respectively. 5 year-EFS for children receiving the RT boost was 57%.
Conclusion: Hypofractionated RT boost was feasible and contributed to obtain durable local control in 15/24 children with measurable residue after first line or second look surgery. An aggressive and integrated local treatment strategy, multiple surgeries and RT including an hypofractionated boost in case of residual disease, is required to improve outcome in children with Ependymoma. This background will be the basis of the next opening SIOP trial for Ependymoma.

O-105

SEVERE NEUROTOXICITY FOLLOWING HYPERFRACTIONATED ACCELERATED RADIOTHERAPY AND THIOTEPA IN THE TREATMENT OF HIGH-RISK MEDULLOBLASTOMA: THE UK EXPERIENCE

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Background/Objectives: The prognosis for children who develop medulloblastoma associated with high-risk features (metastasis, large cell anaplasia, *MYCN* amplification or post-operative residuum $>1.5cm^2$) remains poor.A strategy developed for high-risk

medulloblastoma using induction chemotherapy, Hyperfractionated Accelerated Radiotherapy (HART) followed by either maintenance chemotherapy or two myeloblative courses with thiotepa and stem cell rescue (patients with persistent disease prior to HART), was reported by the Milan group in 2009 with favourable outcomes (5-year event-free and overall survival of 72% and 73% respectively). The approach was subsequently adopted in the UK as a recommended treatment strategy in this disease. We undertook a UK-wide service evaluation to review outcomes following the introduction of this strategy into standard care.
Design/Methods: Neuro-oncologists in all paediatric oncology Primary Treatment Centres in the UK were contacted and an anonymised questionnaire completed for those treated using the strategy from February 2009 to May 2014. Neurotoxicity was defined as ≥ Grade 3 as defined by the Common Terminology Criteria for Adverse Events (CTCAE), version 4.0.
Results: In total, 83 patients were treated from 17 UK centres according to the strategy; 3-year overall survival rate was 54%. Three patients died before receiving HART. In the 55% (n=44) of patients who did not receive thiotepa, none developed severe neurotoxicity. Of those that received thiotepa (n=36) 12 received 1 and 24 two courses; severe neurotoxicity was observed in 33.3% (n=4) and 16.7% (n=4) respectively. Observed neurotoxicities associated with the use of thiotepa and HART included global changes (n=5) and myelitis pattern (n=3).
Conclusion: The favourable survival seen in the original reported series is not replicated in the UK multi-centre setting. The combination of high-dose thiotepa following HART in high-risk medulloblastoma is associated with an unacceptable rate of severe neurotoxicity (22%); suggesting a neurotoxic interaction between these treatment modalities. An international trial in high-risk medulloblastoma is urgently required.

O-106

ATYPICAL TERATOID/RHABDOID TUMORS ARE CHARACTERIZED BY HIGH LEVELS OF EZH2 AND DNMT THAT CORRELATE WITH DNA-METHYLATION AND ARE AMENABLE TO THERAPEUTIC INHIBITION

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Background/Objectives: Atypical Teratoid/Rhabdoid Tumors (AT/RT) are characterized by *SMARCB1*/*SMARCA4* mutations. Being devoid of other mutations we investigated whether epigenetic mechanisms may contribute to the genesis of these tumors.
Design/Methods: As *SMARCB1* is an epigenetic antagonist of the H3K27me3 histone methyltransferase EZH2, we tested by using genome wide analysis of primary tumors (geneexpression- methylom anaysis and ChIP-sequencing), as well as in *in vitro* and *in vivo* models if EZH2 may be suitable for therapeutic inhibition in AT/RT.
Results: In gene expression profiles of 76 primary AT/RT, EZH2, as well as the DNA-methyltransferases DNMT1, DNMT3a and DNMT3b were overexpressed in comparison to normal brain. To epigenetically characterize these tumors, we analyzed genome-wide methylation by Illumina 450k-methylation arrays for 100 AT/RT and Whole Genome Bisulfite Sequencing of 17 cases and found that they display global hypermethylation which might be a result of DNMT overexpression. Moreover, high expression of EZH2 significantly correlated to high expression of DNMTs and DNA-methylation. In line with this, EZH2 co-immunoprecipitated to DNMT1 and DNMT3a in AT/RT cell lines. Secondly, the expression of EZH2 stabilized DNMT expression and recruited DNMTs to promoter regions of tumor suppressor genes. To identify EZH2 targets in primary tumours, 12 AT/RT were subjected to ChIP-sequencing for EZH2 and H3K27me3. Consistent with the EZH2 overexpression in primary tumors, genome wide H3K27me3 occupancy was higher in AT/RT than in various control samples from fetal and adult brain and particularly pronounced at promoter regions. Finally, *in vitro* and *in vivo* tumor cell growth was inhibited and apoptosis was induced either by the genetic inhibition of EZH2 using RNA interference or pharmaceutic inhibition of EZH2 or DNMT.
Conclusion: In conclusion EZH2 is upregulated in AT/RT and can be inhibited therapeutically. Since H3K27me3 and DNA-methylation modifying compounds are accessible for clinical use, these results may impact on therapeutic regimens for patients with AT/RT.

O-107

UPDATING THE PROGNOSTIC IMPORTANCE OF RESECTION STATUS AND CHROMOSOME 1Q GAIN IN CHILDREN TREATED ACCORDING TO THE FIRST SIOP 1999-04 TRIAL FOR PAEDIATRIC INTRACRANIAL EPENDYMOMA

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Background/Objectives: Robust clinical and biological correlates of outcome for childhood intracranial ependymoma are still required. Previous analysis of European paediatric trial cohorts suggested that incomplete surgical resection and chromosome 1q25 gain were markers of recurrence for very young patients, but not for older patients (SIOP ependymoma I). This may have reflected limited cases undergoing biological scrutiny in the latter group. Therefore, biological re-evaluation was performed on an expanded SIOP cohort.
Design/Methods: 89 patients were originally enrolled on the SIOP ependymoma I clinical trial. Following central pathology review, 10 were excluded. Tissue micro-arrays were generated from formalin-fixed, paraffin-embedded material for 71 cases which were then subjected to 1q25 FISH analysis. We also investigated 1q status by Multiplex ligation-dependent probe amplification (MLPA) in a sub-cohort. Results were then correlated with clinical, histological and updated survival data and with MLPA results.
Results: Of the 79 children enrolled, complete surgical resection (CR) was achieved at initial surgery for 35 children (44%). 10-year EFS and OS for CR cases was 52.2% (SE 8.8%) and 70.4% (SE: 7.9%), yet 30.2% (SE 7%) and 46.5% (SE 7.6%) respectively for those with incomplete resection (IR). Of the 71 cases with accompanying tissue, 54 (76%) generated 1q25 results. Both IR (HR 2.12, 95% CIs 1.02 – 4.39, $p = 0.04$) and 1q25 gain (HR 2.26, 95% CIs 1.04 – 4.89, $p = 0.04$) were independent predictors of tumour progression. Indeed, integrating these two markers enabled stratification of cases into three disease progression risk groups (p=0.004). The only independent marker of adverse OS was anaplastic histology (HR 2.34, 95% CIs 1.16 – 4.74, $p = 0.02$).
Conclusion: 1q gain is an independent predictor of poor outcome and in combination with IR identifies a very high risk group. Optimal methodology for identifying 1q gain (FISH vs MLPA) on SIOP II trial will be presented.

O-108

A NEW CLINICAL GUIDELINE (2007) AND NATIONAL AWARENESS CAMPAIGN (2011) ACCELERATED BRAIN TUMOUR DIAGNOSIS IN UK CHILDREN (HEADSMART - BE BRAIN TUMOUR AWARE)

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Background/Objectives: Public and professional concern about delays in diagnosis of childhood brain tumours has led to new referral guidelines and a campaign to raise awareness of early features and the need for timely imaging.
Design/Methods: We investigated the referral pathways of children with a brain tumour 1989-2013 using (a) cancer registrations linked to routine records from primary care and secondary care, (b) referral practice data from a multi-centre audit, and (c) data on total diagnostic interval (TDI) from a service evaluation of HeadSmart.
Results: In a cohort of 181 patients (England, 1989-2006), primary care consultation rates rose 40-fold, from 3.1 per 100 person-months (pm) one year before diagnosis to 148.9 at diagnosis. In a cohort of 3,959 patients (England, 1997-2006), hospital admission rates rose 100-fold, from 1.3 per 100pm at one year before diagnosis to 134.0 at diagnosis. Emergency admissions rose from 35% to 55%. Long delays, repeated presentations in primary care and many ineffective referrals, especially in patients with low-grade brain tumours, were also identified in a multi-centre audit (2006). Headaches or convulsions were the commonest first symptoms at age 4+ years. Ophthalmic signs were more prominent in younger children, and changed most between onset (23% of patients) and diagnosis (46%). Raised intracranial pressure was the most common hospital presentation (40% of patients). During the period 2006-11, the median TDI fell from 13.4 to 6.3 weeks. The greatest impact of HeadSmart is a 65% reduction in median interval between first clinical contact and diagnosis ($p<0.01$; 730 children in 19 UK specialist centres, 2011-13).
Conclusion: Delays in diagnosis were associated with repeated presentations, ineffective referrals and increasing likelihood of urgent admission. The referral guidance and awareness campaign shortened the interval from first contact to scanning. The campaign is ongoing, and it will be disseminated to primary care in 2014-15.

Free Papers 20: Late Effects 2

O-109

SPERM BANKING IN ADOLESCENTS NEWLY DIAGNOSED WITH CANCER: RESULTS FROM THE SBANK10 STUDY

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Background/Objectives: To describe the prevalence of sperm banking among adolescent males newly diagnosed with cancer in the US and Canada, and to identify factors predictive of banking outcomes.
Design/Methods: A prospective single group quasi-experimental study design was utilized to test the contributions of psychological, demographic, developmental, parent, provider, and medical factors on sperm banking outcomes. At-risk adolescent males from 8 leading pediatric oncology centers (13-21 years of age, Tanner stage ≥ 3, N=146), their parents, and medical providers completed self-report questionnaires within one week of treatment initiation. Logistic regression with single covariates was utilized to test each factor as a potential correlate of the two binary sperm banking study outcomes (bank/no bank and attempt/no attempt), and multi-covariate logistic regression was used to calculate odds ratios (OR) and 95% confidence intervals for specified banking outcomes.
Results: Among adolescents (Mean age = 16.49 years, SD = 2.02), 43.8% banked sperm (64/146) and 56.2% did not (82/146). Of those not banking, 14 attempted but were azoospermic (n=3) or unsuccessful (n=11). As such, 53.4% made a sperm banking attempt (78/146), whereas 46.6% (68/146) did not. The overall banking model revealed adolescent history of masturbation (OR=12.23, CI: 2.22-67.37, p<.01) and increased parental self-efficacy to coordinate sperm banking (OR=1.24, CI: 1.03-1.49, p=.02) associated with an increased likelihood of banking. The overall attempt model revealed that higher Tanner stage (OR=23.13, CI: 2.20-243.59, p<.01) associated with an increased likelihood for banking attempt, whereas higher perceived barriers to banking by adolescents associated with a decreased likelihood (OR=0.74, CI: 0.59-0.93, p=.01).
Conclusion: This is the first large study to describe sperm banking practices among newly diagnosed adolescents in the US and Canada. Although findings suggest that banking is underutilized, modifiable factors such as parental self-efficacy and adolescent perceptions of banking barriers were identified. Implications for sperm banking interventions will be discussed.

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FACTORS ASSOCIATED WITH AGING PHENOTYPES IN ADULT SURVIVORS OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA

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Background/Objectives: Childhood cancer survivors are at risk for accelerated aging. We evaluated associations between lifestyle and hormonal status with risk of low bone mineral density (BMD) and frailty among adult survivors of childhood acute lymphoblastic leukemia (ALL).
Design/Methods: Participants included 862 ALL survivors (median age, 31.3 [range: 18.4-59.7] years) who received evaluation at St. Jude Children's Research Hospital as participants in the St. Jude Lifetime Cohort study. Bone density was measured using quantitative computed tomography of L1-L2 vertebrae; low BMD was defined as an age- and sex-standardized Z-score < -1. Prefrailty and frailty were defined as having 2 and ≥3 of the following conditions, respectively: low muscle mass, self-reported exhaustion, low energy expenditure, slow walking speed, and weakness. Logistic regression, stratified by sex, was used to examine associations (odds ratios (OR) and 95% confidence intervals (CI)) between lifestyle (smoking, alcohol consumption, and activity levels) and hormonal status with low BMD and frailty.
Results: Thirty percent of survivors met criteria for low BMD, 3.6% for frailty and 18.6% for prefrailty. After adjusting for body mass index, males with growth hormone deficiency (GHD; OR=1.6, 95% CI=1.0-2.5) or who were current smokers (OR=1.7, 95% CI=1.0-2.9) had increased odds of low BMD compared to those without GHD or non-smokers. Among females, GHD (OR=2.2, 95% CI = 1.3-3.8) and moderate alcohol consumption (OR=2.1, 95% CI=1.1-3.8) were associated with low BMD. After adjusting for current age, the odds of prefrailty/frailty were increased among males with GHD (OR=3.0, 95% CI=1.6-5.7) and who smoked (OR=3.3, 95% CI=1.6-6.4) and among females who were risky drinkers (OR=2.0, 95% CI=1.0-3.8). Survivors with low BMD did not have increased odds of prefrailty/frailty when compared to survivors with normal BMD (p>0.05).
Conclusion: ALL survivors should receive counselling regarding lifestyle habits and undergo screening for hormonal deficits to minimize the risk of low BMD and frailty.

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LATE MORTALITY AND CAUSES OF DEATH AMONG LONG TERM SURVIVORS OF CHILDHOOD CANCER REGISTERED IN THE ITALIAN OFF THERAPY REGISTRY (OTR)

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Background/Objectives: To analyze long term survival and causes of death among 5-year survivors of childhood cancer.
Design/Methods: The Off-Therapy Registry (OTR) of the Italian Association of Pediatric Hematology/Oncology (AIEOP) started in 1980 prospectively enrolling children with cancer (age 0-21 years) at treatment completion. Prevalent cases were also included with the first case diagnosed in 1960. During 2012-14 vital status was ascertained through census offices, and causes of death retrieved from death certificates. Survival analysis allowed for left truncation to limit possible bias due to prevalent cases at the start of OTR. Causes of death other than the one under study were treated as competing risks.
Results: A total of 13,920 5-year survivors were evaluated (M:F ratio 1.24). The median age at diagnosis was 5.2 years (IQR 2.7-9.7). Tumour type distribution was comparable with other series except for a lower frequency of CNS tumours (n=1215; 8.7%). Era of diagnosis was <1980 for 14.0% of the population, 1980-89 for 27.0%, 1990-99 for 46.7%, and 2000-09 for 12.3%.Length of follow-up ranged between 5.0 and 52.9 years, median 19.6 years. At follow-up, 1,162 (8.4%) subjects were dead with a cumulative probability of survival (95%CL) at 20, 30 and 40 years of 92.3% (91.8-92.8); 89.3% (88.6-90.0); 84.6% (83.0-86.1), respectively. Significant reduction in the cumulative risk of death was observed by treatment era, and female gender.Cause specific mortality at 35 years was 5.7% for primary cancer (n=672); 3.4% for secondary malignancy (n=223), 2.5% for other causes (n=132) and 0.6% for external causes (n=44). It was unknown for 91 subjects.
Conclusion: After 30 - 35 years since diagnosis mortality is more likely to be due to other causes of death other than recurrence. We confirm a reduction in late mortality for survivors treated in recent eras.

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POPULATION EVIDENCE TO SUPPORT A MODEL OF CHILD CANCER SURVIVOR CARE

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Background/Objectives: Follow-up of adult-age childhood cancer survivors in British Columbia (BC) occurs mainly in the primary care setting, with little coordination and support. Results from a research program, linking clinical records of all child cancer cases diagnosed in BC from 1970 to mortality, cancer, and health administrative databases for up to 40 years, were used to inform recommendations for strategies to meet the ongoing healthcare needs of this survivor population.

Design/Methods: Results from the BC Childhood, Adolescent, Young Adult Cancer Survivor Research Program were used in a needs assessment; evaluation of ongoing healthcare demand and costs; identification of gaps in care; and determination of the size and characteristics of subgroups requiring different levels of care.
Results: There were approximately 3000 adult-age survivors. The number of survivors transitioning to adult-age care increased each year by 3%. Over 40% lived more than 70 km from the main pediatric hospital. The proportion of at-risk survivors receiving at least one recommended follow-up surveillance test ranged from 0.8% (TSH) to 87% (CBC). At 20 years post-diagnosis, 20% of survivors had no reported hospital-related conditions, and 35% had four or more types of hospital-related conditions. High users of later outpatient services were survivors of CNS tumours, bone sarcomas, or non-ALL leukemia; and those with previous cranial radiation; combination chemotherapy and radiation; combination surgery, chemotherapy and radiation; or autologous or allogenic HSCT. These data contributed to the development of risk-stratified models of care and a business case for implementation.
Conclusion: Working group recommendations led to funding for a formal risk-tiered adult-age childhood cancer survivor follow-up program in BC. This original research demonstrates that population-based longitudinal database linkages of clinical and health administrative data provide high-quality evidence to inform the development of models of quality, sustainable, childhood cancer survivor care, that can improve health care policy and practice.

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VALIDATING PROMIS ANXIETY AND DEPRESSION SHORT-FORMS IN YOUNG ADULT CANCER SURVIVORS: COMPARISON WITH A STRUCTURED DIAGNOSTIC INTERVIEW

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Background/Objectives: To evaluate PROMIS Anxiety and Depression short-forms as screening measures for young adult cancer survivors (YACS), by comparing these measures to results of a structured diagnostic interview.
Design/Methods: 249 YACS (29.50 ±7.33 years) completed the PROMIS Anxiety and Depression Short-forms, and an in-person Structured Clinical Interview for the DSM-IV (SCID). Based on the SCID, participants were classified as having: 1) No significant symptoms; 2) Significant symptoms but no SCID diagnosis; or 3) SCID diagnosis. ROC analyses were used to evaluate concordance between the short-form measures and the SCID and to determine if short-form cut-off score met study criteria for sensitivity (≥.85) and specificity (≥.75).
Results: The Anxiety Short-form had good overall agreement with SCID on anxiety diagnosis (AUC = .81) and moderate agreement on presence of significant anxiety symptoms (AUC = .78). The Depression Short-form had good agreement with SCID on both depression diagnosis (AUC = .89) and presence of significant depressive symptoms (AUC = .83). For detecting a depression diagnosis, a Depression short-form cut-off of T ≥.53.2 came close to meeting study criteria with sensitivity .85 and specificity .73. For detecting an anxiety diagnosis, the Anxiety short-form cut-off T ≥ 52.1 had good sensitivity (.90) but only marginal specificity (.64) indicating many survivors would erroneously screen-in with this cut-off. For identifying survivors with significant anxiety and depression symptoms with or without a diagnosis, the short-form scales performed similarly, but with less robust specificity, and no potential cut-off approached study criteria. Of note, 6 participants with depression symptoms on the SCID reported suicidal ideation not detected on the Depression Short-form which lacks a relevant item.
Conclusion: The PROMIS Short-forms may be useful in assessment of anxiety and depression in YACS but using them as stand-alone screening instruments is likely to misclassify many survivors, particularly those with anxiety disorders.

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GENETIC VARIATION INFLUENCES IMPAIRMENT OF BONE MINERAL DENSITY IN LONG-TERM ADULT SURVIVORS OF CHILDHOOD CANCER

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Background/Objectives: Despite similarities in upfront treatment, impairment of bone mineral density(BMD) varies in long-term adult survivors of childhood cancer(CCS). Because no data are available on the role of genetic variation, we studied whether genetic variation influences this impairment of BMD in CCS.
Design/Methods: This cross-sectional single-center cohort study included 334 adult CCS(median follow-up time after cessation of treatment: 15 years(range 5-39); median age at follow-up: 26 years(range 18-49)). Total body BMD(BMD_{TB}) and lumbar spine BMD(BMD_{LS}) were measured by dual-X-ray absorptiometry(DXA), and BMD was expressed as age-matched and gender-matched standard deviation scores (SDS;Z-score). We selected 12 candidate single nucleotide polymorphisms(SNPs) in 11 genes based on results of previous studies in the healthy population(*COL1A1, TNFSF11, TNFRSF11, TNRFSA11B, VDR, ESR1, WLS, LRP5, MTHFR, MTRR, IL6*). Multivariate analyses included, apart from candidate SNPs, patient and treatment characteristics that were univariately associated with BMD values.
Results: Multivariate analyses revealed that lower $BMD_{TB/LS}$ was associated with lower weight at follow-up($p<0.01$), and BMD_{TB} was associated with previously administered radiotherapy($p=0.01$). Survivors with the homozygous minor allele(GG) genotype of rs2504063(in *ESR1*: estrogen receptor type 1) had a lower BMD_{TB}(-1.17 vs. -0.84; $p=0.01$) than those with the AG/AA genotype, however BMD_{LS} was not different. Carriers of two minor alleles(GG) of rs599083 (*LRP5*: low-density lipoprotein receptor) revealed lower BMD_{TB}(-1.18 vs. -083; $p=0.04$), and lower BMD_{LS}(-0.97 vs. -0.54; $p=0.02$) values than those with the TT/TG genotype. Carriers of *VDR*(vitamin D receptor) haplotype 3 had a lower BMD_{LS} than non-carriers(-0.86 vs. -0.64, $p=0.05$), but BMD_{TB} was not altered.
Conclusion: CCS who are carriers of candidate SNPs in the *VDR*, *ESR1* or *LRP5* genes seem to be more vulnerable to impaired bone mass at an early adult age. In addition to patient and treatment related factors, information on genetic variation may be helpful in identifying survivors who are at risk for low bone density after childhood cancer treatment.

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LONGITUDINAL STUDY IDENTIFIES 3 MIRNA SIGNATURES ALLOWING DIFFERENTIATION BETWEEN PATIENTS WITH WILMS TUMORS AND CONTROLS AT DIAGNOSIS, AFTER SURGERY AND AT TIME OF RELAPSE

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Background/Objectives: Wilms Tumor (WT) is the most common childhood kidney cancer. As treatment according to SIOP includes preoperative chemotherapy without histological confirmation of WT by biopsy, minimal-invasive diagnostic markers confirming WT diagnosis or relapse are highly warranted.
Design/Methods: In our study, we compared miRNA profiles of peripheral blood in patients with WT at five different time points (diagnosis, after preoperative chemotherapy, after surgery, end of therapy, recurrence), with profiles of patients with other malignancies and controls with non-malignant diseases to identify miRNAs with biomarker potential for WT. We measured expression of 883 miRNAs using microarrays in a total of 138 samples and identified differential expressed miRNAs using t-test and miRNA signatures using a Support-Vector-Machine approach.
Results: Our longitudinal study detected 37 significantly deregulated miRNAs in patients with WT compared to controls with 6 miRNAs upregulated (including miRs-197, -320a/b/c/d, and -93*) and 31 miRNAs downregulated (including miRs-144/144*, -18a/b, -20a/b, and -93). We found the highest number of deregulated miRNAs in the comparisons between the first three time points (i.e. at diagnosis, after preoperative chemotherapy, and after surgery) and the controls (i.e. patients with non-malignant diseases or patients with other malignancies). Furthermore, we identified 3-miRNA-signatures that allowed differentiation between patients with WT from non-malignant controls with a classification accuracies of 81%, 92%, and 83% for time points at diagnosis, after surgery and at time of relapse, respectively.
Conclusion: We identified a miRNA profile in peripheral blood of patients with WT under therapy that is significantly different from patients with other malignancies and non-malignant diseases. We report miRNA signatures that show promise as minimal-invasive biomarkers to differentiate WT patients from controls with high accuracies at different time points including the initial WT diagnosis and WT recurrence.

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MODE OF DIAGNOSIS AND OUTCOMES FOR CHILDREN DIAGNOSED WITH RENAL TUMOURS IN THE UK AND IN GERMANY

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Background/Objectives: Publication of geographical comparisons of childhood cancer survival across Europe raised concerns whether the UK had lower population survival rates than countries of similar socio-economic status. For Wilms tumour (WT), this difference reaches 3-6%. Since 2002, the UK participated in a single European clinical trial for renal tumours, allowing direct comparison of possible indicators of late diagnosis.
Design/Methods: The SIOPWT2001 trial enrolled 849 WT patients from UK (to Dec 2011) and 1,507 WT from Germany (ongoing). Since Sept 2012, UK children (n=186) are registered in the clinical observational study (Improving Population Outcomes of Renal Tumours of childhood, IMPORT).
Results: In the SIOPWT2001 trial, median tumour volume (572ml *vs* 381ml) and proportion with metastases at diagnosis (13% *vs* 10%) showed an adverse comparison between UK and Germany, suggesting more advanced disease at diagnosis. This was further interrogated by a retrospective casenote review of 360 patients at 3 UK centres on their mode of diagnosis showing only 14.7% were diagnosed through screening, routine child health surveillance or as an incidental finding when examined for non-tumour related symptoms compared to 27.5% of 947 patients in Germany. 5yr event free survival was not significantly different (84.1% *vs* 82.3%) for children diagnosed in the former group compared to those with tumour-related symptoms in the UK, though the small screening group had 100% EFS. A similar univariable comparison for children diagnosed in Germany showed 90% vs 84% EFS (p=0.05) in favour of those diagnosed without tumour-related symptoms. The IMPORT study collects prospective information categorising the route to diagnosis and so far shows 8% diagnosed following screening/routine surveillance, 14% with non-tumour related symptoms.
Conclusion: International comparisons of route to diagnosis and mode of detection of a common abdominal tumour in relation to routine child health surveillance practices, can inform approaches to improving earlier detection of cancer in children in the UK.

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TCF21 IS HYPERMETHYLATED IN CLEAR CELL SARCOMA OF THE KIDNEY: A GENOME-WIDE TARGET STUDY

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Background/Objectives: Clear Cell Sarcoma of the Kidney (CCSK) is a rare childhood renal tumor. By using whole genomic and mRNA sequencing, we showed that no recurrent genetic mutations or segmental gains/losses could be identified in CCSK. Therefore, we performed genome-wide gene expression- and DNA methylation analyses to find clues pointing to the pathogenesis of the majority of CCSKs.
Design/Methods: Through the "Therapeutically Applicable Research to Generate Effective Treatments" (TARGET) initiative, 13 CCSKs were analyzed for changes in genome-wide gene expression and DNA methylation, in addition to previously performed SNP array analysis, whole genome sequencing and mRNA sequencing. Methylation changes were verified and validated by real-time quantitative polymerase chain reaction following bisulfite conversion in an independent set of 8 CCSK tumor samples.
Results: Integrated analysis of gene expression and DNA methylation identified promoter hypermethylation and low expression of *TCF21* (*Pod-1/capsulin/epicardin*) in all CCSK cases except for one case with a t(10;17)(q22;p13). To verify and validate the methylation status of *TCF21*, sequencing following bisulfite conversion was performed, showing higher *TCF21* methylation levels in CCSKs (3 CCSK samples from the discovery set, 8 CCSK samples from an independent validation set) compared with other pediatric renal tumors (n = 12) and normal kidney samples (n = 2). Expression of *TARID*, the long non-coding RNA responsible for demethylating *TCF21*, was virtually undetectable in CCSKs. Immunohistochemical staining and functional studies are currently being performed.
Conclusion: We raise the hypothesis that hypermethylation of the tumor suppressor gene *TCF21*, a transcription factor involved in mesodermal development which has been shown to be hypermethylated in many adult cancers, and/or decreased *TARID* expression lies within the pathogenic pathway of CCSK.

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TREATMENT AND OUTCOME OF PATIENTS WITH WILMS TUMOUR (WT) REGISTERED IN THE ASSOCIAZIONE ITALIANA EMATOLOGIA ONCOLOGIA PEDIATRICA (AIEOP)-WT-2003 PROTOCOL

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Background/Objectives: The AIEOP-WT-2003 protocol aimed at: reducing chemotherapy for stage I/II WT; improving the outlook for stage III/IV WT (balancing radiotherapy timing/indications and doxorubicin (D) dose reduction), and for anaplastic tumours (designing a new "high-risk" regimen); implementing tumour banking for research purposes and centrally reviewed diagnosis.
Design/Methods: We analysed outcome in 449 unilateral WTs, of 649 newly-diagnosed renal tumours since 10/2003. Treatment was assigned as follows: stage I (including anaplastic cases) and II, 6-week or 22-week vincristine/actinomycin-D (VA), respectively; stage III, 34-week VAD and abdominal radiotherapy; stage IV, preoperative 6-week VAD, abdominal a/o metastatic sites radiotherapy (the last one based on metastatic-response modulation) plus VAD. Stage II-IV anaplastic cases: alternating courses of ifosfamide/D and carboplatin/etoposide in an intensive schedule, plus radiotherapy.
Results: The local diagnosis was reviewed in 81% of cases, and 67% of frozen tumour samples were centrally banked. Five-year DFS and OS for non-anaplastic WT were 86% ±2 and 94% ±1, respectively, after median follow-up of 72 months. DFS (OS) according to tumour stage: stage I (n=117), 90% ±3 (97% ±2); stage II (n=146), 86% ±3 (94% ±2); stage III (n=83), 88% ±4 (97% ±2); stage IV (n=61), 75% ±6 (86% ±5). Five children died without relapsing (3 from secondary cancers, from hepatic venoocclusive disease and surgical complications in 1 case each). For 33 metastatic complete responders to preoperative VAD, for whom lung radiotherapy was omitted, DFS (OS) was 83% ±7 (96% ±4) compared with 65% ±9 (73.5% ±9) for incompletely responders. DFS (OS) was 70% ±7 (74% ±7) in 43 cases with diffuse anaplasia.
Conclusion: These results are comparable with other international studies, however more accurate questions on specific issues deserve larger cooperation to significantly answer. Further reduction of treatment for stage I-II non-anaplastic WT must face with the risk of metachronous tumour.
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GENETIC LANDSCAPE OF ANAPLASTIC WILMS TUMORS WITH DIFFUSE VERSUS FOCAL ANAPLASIA

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Background/Objectives: Presence of anaplasia is a potent marker for adverse outcome in patients with Wilms tumors (WT). While WT patients with focal anaplasia (FA) have identical survival to those with nonanaplastic WT, patients with diffuse anaplasia (DA) show poor outcomes. Beside TP53 mutations, the genome-wide genetic basis of these tumors remains unknown.
Design/Methods: We performed whole-exome sequencing on genomic DNA derived from 12 WT and matched normal DNA from the same patients, using Agilent human V5 (51Mb) capture and the HiSeq sequencing platform. Overall, 9 and 3 matched pairs with DA and FA were assessed, respectively. Chromosome 17p copy number, where TP53 is located, was assessed by a MLPA assay.
Results: Overall, we identified 125 (median 9, range 5-25) non-synonymous somatic single nucleotide variants, of which 54 were predicted to lead to a deleterious protein. No difference was observed in term of total number of mutations between WT with DA and FA, respectively. TP53 mutations were identified in 5 DAWT. In addition, 2 DAWT and 2 FAWT harbored identical hotspot DROSHA mutation (E1147K). Ingenuity Pathway Analysis revealed enrichment for mutations in genes involved in embryonal tumor development (ARMCX3, BCOR, FLT4, KMT2C, REST and TP53) ($p=2.7\times10\text{-}4$). All but one case of DAWT with TP53 mutations harbored TP53 deletion; the case without TP53 deletion had in addition both DROSHA and SIX1 mutations. The 5 patients with TP53 mutations died as compared to one out of 7 without mutation ($p=0.01$).
Conclusion: Our results reveal an exceptionally low mutational load in anaplastic WT, consistent with previously reported results in pediatric solid tumors. DROSHA and TP53 are likely to be mutually exclusive mutations in WT. Updated results with an independent validation dataset will be presented at the meeting.

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OUTCOME OF PATIENTS EXPERIENCING A RELAPSE OF WILMS TUMOUR TREATED BY THE SIOP2001/SFCE PROTOCOL

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Background/Objectives: Overall modern treatment combinations have improved the outcome after Wilms Tumour (WT) recurrence up to 80% for those who relapse after minimal first line therapy and 50% for patients at high risk (unfavorable histology, combined chemo- and radiotherapy regimen). We report the outcome of French patients with relapsed WT included in SIOP2001/SFCE Protocol.
Design/Methods: 772 patients were treated in France between May 2002 and May 2013. Fifty-five patients (7.1%) who experienced a relapse or a progressive disease received a combination of chemotherapy, surgery, radiotherapy according to SIOP2001 guidelines. Intensification treatment as Myeloablative Therapy (MAT) was not formally recommended by SIOP2001 Protocol at relapse.
Results: Forty (72.7%) patients had localized WT (19 stages I/ II; 21 stages III) and 15 (27.3%) had metastatic WT at diagnosis, respectively. Twenty-one patients (38.2%) had unfavorable histology at diagnosis (diffuse anaplasia or blastemal-type), thirty-four (61.8%) favorable. Six (10.9%), 45 (81.8%), 4 (7.3%) patients had a local relapse, a metastatic relapse, or both respectively. Eighteen progressions or relapses occurred during the first-line treatment, 18 relapses within the first 6 months following the end of first-line therapy and 18 after more than 6 months (1 missing data). Thirty-six (65.4%) patients received ICE (ifosfamide, carboplatin, etoposide) or CCE (cyclophosphamide, carboplatin, etoposide) regimens as second line treatment. Twenty-four (43.6%) patients received MAT as intensification treatment. Two-year EFS and OS were 66% and 69.5% respectively. For the patients who underwent MAT the OS was 83.6% and for those who didn't was 58.1%.
Conclusion: Our analysis confirms that more than 65% of relapsed patients can be cured by a combination of chemotherapy, surgery and radiotherapy. The role of intensification treatment with MAT needs a prospective study to find its right place in the treatment of relapsed Wilms tumour.

O-121

CHANGES IN THE CLINICAL FEATURES OF NEUROBLASTOMA 10 YEARS AFTER THE CESSATION OF MASS SCREENING IN JAPAN

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Background/Objectives: Mass screening (MS) for neuroblastoma at 6 months of age in Japan has been halted since 2004. In order to evaluate the effectiveness of MS, we compared the clinical features of neuroblastoma before and after the cassation of MS.
Design/Methods: Six hundred and seventy patients with neuroblastoma who were born and diagnosed between 2004 and 2013 were obtained from the neuroblastoma registry data of the Japanese Society of Pediatric Surgeons (JSPS) (group A: post MS cohort). Two thousand and thirty-six patients with neuroblastoma who were born and diagnosed between 1988 and 1997 were obtained from the data of the Japanese MS study group (group B: during MS cohort). Clinical features such as age at diagnosis, stage and *MYCN* status were compared between the two groups.
Results: There was a significant decrease in the number of patients younger than one year of age (295, group A; 1754, group B) and a significant increase in the number of patients two to three years of age (164, group A; 88, group B) after the cessation of MS. In the patients with stage IV disease (281, group A; 278, group B), there were a significant decrease in the number of patients aged <18 months (91, group A; 159, group B) and a significant increase in the number of patients aged 18 months or older after the cessation of MS (187, group A; 122, group B). As a result, there was a significant increase in the number of patients with stage IV high-risk disease after the cessation of MS (219, group A; 153, group B).
Conclusion: The number of patients aged 2-3 years and patients with stage IV high-risk disease significantly increased after the cessation of MS.

O-122

FEASIBILITY/ TOXICITY AND RESPONSE OF UPFRONT 131I-MIBG THERAPY FOLLOWED BY STANDARD ARM GPOH NB 2004 PROTOCOL IN NEWLY DIAGNOSED HIGH-RISK NEUROBLASTOMA PATIENTS

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Background/Objectives: Meta-iodobenzylguanidine (MIBG) is effective in neuroblastoma (NBL) patients, with response rates (RR) between 20- 60%. To evaluate feasibility, toxicity, efficacy of upfront ^{131}I-MIBG and induction treatment in high-risk (HR) NBL patients.
Design/Methods: In a prospective, multi-centre (AMC and EMC) pilot study (1/1/2005-2011), newly diagnosed HR NBL patients, were treated with 2 courses of ^{131}I-MIBG (if MIBG avid), standard arm of HR GPOH 2004 NBL protocol, myeloablative therapy (MAT) and autologous stem cell rescue (ASCT). ^{131}I-MIBG fixed dose; 1st 7.4 GBq (200 mCi) and 2nd 5.5 GBq (150 mCi). The feasibility of giving ^{131}I-MIBG within 2 weeks after diagnosis, dose intensity of chemotherapy, toxicity of platelets and hematological recovery post MAT ASCT were tested. Response was according to International Neuroblastoma Response Criteria.
Results: Of thirty-two included patients, (age median (range) 35 (0- 137) months), twenty-one patients received the first ^{131}I-MIBG course and 16 patients the second. Eleven patients did not receive MIBG therapy because of; insufficient MIBG uptake, poor clinical condition and hypertension. ^{131}I-MIBG within 2 weeks from diagnosis was feasible in 20/21 (95%) patients. Median cumulative ^{131}I-MIBG dose/ kg was 0.77 GBq (21,0 mCi). Interval between chemotherapy courses was longer in the ^{131}I-MIBG group (median 26 days) than in non ^{131}I-MIBG group (median 23 days). The median nadir of platelets was statistically significant lower at 4 time points in the ^{131}I-MIBG group (11-18 vs. 38-109). Stem cell harvest in both groups was feasible (median harvest CD34 > 2x 10^6/ kg), hematological recovery post MAT ASCT was slower for platelets (>20 × 10^9/L) 25 vs. 14 days but not for neutrophils in the ^{131}I-MIBG group. The RR post ^{131}I-MIBG was 8/21 (38%), post MAT ASCT 15/21 (71%) and overall RR 20/32 (63%).
Conclusion: Combination therapy is feasible/ tolerable and effective in newly diagnosed HR NBL patients.

O-123

EXOME SEQUENCING OF ULTRA-HIGH RISK NEUROBLASTOMA IDENTIFIES MUTATED GENES INVOLVED IN NEURON DEVELOPMENT AND DIFFERENTIATION

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Background/Objectives: Neuroblastoma often presents with widespread metastatic disease, resulting in survival rates of less than 50%. The mutated genes associated with highly aggressive tumors remain unknown.
Design/Methods: To determine the spectrum of somatic mutations in ultra-high-risk neuroblastoma (high-risk patients with any adverse event within 36 months from diagnosis), we performed whole-exome sequencing (110x coverage) by Illumina sequencer on a discovery set of 19 tumor/blood DNA pairs from patients with ultra-high-risk neuroblastoma. As validation set, we used whole-exome sequencing data from 14 and 11 tumor/blood DNA pairs of ultra-high-risk and of non-ultra-high-risk patients (with no adverse events after 36 months from diagnosis) sequenced by a different platform (Ion Proton, 80x coverage). The putative deleterious mutations (missense, frameshift, stop gain/loss) and cancer driver genes were selected by using Cravat and CHASM programs.
Results: We identified 134 genes with deleterious mutations and 37 of these were predicted to be cancer driver genes; only ALK was mutated in two different patients. Five genes were annotated as known therapeutic targets (ALK, ERBB3, PTEN, PTK2, FGFR1). We found numerous pathways and biological processes implicated in neuron development and differentiation. In a separate validation set of 14 tumor/blood DNA pairs of ultra-high-risk neuroblastomas, 64 out of 134 genes carried deleterious mutations. Pathway analysis confirmed the enrichment of neuron development and differentiation-related functions. Conversely, in a set of 11 non-ultra-high-risk patients, 60 out of 134 genes carried deleterious mutations and were highly enriched in canonical carcinogenesis-related pathways such as receptor tyrosine kinase signaling, response to oxidative stress and DNA repair. An ultra-deep targeted sequencing of the selected 134 genes on 50 additional tumor/blood DNA pairs from ultra-high-risk and non-ultra-high-risk patients is currently on-going.
Conclusion: Our study identifies mutated genes and highlights the dysregulation of neuron development and differentiation in a sub-set of patients with a highly aggressive neuroblastoma.

O-124

BENIGN COURSE OF DISEASE IN LOCALIZED NEUROBLASTOMA SHOWING RELAPSE OR PROGRESSION

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Background/Objectives: Recent strategies for localized Neuroblastoma aim to reduce cytotoxic treatment. This may lead to an increase of progressions manageable with limited treatment. On the other hand some patients may experience multiple progressions with a fatal outcome. We were interested in the differences between these groups.
Design/Methods: Patients with localized Neuroblastoma without MYCN-amplification registered between 1995 and 2010 in the German Neuroblastoma trials were analysed. Progressions and relapses were classified as locoregional, progression to stage 4S or to stage 4. Locoregional events were further classified into those manageable with one line of surgery or chemotherapy versus multiple episodes requiring more than one line of therapy.
Results: Of 896 patients with localized neuroblastoma, 161 experienced relapse or progression (124 locoregional, 16 to stage 4S, 21 to stage 4; 5-year-EFS 0.81±0.01; 5-year-OS 0.95±0.01). Five patients with locoregional progression died during or shortly after the first event, 78 were managed with one line of relapse treatment (surgery only in 28 patients), and 41 patients experienced more than one event (two events: n=16, three events: n=9, >3: n=16). Thirteen patients developed distant metastases in consecutive events. Compared to patients with multiple episodes of progression, patients with only one episode were younger (8 vs. 59 months, $p<0.001$), showed less freqently 1p aberrations (7% vs. 24%, p=0.02) and tended to present less often with stage 3 tumors (44% vs. 63%, p=0.054).Overall survival was excellent for patients with progression to stage 4S and with manageable locoregional events (one patients died from secondary malignancy), but unsatisfactory for patients with multiple locoregional events (5-year-OS: 0.59±0.08) or with progression to stage 4 (5-year-OS: 0.57±0.11).
Conclusion: In a substantial portion of patients, locoregional progressions or progressions to stage 4S were manageable assuring an excellent prognosis. Due to such "benign progressions", event-free-survival estimates in localized neuroblastoma may be misleading and have to be interpreted with caution.

O-125

METRONOMIC THERAPY AS LOW TOXIC AND EFFECTIVE TREATMENT FOR RECURRENCES OF HIGH RISK NEUROBLASTOMA

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Background/Objectives: Many patients with recurrences from high risk neuroblastoma have been treated with very limited success utilizing the "maximum tolerated dose (MTD) concept". It is known from breast and other cancers that low toxic continuous use of cytostatic and other drugs may overcome resistances. This metronomic approach is thought to target the microenvironment (immune cells, vasculature, stroma) and the cancer cells. Here we report the first results with pilot patients of a new metronomic concept.
Design/Methods: 20 patients with recurrences from high risk neuroblastoma (HR-NB) were treated with metronomic concept (celecoxib 2×200 mg/m^{2}xd oral cont., cyclophosphamide 25 mg/m^{2}xd oral cont., vinblastine 3 mg/m^{2}xd every 2 weeks, etoposide 25 mg/m^{2}xd oral d1-21 every 2nd month x4) up to 24 months. The secondary progression free and overall survival was compared to 307 patients with recurrent stage 4 neuroblastoma >18 months at diagnosis treated according to the MTD concept (palliative excluded) and weighted by time from diagnosis to recurrence (18 months) and number of sites of recurrences (1 vs.>1).
Results: One of the patients had 1 and 19 had 2-4 recurrences before start of metronomic therapy. 5 patients had one site, 11 two, and 1 three sites of recurrence (primary tumor 12, osteomedullary 12, CNS 3, liver 1, lymph nodes 1). Three patients were in CR after pretreatment of the relapse and therefore not included in the survival analyses. The 1 year EFS of the metronomically treated patients was 64±12% compared to 37±3% of the control group (logrank p=0.271) and the 1 year OS was 79±11% for the metronomic and 59±3% for the control patients (logrank p=0.052). The reported toxicity was minimal except grade 2-3 thrombocytopenia/ leukopenia/anemia (all heavily pretreated) and treatment was realized in an outpatient setting.
Conclusion: The metronomic approach is promising concept regarding outcome in HR neuroblastoma and has minimal toxicity. A prospective study is underway.

O-126

DEVELOPMENT OF A SCORING SYSTEM BASED ON A PROGNOSTIC INDEX FOR RISK ASSESSMENT OF PATIENTS WITH NEUROBLASTOMA

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Background/Objectives: Accurate risk stratification for patients with neuroblastoma still remains a challenge. While current algorithms consider a variety of clinical, histopathological and genetic markers for treatment allocation, the ideal strategy to combine these markers has remained elusive. We here aimed to develop a risk assessment system that is built on a computational model taking hazard ratios of individual prognostic markers into account.
Design/Methods: To develop a prognostic model for predicting event free survival (EFS), a large cohort of patients with neuroblastoma was divided into a training set for model building (n=411) and a validation set (n=209). Potential prognostic factors comprised stage, age, *MYCN* status, 1p status and four different gene expression-based classifiers that had been generated previously on an independent cohort. To build a reliable prognostic index (PI), variables were selected by the LASSO method (Least Absolute Shrinkage and Selection Operator), followed by backward selection using multivariable Cox regression. A risk score with three groups (low-, intermediate- and high-risk) was built based on an optimal stratification of the PI.
Results: Variable selection by LASSO identified stage, *MYCN* status, age and two gene expression-based classifiers as the most accurate variables for prediction of EFS. These variables were considered for further selection by multivariable analysis to finally build a new scoring system based on hazard ratios of the best performing markers. The final risk score was determined by two different gene expression-based classifiers (SVM_th24 and SVM_th44) only, showing highly accurate outcome prediction of patients of the

training cohort (5-year EFS, low-risk 83.2±2.6, intermediate-risk, 64.8±9.0, high-risk 32.0±4.0; p<0.001).
Conclusion: Results from the training set indicate that our approach provides an innovative scoring system that is highly accurate in predicting outcome of patients with neuroblastoma, and that gene expression-based classifiers are key determinants of the disease course. Validation of these findings in the independent validation cohort is pending.

Free Papers 23: New Biomarkers, Pre-Clinical Models & Treatments

O-127

HAILEY FISH - A ZEBRAFISH MODEL OF MALIGNANT RHABDOID TUMOR

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Background/Objectives: Malignant Rhabdoid Tumor (MRT) is one of the most aggressive and lethal pediatric malignancies. While kidney and brain are the most frequent primary sites of origin, MRT can develop at any anatomical location. Biallelic inactivation of the tumor suppressor gene *SMARCB1* (also known as *INI1*/*BAF47*/*SNF5*), is well recognized as the primary recurrent genetic event involved in the development of MRT. *SMARCB1* encodes a subunit of the SWI/SNF ATP-dependent chromatin-remodeling complex, The zebrafish (*Danio rerio*) is an important vertebrate organism used in biomedical research. In recent years, zebrafish has emerged as an attractive animal model in the study of cancer biology. In contrast to other vertebrates (including humans) bony fish (teleost) have two paralogues of *smarcb1* gene: *smarcb1a* and *smarcb1b*. The Smarcb1 proteins are highly conserved; suggesting shared cellular functions in fish and mammals. Because MRT is rare, a zebrafish model would be significant to explore questions regarding tumor biology and in developing new therapeutic strategies.
Design/Methods: Using TALEN and CRISPR mediated genome editing we have successfully mutagenized *smarcb1a* and *smarcb1b* genes.
Results: We have observed tumor development in *smarcb1b* mutagenized fish. Histological analyses revealed that zebrafish develop tumors that are morphologically similar to their human counterparts. We are expanding this study by targeting *smarcb1a* gene to compare tumors developed by individual and compound heterozygotes. We expect that double heterozygotes will develop tumors more easily and in the broader range of tissue than each individual heterozygote.
Conclusion: By comparing the expression profile of fish tumors and human MRT we hope to illuminate novel pathways involved in disease pathogenesis. In addition, our zebrafish model of MRT will be used to determine the cell of origin of this tumor and will serve as an *in vivo* drug-screening tool.
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TGF-BETA SIGNALING IS INVOLVED IN THE DETRIMENTAL EFFECTS OF SMARCB1 DEFICIENCY IN ATYPICAL TERATOID/RHABDOID TUMORS

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Background/Objectives: In the majority of atypical teratoid/rhabdoid tumors (AT/RT) inactivation of chromatin remodeling complex member SMARCB1 is the sole recurrent genetic event. Little is known, however, on downstream pathways which might represent targets for treatment.
Design/Methods: Using *Drosophila melanogaster* and the Gal4-UAS system, modifier screens were performed in order to identify pathways involved in the lethal phenotype associated with knockdown of *snr1*, the fly homolog of *SMARCB1*. The role of human homologs of identified genes was next investigated in human rhabdoid tumor cell lines as well as AT/RT tumor samples from the European Rhabdoid Tumor Registry EURHAB.
Results: The lethal phenotype associated with *snr1* knockdown in *Drosophila melanogaster* could be shifted to later stages of development upon additional knockdown of *babo*, the fly homolog of TGFbeta receptor type I. Similarly, pharmacological inhibition of TGFbeta receptor type I using SB431542 reversed the detrimental effect of snr1 knockdown in the fly model. TGFbeta signaling is transduced to the nucleus by SMAD proteins. In human AT/RT samples, SMAD family members were found to be highly expressed. In SMARCB1-deficient AT/RT cells, silencing of *SMAD3* and *SMAD6* expression reduced TGFbeta signaling activity (luciferase assay) and resulted in decreased proliferation (MTT and BrdU assay).
Conclusion: TGFbeta signaling is involved in the detrimental effects of SMARCB1-deficiency. Our results demonstrate that fly models can be employed for the identification of clinically relevant pathways in human cancer and provide a rationale for the investigation of TGFbeta directed treatments in AT/RT. Supported by Deutsche Krebshilfe (DKH110266) and IZKF Münster (Ha3/019/15).

O-129

BRENTUXIMAB VEDOTIN PRESENTS PROFOUND ANTI-TUMOR EFFICACY IN CD30+ AND CO-CULTURED CD30- GERM TUMOR CELLS

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Background/Objectives: Brentuximab vedotin (BV) consists of the potent antimitotic drug monomethylauristatin E (MMAE) attached to an anti-CD30 monoclonal antibody and thereby rendered inactive. After CD30-binding, internalization and linker-cleavage cytotoxic MMAE is intracellularly released and diffuses in the tumor microenvironment. While demonstrating significant activity in lymphoma, the efficacy of BV is yet unexplored in other CD30+ cancers such as germ cell tumors (GCT). Thus, in children with CD30+GCT who are at particular risk for treatment-related sequelae, BV may be a therapeutic option.
Design/Methods: CD30 was analyzed in 12 human GCT cell lines by quantitative RT-PCR and immunohistochemistry. Cytotoxicity of BV and free MMAE was measured by cytometry-based Hoechst assay differentially measuring viable CD30+GCT27 and CD30-JAR cells over time.
Results: CD30 is expressed in 7/12 GCT cell lines and is predominately detectable in embryonal carcinoma (EC) compartments. Treatment of CD30+GCT27 led to a time- and BV dose-dependent reduction of cell viability down to 68.6±6.9%(48h), 14.2±1.0%(72h) and 3.1±0.1%(96h) compared to daily controls at 250 ng/ml BV. In contrast, CD30-JAR cells unable to internalize BV only respond to free MMAE with residual cell viability of 86.2±18.1%, 19.2±2.5% and 7.0±2.2%, respectively. Of note, in co-culture not only CD30+GCT27 but also CD30-JAR cells exhibit a profound cytotoxic response to BV in a time and dose-dependent manner. After 96h of treatment with 250 ng/ml, 500 ng/ml and 1000 ng/ml BV 80.9±6.7%, 42.8±4.7% and 16.5±2.9% of CD30+GCT27 cells were still alive while viability of CD30-JAR cells was reduced to 56.1±22.5%, 34.5±18.1% and 18.8±11.7%, respectively. This indicates that MMAE released from CD30+GCT27 cells not only destroys the targeted cell population but also co-cultured CD30-JAR in a bystander fashion with comparable potency.
Conclusion: Based on these in vitro findings, Brentuximab vedotin may constitute a novel treatment approach warranting future clinical evaluation in children with malignant GCTs not only of pure but also mixed CD30+/CD30-histology.

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MYC AND MITOCHONDRIAL METABOLISM IN CHILDHOOD NEUROBLASTOMA

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Background/Objectives: Neuroblastoma, which arises from the sympathetic nervous system is one of the most aggressive solid tumors of early childhood. Amplification of the *MYCN* oncogene has been found in around 30% of neuroblastoma patients and it is associated with rapid tumor progression and poor prognosis. New treatment options are urgently needed for this group of patients. As metabolic adaptations are crucial for cancer cell survival during tumor progression, identifying metabolic discrepancies of aggressive tumors may be central in order to find new treatment strategies.
Design/Methods: We have treated neuroblastoma cells with a small c-MYC inhibitor, 10058F4, or with shMYCN-RNA and analyzed apoptosis, cell cycle progression, and differentiation. We have also performed proteomic analyses and used the results from these data for further functional studies including Seahorse experiments using a set of metabolic inhibitors.
Results: Our findings suggest that a small chemical molecule, 10058-F4, previously identified as a c-MYC inhibitor also targets the MYCN/MAX complex resulting in apoptosis and neuronal differentiation in *MYCN*-amplified neuroblastoma cells. Importantly, we found that inhibition of MYCN results in changes in neuroblastoma cell metabolism including mitochondrial dysfunction leading to accumulation of

intracellular lipid droplets. Using functional assays we found that MYCN contributes to metabolic plasticity in neuroblastoma cells.
Conclusion: Taken together, our results highlight that MYCN regulates important metabolic pathways in *MYCN*-amplified neuroblastoma, which may be the basis for development future therapies for this patient group.

O-131

SYNERGISTIC ANTITUMOR ACTIVITY OF TOPOTECAN AND EVOFOSFAMIDE (TH-302) MEDIATED BY OXIDATIVE STRESS IN PEDIATRIC SOLID TUMORS

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Background/Objectives: Previous studies have shown that topoisomerase I inhibitor, topotecan, induces oxidative stress in breast cancer cells. Topotecan treatment may yield increased hypoxia in tumors, and potentiate antitumor effects of evofosfamide (TH-302), a hypoxia-activated prodrug of bromo-isophosphoramide mustard. In this study, we assessed the oxidative stress in pediatric tumor cells after topotecan treatment. We also investigated the antitumor efficacy of combined topotecan and evofosfamide treatment in preclinical tumor models.
Design/Methods: A panel of twelve neuroblastoma (NBL), rhabdomyosarcoma (RMS), osteosarcoma and Ewing's sarcoma cell lines were cultured and exposed to topotecan, both as a single agent and in combination with evofosfamide, for 72 hours. Cell viability was measured using AlamarBlue assay. Tumor cell oxidative stress was determined by the 2, 7'-dichlorofluorescein diacetate (DCFDA) assay under topotecan treatment with/without the presence of evofosfamide. In vivo antitumor activity was evaluated in NOD/SCID mouse models. Cleaved caspase-3 was used as the apoptotic *marker in vivo*.
Results: All tested tumor lines showed anti-proliferative responses to topotecan with the IC_{50}s ranging from 3.6nM to 3.7μM. Adding topotecan to the evofosfamide treatment significantly increased cytotoxicity in all tumor cells ($p<0.05$). Our data indicated increased oxidative status, as revealed by increased reactive oxygen species measured by DCFA assay in tumor cells exposed to topotecan when compared with control cells ($p<0.01$). In NBL and RMS xenograft models, adding topotecan more significantly inhibited tumor growth comparing to single-agent evofosfamide or topotecan treatment ($p<0.01$). Complete tumor regression was observed in CHLA-20, SK-N-BE(2) and RH4 xenograft models with combined treatment. In the SK-N-BE(2) metastatic model, combined treatment group also showed improved animal survival than single-agent treatments ($p<0.01$). Increased tumor apoptosis was confirmed by cleaved caspase-3 immunostaining with combined treatment.
Conclusion: Topotecan increases oxidative stress in pediatric solid tumor cells. Synergistic therapeutic efficacy can be achieved when combining topotecan with hypoxia-activated prodrug evofosfamide.

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BIOMARKER IDENTIFICATION IN CEREBROSPINAL FLUID PROTEOME FROM CENTRAL NERVOUS SYSTEM (CNS) PEDIATRIC TUMOURS

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Background/Objectives: Sensitivity of combined cerebrospinal fluid (CSF) cytology and neuroimaging studies to diagnose leptomeningeal dissemination in CNS tumours –which is a key information to drive treatment- is relatively low. Changes in CSF proteome have been shown to reflect CNS pathological processes. We seek to characterize the CSF proteome of pediatric CNS tumours, to identify CSF biomarkers predictive of tumour proclivity to leptomeningeal spread, of patient recurrence, other than to assist diagnosis.
Design/Methods: CSF samples collected by lumbar puncture (18 medulloblastoma, 1 high-grade glioma, 5 ependimoma, 2 PNET, 1 atypical teratoid rhabdoid tumor), either at initial diagnosis (n=27) or at tumour recurrence (n=3), and 13 controls (extra-CNS non Hodgkin lymphoma) were processed with core-shell hydrogel nanoparticles and then analyzed with reverse-phase liquid chromatography/electrospray tandem mass spectrometry (MS/MS). Several physiological, technical and statistical challenges were considered and faced.
Results: Among the 559 non redundant proteins identified by MS/MS analysis, 147 were not present in the CSF database (http://www.biosino.org) and 91 were expressed or not in all the 40 subject (not discriminant proteins). The univariate selection procedure identified 47 significant proteins in at least one of the performed comparisons (cases versus controls, metastatic or not metastatic cases versus controls, respectively). Twenty-six 26 proteins out of 47 were afterwards selected because of their biological relevance. Fourteen of them were subjected to quantitative expression analysis on an independent validation cohort (60 cases, 14 controls), using western blotting, reverse phase protein arrays (RPPA) and Enzyme-Linked Immunosorbent Assay (ELISA).
Conclusion: Measuring biomarker performance in CNS pediatric tumours demonstrated to be a difficult task. Combining a unique dataset of CSFs from pediatric CNS tumours with a novel enabling nanotechnology allowed us to identify promising CSF proteins, possibly linked to CNS tumors.
Aknowledgments: Italian Ministry of Health; Associazione Bianca Garavaglia onlus

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O-133

CRANIO-FACIAL SECOND PRIMARY TUMORS IN HEREDITARY RETINOBLASTOMA PATIENTS PREVIOUSLY TREATED WITH EXTERNAL BEAM RADIOTHERAPY

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Background/Objectives: About half of children diagnosed with retinoblastoma (Rb) are carriers of a constitutional alteration of the *Rb1* gene. The prognosis of Rb is excellent, but carriers of this mutation have higher risk than general population to develop further malignancies, particularly in irradiation field if they have been previously treated by external beam radiotherapy (EBRT). These cranio-facial second primary tumors (SPTs) in irradiation field have a very poor prognosis.
Design/Methods: This retrospective monocentric study includes 219 patients diagnosed with hereditary Rb and treated by EBRT between 1968 and 2011 in the Institut Curie. Clinical, therapeutical, radiological and histological data were recorded. Radiological and histological centralized reviews were performed. Cranio-facial SPTs rate was estimated using the Kaplan-Meier method.
Results: Median follow-up was 241 months [5.3 - 461.2]. During the follow-up, 52 patients developed a cranio-facial SPT and a third tumor was diagnosed in 4 patients. Among the 52 SPTs, 46 were malignant (88%) and 6 benign (12%). Histologically, the most frequent subtypes were undifferentiated sarcomas in 22 patients (42%) and osteosarcomas in 17 patients (33%). Predilection sites were: facial bones (38%), orbit (33%) and ethmoid sinus (12%). At 10, 15 and 20 years after EBRT, the SPT rate was equal to 6.7% $CI_{95\%}$ [3.3% – 10.0%], 12% $CI_{95\%}$ [7.5% – 16.5%] and 24% $CI_{95\%}$ [17.5% – 30.0%] respectively. At 1, 2 and 5 years after STP diagnosis the overall survival was estimated to 81.6% $CI_{95\%}$ [71.5% - 93.2%], 75.0% $CI_{95\%}$ [63.5% - 88.3%] and 52.3% $CI_{95\%}$ [39.1% - 69.8%], respectively.
Conclusion: Undifferentiated sarcomas and osteosarcomas are the most common cranio-facial SPTs in irradiated hereditary Rb, which develop in specific locations. Their poor prognosis explains why current protocols avoid using EBRT –actually its indication has become exceptional– and justifies the efforts in early detection to try to improve their outcome.

O-134

CONSERVATIVE TREATMENT OF INTRAOCULAR BILATERAL RETINOBLASTOMA: A PROSPECTIVE PHASE II TRIAL FOR MACULAR OR PARAMACULAR INVOLVEMENT ON BOTH EYES OR ON THE ONLY SAVED EYE

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Background/Objectives: Chemotherapy associated with focal treatments for intraocular retinoblastoma, has allowed to achieve a higher rate of eye preservation without the use of external beam radiotherapy (ebrt). In order to decrease the possible long term sequels of laser scars for macular-paramacular tumors, a protocol of laser reduction was initiated.
Design/Methods: Children affected by intraocular bilateral macular-paramacular retinoblastoma (defined by a distance to macula of 3mm of less), on both eyes or on the only saved eye, were included in a prospective, nonrandomized, phase ii trial, conducted at the Institute Curie. The protocol combined 6 cycles of 3 drugs (vincristine, carboplatin and etoposide), with thermotherapy macula-sparing associated from the third cycle.
Results: Nineteen patients (26 eyes) were included from July 2004 to November 2009. Median age at diagnosis was 6 months. According to Reese-Ellsworth classification, 13 eyes were group I-IV and 13 group V (Vb for 5 eyes). According to international retinoblastoma classification, 16 eyes were group b-c and 10 group d.
Macular-paramacular tumours were treated with chemotherapy alone in 9 eyes, chemotherapy associated to thermotherapy macula-sparing from the third cycle in 17 eyes. Four eyes experienced macular relapse during the first year from the end of treatment. At a median follow-up of 77 months, 23 eyes (88.5%) were salvaged without

EBRT or enucleation (2 eyes needed enucleation and 1 EBRT). The median visual acuity (VA) of the 24 eyes preserved was 20/50 at a median age of 7.2 years. Nine eyes presented VA ≥ 20/40, 9 between 20/40 and 20/200, and 6 eyes had VA < 20/200. No severe treatment side effect was observed.
Conclusion: Six cycles of 3 drugs chemotherapy associated with macula-sparing thermotherapy achieves good local control, improving the rate of eye preservation without EBRT, and moreover, decreases macular damage allowing to often obtain satisfactory visual results.

O-135

FEMALE SEX, BILATERAL DISEASE, AGE BELOW 3 YEARS AND APPREHENSION FOR ENUCLEATION CONTRIBUTE TO A HIGH RATE OF TREATMENT ABANDONMENT IN PATIENTS WITH RETINOBLASTOMA

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Background/Objectives: Aim was to study the rate and cause of treatment abandonment in patients with retinoblastoma, a major obstacle to treating retinoblastoma in developing countries.
Design/Methods: The study was retrospective and conducted in a referral center in North India. Non-compliance was defined as adherence to <3 cycles of chemotherapy and/or defiance of recommended local treatment. Two cohorts of patients were studied. One was a larger cohort (n=602) of all patients diagnosed with retinoblastoma in the institution from 2000 to 2014. Limited variables (Age, sex, laterality) were examined in the larger cohort, as it was unfeasible to explore all factors influencing compliance due to incomplete data or lost contact. Detailed interview was performed with care-givers in a smaller cohort of 104 patients (compliant: 60; non-compliant: 44), with whom contact was possible.
Results: One-hundred and seventy (28%) patients were non-compliant. Patients below 3-years were more likely to be non-compliant (32.5%) compared to older patients (22.8%) (p=0.01). Compliance was greater among males (64%) than females (36%) (p=0.017). Patients with unilateral disease were more compliant (72%) compared to those with bilateral disease (28%) (p=0.009). Apprehension for enucleation was expressed more frequently in the non-compliant (64%) than the compliant group (8%) (p=0.0001). A larger proportion (61.4% vs. 13.3%) of non-compliant patients stated difficulty in attending outpatient services of different departments for multimodality treatment (p=0.003). The mortality in compliant versus non-compliant patients was 7% and 68%, respectively (p=0.0001). Variables that did not influence compliance included, symptom-to-diagnosis interval (p=0.59), residence-to-hospital distance (p=0.49), rural background (p=0.35), financial limitation (p=0.23), socio-economic status (p=0.7), number of siblings (p=0.41) or extra-ocular disease (p=0.32).
Conclusion: The rate of treatment abandonment in 602 patients over a 15-year period was a sizable 28%. The factors that contributed to non-compliance included, female sex, bilateral disease, age <3-years, apprehension for enucleation and difficulty in attending outpatient services of different departments.

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PARENTS' PERSPECTIVE OF QUALITY OF LIFE IN RETINOBLASTOMA SURVIVORS: A CROSS-SECTIONAL STUDY OF 122 PATIENTS

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Background/Objectives: Retinoblastoma (Rb) is the most common intraocular tumor in childhood. With current modalities, the cure rates are high and hence the number of survivors is increasing. However, the data on quality of life (QOL) in this population are minimal.
Design/Methods: We analyzed the QOL in 122 retinoblastoma survivors using the parent-proxy report of PedsQL™ 4.0 generic core scale in local language, which has been validated in Indian population. The questionnaire was filled by parents of children of more than 5 years of age who had completed treatment for more than 12 months. The questionnaire consists of 23 questions on physical, social, emotional and school domains on a scale from 0 to 4. This was converted to a scale from 0 to 100, where higher values represented better QOL. This was compared with parent-reported QOL of 50 siblings. Factors predicting the QOL were assessed.
Results: The median age of Rb survivors was 98 (range, 60-247) months and 68% were males. Seventy-nine percent were International Retinoblastoma Staging System stage 1 and 25% had bilateral disease. Fourteen percent had extraocular involvement and 22% had received radiotherapy. The overall parent-reported QOL was significantly worse in Rb survivors as compared to controls (74.4 ± 8.5vs85.1 ± 4.6, p< 0.001). All the 4 health domains (physical, emotional, school and social) were found to be significantly affected when compared with controls. None of the baseline and treatment related factors predicted worse QOL in the survivor group.
Conclusion: QOL is often a neglected aspect in survivors of pediatric solid tumors. We found a significantly worse parent-reported QOL in Rb survivors, including the physical and psychosocial aspects. However, no predicting factors for worse QOL were found in this group. Although a high survival rate has been achieved in early stage Rb, efforts need to be made to improve QOL.

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LONG TERM NON-VISUAL OUTCOMES IN SURVIVORS OF RETINOBLASTOMA

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Background/Objectives: With multi-modality approach, the outcomes of patients with retinoblastoma have improved. With increasing number of survivors, the long-term aspects need to be addressed. Sensory-neural hearing loss has been reported in 0-79% of retinoblastoma survivors, attributed to carboplatin. However, data on short-stature in retinoblastoma survivors are limited.
Design/Methods: We conducted a cross-sectional study to assess height and hearing loss in retinoblastoma survivors, who had completed therapy for more than 1 year and were more than 5 years of age. Clinical and treatment related data were obtained from the database.The recorded height was compared with median height for age and sex as per the WHO growth standards. Z-scores were calculated for all patients and a patient with z-score of less than -2 was considered short-statured. Baseline clinical and treatment related factors were analyzed for any association with short-stature. Hearing loss was assessed by pure tone audiometry upto 8,000 Hz.
Results: One-hundred thirty-eight patients with a median follow-up was 5 years were assessed.One-third (46/138) of retinoblastoma survivors were short-statured. The mean height of this group was significantly shorter than the mean 50th percentile height for same age and sex (119.7 ± 14.8 cm vs 129.9 ± 15.5 cm, p<0.001). Previous chemotherapy was found to be associated with short stature (36% vs 11%, p=0.04), whereas no association was observed with radiotherapy (32% vs 38%, p=0.57). Pure tone audiometry was performed in 116 survivors. One of 116 survivors (<1%) was found to have sensory-neural hearing loss at high frequency (6,000- 8,000 Hz). The cumulative dose of carboplatin received by this patient was 3360 mg/m^2.
Conclusion: Short stature affects a significant number of retinoblastoma survivors and is significantly associated with previous chemotherapy. Sensory-neural hearing loss is uncommon, affecting less than 1% of survivors. We therefore recommend assessment of stature and appropriate endocrinology referral at follow-up visits of retinoblastoma survivors.

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DO MITOCHONDRIAL D-LOOP MUTATIONS PLAY A ROLE IN HUMAN RETINOBLASTOMA?

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Background/Objectives: Preserving vision remains a challenge for ophthalmologists treating children with retinoblastoma. Alteration in mitochondrial DNA plays an important role in the development and progression of cancer. The Displacement Loop (D-loop) region of mitochondrial DNA is the regulatory region for its replication and transcription. It is considered to be a mutational "hot spot" in human cancers. It is the most polymorphic region of human mtDNA genome. Mutation rate is much faster in mitochondrial genome than nuclear genome. We aimed to characterize somatic variations/mutations in the D-loop region of mitochondrial DNA and their impact on survival in retinoblastoma patients.
Design/Methods: The entire D-loop region of mtDNA was amplified in polymerase chain reaction and variations were evaluated in 60 retinoblastoma patients by direct DNA sequencing and their results were analyzed by Mitomap database. Somatic mutations were correlated with clinical, histopathological parameters and patient survival. Kaplan-Meier method was used to draw the survival curves.
Results: In 60 retinoblastoma patients, 516 variations in 441 positions were found when compared to Mitomap database. All variations were single nucleotide substitutions. Majority of these somatic mutations of mtDNA were homoplasmic as compared to heteroplasmic. The most common variations were T to C and C to T followed by A to G. 368/441 (83.44%) variations was found in hypervariable regions of mitochondria. There were 5.81% novel variations observed on comparison with the MITOMAP database. The most common instabilities observed at the first polymorphic C track.

A73G (83.33%) were the most frequent variations in which A263G was statistically significant with overall survival of patients.
Conclusion: This is the first study to show a high frequency of mtDNA variations in retinoblastoma. Our results strongly indicate that pathogenic mtDNA mutations may be a potential prognostic marker for retinoblastoma. Furthermore, dysfunctional mitochondria may play an active role in cancer development and the patient's response to radiotherapy/chemo-radiotherapy.

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UROLOGICAL OUTCOME AFTER HIGH DOSE RATE BRACHYTHERAPY FOR BLADDER-PROSTATE RHABDOMYOSARCOMA IN CHILDREN

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Background/Objectives: To evaluate urological outcome after high dose rate brachytherapy (HDR-BT), as part of multi-modality treatment for Bladder-Prostate Rhabdomyosarcoma in children.
Design/Methods: Five children, 1 girl and 4 boys, aged 0-8 years, received primary treatment for Bladder-Prostate Rhabdomyosarcoma (BP-RMS) with multimodality treatment including HDR-BT at the Karolinska University Hospital between 2004 and 2014. The tumor size was 1.5-5.5 cm and none of the patients had neither local invasion outside of the bladder and prostate nor metastases at diagnosis. All patients were pre-treated according to CWS protocols. Surgery was limited to placement of BT-catheters in 3 out of 5 patients. HDR-BT was given twice daily during the first five post-operative days (HDR Micro-Selectron, Nucletron, The Netherlands) to a total dose of 24-42 Gy. Additional external beam radiation was given in 3 cases and the combined total radiation dose was 39-58 Gy.
Results: After follow-up of 12-132 months, all 5 patients are alive with no evidence of disease. One patient has undergone total cystoprostatectomy due to incomplete response to primary treatment. Follow-up with ultrasonography has shown no upper tract dilatation or residual urine in 4 patients and mild non-progressive upper tract dilatation in one patient after cystoprostatectomy with temporary ureter-cutaneostomies. Plasma creatinine levels (range 31-59) and Cystatine-C based GFR estimates (>90) are normal for age in all patients. Urine flow measurements have shown bell shaped curves and maximal flow rates in the normal range (13.8-19.3 ml/s) in 4/4 patients treated without radical surgery. 3 out of 4 boys report normal erections.
Conclusion: We report the medium-term urological outcome after HDR-BT for BP-RMS in children. The occurrence of urological squelae in this cohort of patients is surprisingly low. Avoidance of surgery to the bladder neck and trigonum might contribute to this finding.

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PREDICTORS FOR OUTCOME AND IMPACT OF LYMPH NODE SURGERY IN LOCALIZED EMBRYONAL PARATESTICULAR RHABDOMYOSARCOMA – A REPORT FROM THE CWS-86, -91, -96, AND -2002P TRIALS

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Background/Objectives: Patients with paratesticular rhabdomyosarcoma (PRMS) are known to have an excellent prognosis. Retroperitoneal lymph node (LN) involvement is common in patients > 10 years, but the optimal treatment of retroperitoneal LN disease remains unclear. The aim of the study was to evaluate predictors for outcome and the role of LN surgery in patients with localized embryonal rhabdomyosarcoma (eRMS) treated within four consecutive Cooperative Soft Tissue Sarcoma (CWS) trials between 1986 and 2008.
Design/Methods: 147 patients with PRMS and complete data set suitable for this analysis were included. All patients were treated according to the treatment protocols of the CWS trials including multiagent chemotherapy, tumor resection and / or radiotherapy. IRB approval was obtained for all trials.
Results: The outcome of the patients was excellent (5-year-EFS: 89.8%±2.6). Positive predictors for outcome were age ≤10 years and a tumor size <5cm (EFS: 96.7%±2.3, p=0.008). Primary lymph node sampling of inguinal / iliacal lymph nodes was done in 15/147 patients, of which 12 were positive and 3 were pNx. The EFS (85.1%±9.7) was comparable to patients, who did not undergo inguinal lymph node surgery (EFS: 88.5%±3.2, p=0.619) without additional local therapy in most patients. Thirty-two patients underwent secondary retroperitoneal lymph node dissection. Viable tumor was only found in 8/32 patients, who had an inferior outcome compared to the 24 other patients (EFS: 50%±17.7 vs. 76.8%±9.2). 4/8 patients were >10 years.
Conclusion: The outcome of patients suffering from PRMS is excellent and is hardly improvable. Positive predictors for outcome are age ≤10 years and tumor size <5cm. Primary lymph node sampling seems to have no impact on the EFS and should not be recommended. Secondary retroperitoneal lymph node dissection revealed a high number of unnecessary procedures, but patients with positive lymph nodes had a poor prognosis and require additional local therapy.

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FDG-PET/CT IMPROVES STAGING IN EXTREMITY RHABDOMYOSARCOMA

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Background/Objectives: The objective of this retrospective study was to compare FDG-PET/CT with conventional imaging (CI) in initial staging and evaluate if the staging modality is associated with a difference in event free and overall survival.
Design/Methods: We included all patients with extremity rhabdomyosarcoma from 2000-2014 in the 4 surgical pediatric oncology centers in the Netherlands. Patients charts were evaluated for patient and tumor characteristics, radiology reports and outcome.
Results: We included 20 patients with a rhabdomyosarcoma of the extremities. In 10 patients a FDG-PET/CT scan was performed in addition to conventional imaging. In the other 10 patients staging was performed by conventional imaging (ultrasound, MRI and/or CT scan) only. Patient and tumor characteristics were comparable in the two groups. Follow up of surviving patients was different in the two groups (median of 30 (11-73) vs 96 (17-47) months) because FDG- PET/CT was only performed since 2007. No patients had distant metastases. In the FDG-PET/CT staged group 5/10 patients were staged as N0 (without lymph node metastases) and 5/10 patients as N1 (with lymph node metastases). In the CI staged group 8/10 patients had no lymph node metastases and 2/10 had lymph node metastases. Of the 5 N0 patients in the FDG-PET/CT group no patient had a relapse and all patients are alive. Of the 8 N0 CI staged group 6 patients had a relapse and 4 of these patients died.In N0 patients the EFS was significantly better in FDG-PET/CT staged patients (p=0.01), OS was not significantly better (p=0.06).
Conclusion: Patients without lymph node metastases staged with FDG-PET/CT have a significantly better outcome than N0 patients staged with conventional imaging only. So FDG-PET/CT should be a part of staging patients with extremity rhabdomyosarcoma.

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TREATMENT AND OUTCOME OF PATIENTS WITH THORACIC RHABDOMYOSARCOMA – A REPORT FROM THE COOPERATIVE SOFT TISSUE SARCOMA TRIALS CWS-81, -86, -91, -96, -2002P AND SOTISAR

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Background/Objectives: Rhabdomyosarcoma (RMS) is the most common pediatric soft tissue sarcoma and can also be observed at the thoracic wall or within the chest. Surgical management of these tumors can be challenging. The aim of the study was to analyze patients treated within six different Cooperative Soft Tissue Sarcoma (CWS) trials suffering from intrathoracic and chest wall RMS regarding treatment, outcome and surgical procedures.
Design/Methods: 2525 pediatric patients suffering from rhabdomyosarcoma were enrolled into five different CWS trials from 1981 to 2014. 53 patients with localized disease were identified with diagnosis of intrathoracic or chest wall RMS, of which 20 were male and 33 were female. One patient was excluded due to an incomplete data set. A retrospective chart analysis was carried out. IRB approval was obtained for all trials.
Results: The median age of the patients was 8.6 years [0-19]. The 5-years overall survival rate was 58.7%±7.4. The 5-years event free survival (ES) was 47.8%±7.4. 34 patients had tumors located at the chest wall (ES: 58%±8.6) and 18 patients within the thoracic cavity (ES: 23.2%±11.6). 31 patients were younger than 10 years (ES: 43.6%±9.6) and 21 were older (ES: 54%±11.4). Patients with a tumor size ≤5 cm (n=17) had a better

outcome (ES: 70.1%±11.2) compared to those with a size >5 cm (ES: 36.5%±8.8). Interestingly, patients with embryonal RMS had a worse outcome (n=29; ES: 38.1%±9.7, relapse: 14/29) compared to alveolar RMS (n=23; ES: 57.5%±11.2, relapse: 4/23). Incomplete primary and secondary resections were performed in 44%.
Conclusion: Thoracic RMS belongs to the sites with unfavorable prognosis with a high rate of incomplete resections and relapses. Local control of these tumors needs to be urgently improved regarding completeness of resections and local radiotherapy.

O-143

STAGE III DISEASE IN PEDIATRIC NON-RHABDOMYOSARCOMATOUS SOFT TISSUE SARCOMA IS AN INDEPENDENT PREDICTOR OF POOR OUTCOME DESPITE SURGICAL RESECTION

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Background/Objectives: Pediatric non-rhabdomyosarcomatous soft tissue sarcomas (NRSTSs) are rare tumors which are not well studied.
Design/Methods: All children with NRSTSs treated between June 2003 and December 2012 were analysed for treatment outcome and prognostic factors.
Results: A total of 70 patients were analysed with median age of 15 years (range;1-18 years).The most common histological subtypes were synovial sarcoma (34%), neurofibrosarcoma (13%) and fibrosarcoma (8%). Median tumor size was 7.6 cm (2-20 cm), with 69% patients having tumor size > 5 cm. Staging was done according to American Joint Committee on Cancer Staging System generally used for adult sarcomas. Forty-nine (70%) patients underwent surgical resection, out of which 45 patients had localized disease. The 5-year EFS and OS rates were 42% and 55%, respectively for whole cohort and 55% and 69% respectively for surgically resected group. For surgically resected group, univariate analysis identified stage III disease (p -0.01, HR 2.89; 95% CI 1.2 -6.9) associated with poor EFS. For OS, univariate analysis identified tumor size > 5cm (p-0.05) and stage III disease (p <0.001) as adverse prognostic factors, however in multivariate analysis, only stage III disease (p - 0.002; HR 5.3; 95% CI 1.8-15.5) emerged as poor prognostic factor for OS.
Conclusion: Stage III tumors faired worse even after curative resection. Thus, this subgroup of NRSTSs requires careful patient selection for therapeutic decision making if any mutilating surgery is being considered. There is also a need for development of better staging system for children with NRSTSs.

O-144

EXTREMITY AND NON-EXTREMITY SYNOVIAL SARCOMA IN CHILDREN

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Background/Objectives: Synovial sarcoma is the most common non-rhabdomyosarcoma soft tissue sarcoma in children and adolescent, accounting for 10% of all soft tissue sarcomas. The outcome of patients with non-extremity SS is generally poor than that of patients with extremity tumours.
Design/Methods: The records of patients with extremity (n=20) and non-extremity (n=9) synovial sarcomas treated between February 2006 and October 2014 were analysed.
Results: Complete surgical resection with histological clear margins was achieved in all patients with extremity tumour, 14 as initial and 6 as delayed surgery after chemotherapy. In patients with non-extremity tumours, initial excision was performed in five and delayed surgery in four patients. The median follow up duration was 47 months. There were no local recurrences in patients with extremity tumours while distant metastases occurred in five patients. Two patients with non-extremity tumours had local recurrences and one had distant metastases. The 5-year overall survival and event free survival was 80% and 67.8% respectively for the entire cohort. The 5-year overall survival and event free survival were, respectively 88.2% and 69% for extremity tumours and 62.5% (p=0.2) and 63.5% (p=0.7) for non-extremity tumours.
Conclusion: Local recurrence was the commonest failure in non-extremity tumours while distant relapses were the only failures in patients with extremity tumours. Although there was a trend towards better survival in patients with extremity tumours, it was not statistically significant.

IPSO Session 2: Renal Tumours

O-145

NUTRITIONAL STATUS OF CHILDREN WITH WILMS TUMOUR ON ADMISSION TO A SOUTH AFRICAN HOSPITAL AND ITS INFLUENCE ON OUTCOME

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Background/Objectives: In developing countries the prevalence of malnutrition on admission amongst paediatric patients with cancer can be as high as 69%. High rates of malnutrition occur due to factors such as poverty, co-morbidities, late presentation and advanced disease process. Weight has been shown to be an inaccurate parameter for nutritional assessment of patients with solid tumours as it is influenced by tumour mass. This study aimed to assess the prevalence of malnutrition amongst our patients with Wilms Tumour (WT) and the level of nutritional support received within 2 weeks of admission, as well as the influence of nutritional status on outcome.
Design/Methods: Seventy six children diagnosed with WT and admitted to Inkosi Albert Luthuli Central Hospital between 2004 and 2012 were studied prospectively. Nutritional assessment took place before starting treatment and included weight, height, Mid-Arm Circumference (MAC) and Triceps Skinfold Thickness (TST). Outcome was determined at 2 years after date of admission. Time until commencement of nutritional resuscitation, and nature thereof, were recorded.
Results: Stunting and wasting were evident in 12 and 15% of patients respectively. By including MAC and TST, the prevalence of malnutrition was shown to be 57%. Malnourished children had significantly larger tumours than those who were well nourished. Malnutrition was not a predictor of poor outcome and did not predict advanced disease. In relapse-free patients, nutritional status was not related to treatment toxicity. Eighty four percent of patients received nutritional resuscitation within 2 weeks of admission.
Conclusion: Nutritional assessment in children with solid tumours should include MAC and TST. Malnutrition at the time of admission was not shown to be related to poorer outcome after 2 years. This may be due to the effects of early aggressive nutritional resuscitation as part of management by a multidisciplinary team, although numbers are small.

O-146

THE CHALLENGE OF DIFFERENTIAL DIAGNOSIS BETWEEN WILMS TUMORS, NEUROBLASTOMAS AND NON-WILMS RENAL TUMORS

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Background/Objectives: To evaluate cases that have been initially treated as WT and in fact proved to be another histology, in order to reduce the mistaken diagnosis thereby avoiding neuroblastoma or non-Wilms renal tumors to receive unnecessary preoperative chemotherapy.
Design/Methods: Retrospective analysis of 446 medical records and images of WT, neuroblastoma and non-Wilms renal tumors diagnosed in children admitted at Pediatric Oncology Institute-GRAACC/ UNIFESP from 1984 to 2012. The clinical characteristics and the image exams of the patients who attended to the inclusion criteria were studied and reviewed.
Results: 5 patients were mistakenly diagnosed and treated as a WT. They had neuroblastoma or another renal tumor, showing a 98.87% accuracy on the diagnosis performed. All 5 patients were males and less than three years old. Among the studied patients, 4 presented unilateral renal involvement and 1 presented bilateral renal involvement. None had metastasis at diagnosis.
Conclusion: In some cases it can be difficult to perform the differential diagnosis between WT, neuroblastoma and other renal tumors based only on the clinical and image data. We had 1,12% of mistakenly diagnosed cases, which demonstrates the efficacy on the diagnosis performed at IOP-GRAACC/UNIFESP. Certainly, future studies with more patients will enable a deeper view of neuroblastoma or other non-Wilms renal tumors treated as a WT frequency, as well as their impact in survival.

O-147

OUTCOME OF CHILDREN WITH STAGE IV WILMS TUMOR TREATED ON AIIMS-WT-99 PROTOCOL

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Background/Objectives: To evaluate the outcome of children with stage IV Wilms tumor (WT) on AIIMS-WT-99 study.
Design/Methods: All children with Stage IV WT registered from October 2000 through December 2012 were included. Tumors deemed resectable, underwent upfront resection. Unresectable/inoperable tumors received pre-resection chemotherapy (Vincristin+Dactinomycin+Doxorubicin). Adjuvant pulmonary and flank radiotherapy was advised to all patients. Metastatectomy was performed for lung nodules that remained after chemotherapy and radiotherapy. Kaplan Meier survival estimates for 5-year overall survival (OS) and event free survival (EFS) were calculated. Events were defined as death, recurrence or progression of disease.
Results: Of 219 children of WT, during this period, 36 (16%) were stage IV tumors. Pulmonary metastases were present in 33 of whom 5 also had concomitant liver metastases. Isolated liver metastases were present in 3. Nine patients underwent upfront resection followed by adjuvant chemotherapy and radiotherapy. Radiotherapy for metastatic disease was administered to 26/36 patients. Pulmonary metastatectomy was performed in 5 patients. Eighteen of 36 (50%) patients were alive at last follow-up, giving a 5-year OS of 48%(95CI 41.3-75.9) with a mean survival time of 59 months(limited to 115months). Of these 18 alive, only 15 were disease free, while the remaining 3 had recurrent or progressive disease. 16/28 (57%) patients with lung only metastases achieved a disease free status while of the 8 with liver metastases only 1 achieved disease free status. Twenty events were recorded (11 recurrences and 9 disease progression). The 5-year EFS was 42.4% (95% CI 33.4-67.6) with a mean survival time of 50.49 months limited to 115 months.
Conclusion: On the current multimodal therapy, Stage IV WT had a poor 5-year EFS (42.4%), especially those with liver secondaries. Fifty-five percent of patients developed progressive or recurrent disease. This highlights the need for more aggressive therapy for these patients.

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MINIMALLY INVASIVE TUMOR NEPHRECTOMY FOR NEPHROBLASTOMA

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Background/Objectives: Despite the lack of guidelines within current treatment protocols, minimally invasive nephrectomy is increasingly being used as technique for tumor removal in nephroblastoma. Several issues have to be considered concerning this approach. We analyzed children undergoing laparoscopic WT resection at our institution. Technical aspects for a safe procedure and an adequate Lymph node sampling are highlighted.
Design/Methods: IRB approval was obtained. Between August 2010, and March 2015, 8 children underwent transperitoneal laparoscopic nephrectomy for WT. Patients' data, tumor characteristics, surgical, and oncological outcome were assessed. LN sampling was reviewed with special emphasis.
Results: Mean age at surgery was 28.31 months (range 12-57.5). All children received neoadjuvant Actinomycin-D/Vincristin. All tumors showed response to chemotherapy; mean tumor volume was 296.13 ml (162-850) at diagnosis and 81.13 ml (15-207) at surgery. Complete tumor resection was achieved via a 4 trocar-technique in all children, resulting in local stage 1 in all cases. No tumor rupture occurred. Resected specimens were retrieved from the abdomen via Pfannenstiel incision using a retrieval bag. Adequate lymph node sampling (6 or more) was performed before dissection of the kidney and was realized in all cases by applying surgical steps similar to other procedures on the upper urinary tract (elevation with stay sutures, vascular dissection before tumor mobilization, positioning of trocars, and others). Mean operating time was 147 minutes (93-190). There were no complications and all children are alive without evidence of disease after a mean follow up of 24.1 months (0-54).
Conclusion: Minimally invasive surgery is a safe option for WT resection provided that patients are carefully selected and operating surgeons have sufficient expertise in pediatric oncology and minimally invasive urology. Adequate LN sampling is possible via the minimally invasive approach. However the laparoscopic technique must not be reason for not complying with the general guidelines for WT surgery.

O-149

DEVELOPMENT OF RENAL DYSFUNCTION LONG AFTER NEPHRECTOMY FOR CASES WHERE ADJUVANT THERAPY WAS NOT A CONFOUNDING PROGNOSTIC FACTOR

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Background/Objectives: The prevalence of mild-to-moderate renal dysfunction in Wilms tumor patients surviving beyond the age-related physiological renal function decline may be due to adjuvant therapy rather than 50% reduction in renal parenchyma. We aimed to evaluate renal function in adult patients who underwent nephrectomy during childhood and received or did not receive postoperative radiotherapy.
Design/Methods: We assessed the estimated glomerular filtration rate (eGFR) and blood pressure in 13 patients older than 30 years who underwent nephrectomy during childhood for medical causes (Group A), and in 13 Wilms tumor patients surviving beyond the age of 30 years after nephrectomy and postoperative radiotherapy (Group B). The primary outcome of the study was the evaluation of renal function amongst the two groups. Data are expressed as mean±SD or numbers.
Results: There were no significant differences in age at surgery (2.41±4.1 vs. 3.88±2.8 years; p=0.3) and age at follow-up (40.92±7.74 vs. 43.15±6.46 years; p=0.43) between Group A and Group B. Likewise, eGFR (85.69±19.22 vs. 78.30±20.62 mL/min/1.73 m^2; p=0.35), systolic blood pressure (117±11.19 vs. 124.23±16.81 mmHg ; p=0.22) and diastolic blood pressure (74.9±7.31 vs. 80 ± 9.12 mmHg; p=0.14) were similar at follow-up. Renal dysfunction was documented in 8 patients of Group A and 11 of Group B (p=0.37). Systolic hypertension (blood pressure ≥130 mmHg) and diastolic hypertension (blood pressure ≥ 80mmHg) were found in 2 vs. 5 (p=0.37) and in 4 vs. 9 patients (p=0.11), respectively.
Conclusion: Present data suggest that children who undergo nephrectomy for oncological or non-oncological causes, require a life-long nephrologic surveillance because renal dysfunction is a dose-dependent predictor of morbid cardiac events and overall mortality.

O-150

DECREASING THE INCIDENCE OF POST OPERATIVE INTESTINAL OBSTRUCTION IN WILMS TUMOR: A MODIFIED SURGICAL APPROACH

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Background/Objectives: Intestinal obstruction is one of the main postoperative complications in Wilms tumors. The authors postulate that manipulation of the small intestine (SI) and cutting of anatomical peritoneal reflections opens a way for SI migration to the the retroperitoneal space and predisposes for obstruction. The modified approach describes a technique that entails a conservative approach towards SI manipulation and cutting of the peritoneal reflections/evaluating the role of the aforementioned surgical approach regarding its technical utility and the incidence of postoperative intestinal obstruction.
Design/Methods: A retrospective review of all patients with Wilms tumor who underwent surgery between January 2012 and December 2014 using this approach. Data collected included demographic data, tumor characteristic(size, stage), intraoperative tumor rupture, post operative radiotherapy and postoperative intestinal obstruction.The technique used the transverse incision , once in the peritoneal cavity we cut the peritoneal reflections short of the ceacum or short of the sigmoid . The phrenocolic ligament is as well reserved. The colon is reflected over SI packing it, proceeding to nephrectomy and lymph node sampling.
Results: The study included 65 patients (31 male,34 female).Mean age was 3.2 years (0.6 - 11). Upfront surgery were done in 24 patients(36.9%) while 41 patients (63.1%) received preoperative chemotherapy .The mean tumor largest diameter was 13 cm. (9 - 18). Local staging were, I 10 patients(15.4%) , II 9 patients (13.8%) III 46 patients(70.8%) . forty nine patients (75.4%) received Post operative flank irradiation. No intraoprtative tumor rupture occurred. During the follow up period (3 months - 3 years) one patient (1.5%) developed postoperativ inusssusception.
Conclusion: The modified surgical approach allows minimal manipulation of SI and prevents it's migration to the retroperitoneal space which contributes to decreasing the incidence of postoperative intestinal obstruction with no increased risk of tumor rupture.

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GASTROSTOMY COMPLICATIONS IN PEDIATRIC CANCER PATIENTS: A RETROSPECTIVE SINGLE-INSTITUTION REVIEW

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Background/Objectives: Complications in pediatric cancer patients after a gastrostomy (GT) placement have not been widely investigated. We aimed to evaluate the complication rate and nature of complications in this population.
Design/Methods: Medical records of pediatric cancer patients having a GT placed at our institution between 1998 and 2013 were retrospectively reviewed. Variables analyzed included gender, age at procedure, primary cancer diagnosis, surgical procedure, duration of GT usage, ANC level at procedure and complications.
Results: One hundred seventy-one patients (92 males, 79 females) who underwent 181 GT placements (110 open, 59 endoscopic and 12 laparoscopic) were identified. Median age was 6.0 years (range, 0.2-21). One hundred one patients had a central nervous system tumor, 45 had a solid tumor and 25 had leukemia/lymphoma. Median ANC level was 3300/mm^3 (range, 0-38988). Median duration of GT usage was 8.0 months (range, 0.2-142). Complications occurred in 106 patients (61.9%). Major complications, including intrabdominal complications (2.2%) and GT site infections (23.7%) occurred in 46 patients (11 perioperative). Minor complications occurred in 64 patients, the most common of which were granulation tissue (28.8%) and GT site leakage (21.4%). Younger age at GT placement was associated with increased risk of developing a complication (0.048) and open GT was associated with increased risk of GT site infection (0.003). No statistical significance was observed between complications and gender, primary cancer diagnosis, surgical procedure, duration of GT usage and ANC at procedure.
Conclusion: A significant number of complications are seen after GT placement in pediatric cancer patients, however the incidence of complications in our report is similar to previously reported series in non-cancer patients. Younger patients were more likely to have complications and GT site infections were more common after open GT procedures. New guidelines have been established in order to decrease the complication rate in this specific population.

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EFFICIENCY OF PHOTODYNAMIC TREATMENT FOR RECURRENT SOLID TUMORS IN CHILDREN

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Background/Objectives: To assess results of photodynamic treatment (PDT) with photosensitizers of chlorine family in children with solid tumors.
Design/Methods: PDT was conducted to 9 patients with recurrent solid tumors. The mean age was 1.8.PDT was intraoperative after tumor removal. We used laser equipment "Lakhta Milon" (Russia). Output laser power was 2.5 W. During treatment the laser power density ranged from 0.1 to 0.8 W/sm^2. We used different doses of photo energy - from 300 to 400 J/sm2, and for tumors deep infiltrating growth - up to 500 J/sm2.Administered photosensitizer dosage was 0.6-0.8 mg/kg of the patient's body weight. Exposure duration depended on tumor size and was from 10 to 30 min. For tumor exposure we used the light guide with end-formed microlens. Case follow-up and dressing changes were outpatient. Number of appointments starting with primary inspection and up to results of assessment of the chosen treatment (3 years later) was from 10 to 15, in average.
Results: Assessment of PDT efficiency involved the following criteria: full absence of local recurrence of the tumor; absence of visible and palpable sings of the tumor growth; local recurrence in 6 months; no effect - continued tumor growth within near post-operational period. Direct results of PDT were assessed during 1 year. For most cases, this period was long enough for recurrent tumor detection. Absence of recurrent tumor was observed in 7 (77.7%) patients, recurrence was observed in 2 patients. Recurrence was detected only in patients with Wilms' tumor of neuroblastoma. Follow-up monitoring of 7 patients for 6 months to 3 years did not reveal any recurrence.
Conclusion: The study shows high efficiency of PDT for solid tumors in children at advanced stages. In this respect, 82.4% children had no tumor recurrence within 3 years. PDT should be implemented more widely in treatment for residual and recurrent tumors.

IPSO Session 4: (PBC-Session): Best of IPSO

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A SUBSET OF IMAGE DEFINED RISK FACTORS PREDICTS COMPLETENESS OF RESECTION IN CHILDREN WITH HIGH-RISK NEUROBLASTOMA: AN INTERNATIONAL MULTICENTER STUDY

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Background/Objectives: Image defined risk factors (IDRFs) were promulgated as a means for predicting the feasibility and safety of complete primary tumor resection in children with neuroblastoma (NB). It is unknown whether the presence or absence of individual IDRFs has a differential effect on resectabilty or patient outcome. A multicenter database of patients with high-risk NB was interrogated to answer this question.
Design/Methods: Patients with high-risk neuroblastoma (age <20 years) were eligible if cross-sectional imaging was performed at least twice prior to resection. IDRFs and primary tumor measurements were recorded for each imaging study. Extent of resection was determined from imaging studies and/or operative reports.
Results: There were 211 of 229 patients with IDRFs at diagnosis and 169 patients with IDRFs present at pre-surgery. Although there was no significant correlation between the overall presence or absence of IDRFs and completeness of resection, a >90% resection was significantly more likely in the absence of two overlapping subsets of IDRFs either at diagnosis or pre-surgery. Both subsets of nine included invasion of the pancreaticoduodenal block or porta hepatis; encasement of the aorta, its major abdominal branches, the vena cava or iliac vessels; and invasion of both renal vascular pedicles. In addition, involvement of the diaphragm was significant at diagnosis and encasement of the origin of the superior mesenteric artery (vs. its branches) was significant at pre-surgery. There were no significant differences in 5-year event-free and overall survival when patients were stratified by the presence vs. absence of any IDRF either at diagnosis or pre-surgery.
Conclusion: A subset of IDRFs present either at diagnosis or after induction chemotherapy significantly influences the probability of a complete resection in children with high-risk NB. There were no significant differences in 5-year event-free and overall survival when patients were stratified by the presence vs. absence of any IDRF at diagnosis or pre-surgery.

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DEATH RECEPTOR EXPRESSION AND SENSITIVITY TARGETED IN DESMOPLASTIC SMALL ROUND CELL TUMOR

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Background/Objectives: Background: Desmoplastic Small Round Cell tumor is a rare tumor of childhood and adolescence for which cytotoxic chemotherapy, aggressive surgery, and radiotherapy have improved the survival only to approximately 50-60%. There is no known targeted chemotherapy for DSRCT. Here we describe a death receptor dependent apoptosis pathway in DSRCT cells that has not previously been described.
Design/Methods: Methods: JN-DSRCT cells were confirmed to have the t11;22 translocation and Wilms characteristic fusion protein. Flow cytometry was used to confirm expression of death receptor 4 and 5, and decoy receptors 1 and 2. Immunohistochemistry and immunofluorescence was used in DSRCT tissue to verify expression of DR-4 and DR-5. Clonogenicity assay was used to assess cytotoxicity of a novel DR-5 antibody, ONC 201. Expression of cleaved caspase 3 and 8, and cleaved PARP levels of JN-DSRCT cells after ONC201 treatment, were assessed using Western Blotting. An orthotopic xenograft model of luciferase transfected DSRCT in NOD-SCID-Gamma mice was then used in ONC201 treatment.
Results: DR-5 and less so DR-4 are highly expressed in DSRCT cells. Dose dependent cytotoxicity was demonstrated in vitro using ONC-201. The mechanism of cell death was confirmed to be the intrinsic pathway as verified by dose dependent increased levels

of cleaved caspase 3, 8, and PARP. ONC201 treatment of mice in-vivo showed at least stable disease.
Conclusion: In DSRCT, the death receptor 5 is highly expressed and the intrinsic apoptosis pathway are activated and sensitive to ONC201. This novel finding shows ONC201 and other DR-5 targeted therapy may be effective in the treatment of DSRCT.

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HIGHER INCIDENCE OF SURGERY-RELATED COMPLICATIONS IN WILMS TUMOR NEPHRECTOMY FROM CLINICAL RECORDS ANALYSIS COMPARED TO CENTRAL DATABASE REGISTRATION

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Background/Objectives: Reliable data about surgical complications in the treatment of Wilms tumors (WT) is essential in the evaluation and implementation of treatment protocols. The purpose of this study is to address the question whether central database registration is reliable and a useful tool to estimate and compare figures concerning surgery-related complications in WT nephrectomy.
Design/Methods: Clinical records of all patients treated according to the SIOP 2001 protocol in the 3 major centers in the Netherlands were analyzed for surgery-related complications. These were compared to the prospectively reported data collected in the central SIOP 2001 database. Data from the clinical records was considered the gold standard. Complications were graded according to the Common Terminology Criteria for Adverse Events version 4.0.
Results: One hundred and sixty-six patients treated between 2001 and 2013 were included. Baseline characteristics between patients with and without complications were similar. From the clinical records, a total of 38 patients with 53 surgery-related complications of which 8 peri-operative were identified compared to 8 patients ($p<0.001$) with 18 complications of which 3 peri-operative ($p=0.52$) respectively from the SIOP 2001 database. Forty-one short term (<30 days) and 4 long-term complications were observed from the clinical records compared to 15 ($p<0.01$) and none ($p=0.045$) respectively identified from the SIOP 2001 database ($p<0.1$). The most frequently observed complications were post-operative ileus (n=9) and chyloperitoneum (n=5). Intra-operative tumor rupture occurred in 4 (2.4%) patients. Patients with complications received the first post-operative chemotherapy on average 15.3 days after surgery. This was significantly longer than patients not experiencing surgery-related complications: 13.1 days ($p=0.031$).
Conclusion: Central reporting of surgical complications appears to be inaccurate. Treatment policies should therefore be based on clinical records rather than on the central database.

IPSO Session 5: Miscelleanous

O-156

GENETICS OF FAMILIAL OVARIAN TERATOMA IN CHILDREN

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Background/Objectives: Owing rarity of data about the genetics of familial forms of ovarian teratoma, the aim of this study was to review 12 years of our experience in their management and to perform genetic studies in familial cases.
Design/Methods: We retrospectively reviewed all the ovarian tumors operated on in a single center between 2000 and 2012. We focused on ovarian teratoma and looked for familial forms by systematically reviewing clinical notes and re-contacting patients. Capture of exons from genomic DNA was performed with the 51 Mb SureSelect Human All Exon Kit V5 (Agilent technologies) and sequencing was performed on a HiSeq2500 (Illumina) machine. An in-house software (PolyWeb) was used for filtering variants under relevant genetic models in each family.
Results: 110 ovarian tumors were operated on between 2000 and 2012. 19 were malignant (germ cell tumors, yolk sac tumors, and immature teratoma), 91 were benign tumors from which 74 were teratomas. We identified 10 cases with a familial history of ovarian tumors: 8 benign and 2 with malignant component. Familial history consisted in: mother with a unilateral or bilateral synchrone mature teratoma (n=3), maternal or paternal aunt with unilateral mature teratoma (n=2), paternal cousins with mature teratoma or serous cystadenoma (n=2), Prader Willi syndrome (n=1), maternal uncle with testicular seminoma (n=1), maternal grandfather with testicular seminoma (n=1). All patients are disease free at a mean follow up of 3.7 years (range 1-8). An exome sequencing was performed in 8 families but failed to identify any common variant. However, we found an interesting variant in the gene p53-induced protein with a death domain (*PIDD1*), known to act in the DNA-damage response, within one family.
Conclusion: We failed to find a frequent genetic cause of familial forms because there may be a high genetic heterogeneity underlying ovarian teratoma. Enlargement of this cohort is now mandatory

O-157

RISK FACTORS FOR SEVERITY IN PATIENTS DIAGNOSED WITH NEUTROPENIC ENTEROCOLITIS

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Background/Objectives: To characterize the episodes of Neutropenic Enterocolitis (NE) that occurred in the Pediatric Oncology Institute – GRAACC/ UNIFESP, Brazil.
Design/Methods: A retrospective descriptive cohort study. 38 patients with NE from 2007 to 2013. Age; sex; diagnosis; clinical presentation; chemotherapy interval; neutropenia history in interval less than 30 days; use of stimulating factor colonies and corticosteroids; realization of radiotherapy and transplantation; Complete blood count and absolute reactive protein c diagnosis; Computed tomography (CT); Conservative or surgical treatment; length of stay; use of NPP; fasting time more than 5 days; and clinical outcome. We used the logistic regression method with the SPSS21 program for univariate (UV) and multivariate (MV) analysis.
Results: One thousand five hundred twenty two patients were analyzed (25% were leukemias), 2.49% had a diagnosis of NE. The average age was 11.4 years, with no gender predominance. 40% of cases are related to hematological malignancies and 60% with solid tumors. ICU stay was required in 58.3% of the episodes and was associated in the UV analysis of neutropenia history in interval less than 30 days ($p = 0.014$); fasting time more than five days ($p = 0.01$); PCR ($p = 0.037$); and ascites valued at initial CT ($p = 0.024$). The same factors were significant in MV analysis, except for ascites. Surgery was performed in 11.6% of cases and the death rate due to NE was 7.9%.
Conclusion: An increased incidence of NE in patients with solid tumors was observed and may be associated with the intensity of current chemotherapy protocols. Clinical, laboratory and radiological factors are associated with ICU admission and recent neutropenia, absolute value of CRP, fasting time and ascites indicate severity. This experience led to a standardized follow up protocol.

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SURGICAL APPROACHES AND OUTCOME IN PEDIATRIC SUPERIOR MEDIASTINALTUMORS

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Background/Objectives: Superior mediastinal tumors in pediatric are heterogeneous group of tumors with marked variation in pathology,extension and response to chemotherapy. Different surgical approaches were described for resection of these tumors. Objectives: To evaluate the indications, advantages, limitations and outcome of different surgical approaches to tumors originating from or extending to superior mediastinum in pediatric.
Design/Methods: We retrospectively reviewed all cases who had surgery for superior mediastinal tumors in our hospital between Jan. 2008 to Dec.2013. We reviewed demographic data, clinico-pathological features, radiologic findings, operative techniques and outcome in all cases.
Results: The study included 18 patients (11males, 7 females). The age range was (0.2-16 years). The commonest pathology was germ cell tumors (6 cases), followed by neuroblastoma (4 cases), soft tissue sarcoma (STS) (3 cases), thymolipoma (2 cases), infantile fibromatosis (1 case), calcified fibrous tumor (1 case) and thymic carcinoma (1 case). The mean of largest tumor diameter at time of resection was 11 cm (5-26 cm). Extended lateral thoracotomy was used in 6 cases. Other approaches included trapdoor incision (5 cases), clamshell incision (4 cases), cervical approach (2 cases) and double level lateral thoracotomy (1 case). Fourteen cases had initial biopsy while 4 cases had upfront surgery based on radiologic findings. Neoadjuvant chemotherapy was given in 10 cases. There was no perioperative mortality and post operative morbidity was 16%. At the end of Dec. 2014, 16 cases were alive free of disease while one case with STS developed local recurrence and the case of thymic carcinoma died of distant metastases.
Conclusion: Tumors originating or extending to superior mediastinum in pediatric are challenging. Every case should be evaluated according to tumor extension and

pathology for proper selection of the best surgical approach which achieve best exposure for adequate resection and least morbidity.

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MALIGNANT MELANOMA IN CHILDREN AND ADOLESCENTS – A NATIONWIDE OUTCOME REPORT

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Background/Objectives: The incidence of skin cancer notably Malignant Melanoma (MM) and Non Melanoma Skin Cancer is increasing in England and while it remains predominantly an adult cancer (4% of overall paediatric cancers) - timely referral, treatment and advice must be clearly established. This study reports nationwide data for patients under 18 years who presented with MM in England during the era(s) 2005 -2013.
Design/Methods: Skin cancer data (ICD10 C43 – malignant melanoma - MM) - were extracted from the National Cancer Registry Service. Tumour morphology, anatomical site, gender, type of first treatment, Breslow thickness at presentation and lymph node operation(s) including mortality rate(s) were analyzed.
Results: Two hundred thirty one patients with MM were diagnosed in England and of these seventy seven were superficial spreading melanoma and twenty nodular melanoma(s). The majority of index cases occurred in 11-17 year old patients (n= 204) with a male to female ratio of 1 : 1.6 for MM. Anatomical site showed 34% of MMs in males were on the trunk region while 35% were on the lower limb(s) in females. Thirty four percent of patients had a Breslow thickness > 2mm with 18% also > 4mm. Main procedures undertaken were excision of which 44% had at least two operations performed. Thirteen percent of patients underwent varied lymphadenectomy operations(s). Eighteen deaths (8%) occurred within 0 - 6 years from primary diagnosis.
Conclusion: This study highlights national data, clinical management and outcomes(s) of MM in a paediatric population. The findings usefully serve a public health warning. Whilst a ban on sun bed use has been introduced in the UK for those < 18 years this policy has not led to an overall decline in 'tanning burns' for young people who continue this practice(1).
[1]N.Bowtell et al, NCIN Conference 2014.

O-160

PULMONARY PLEUROBLASTOMA IN CHILDREN: IS A CONSERVATIVE SURGICAL STRATEGY POSSIBLE?

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Background/Objectives: Due to the rarity of this tumor, management and surgical treatment for pulmonary pleurobalstoma (PPB) are not completely defined, as attested by recent discussions in the EXPERT group. The aim of this study was to analyze a homogenous series treated for PPB in order to propose some surgical principles of treatments.
Design/Methods: From 2000 to 2014, nine patients were operated. There were 6 boys and 3 girls with a median age at diagnosis of 2.3 years (range 6 months – 13 years).
Results: PPB classification was 2 subtype I, 6 subtype II and 1 subtype III. Circumstances of diagnosis were congenital lung malformation in 3 cases, pneumothorax in 2 cases and thoracic mass in 4 cases. In 4 patients, chest tube was placed at diagnosis. First surgery was considered as complete in 4 cases and incomplete in 5 cases and was followed by chemotherapy in all(IVA=2 or IVADo=7). Four of these five incomplete resections underwent a second look procedure, avoiding radiotherapy. The fifth, aged 13 years at diagnosis, died after 11 months from uncontrolled tumoral progression. Two patients presented recurrence, one initially considered as complete resection and the other as incomplete. They were treated both by complementary surgery, second line chemotherapy and radiotherapy. None had chest tube insertion at diagnosis. 8/9 patients are alive, without disease, with a median follow-up of 16 months.
Conclusion: Rupture of PPB at diagnosis is frequent, either spontaneous or linked to a chest tube insertion, but does not seem to impair the prognosis. Second look surgery is of high interest for the decision of adjuvant radiotherapy. Regarding the high chemosensitivity of PPB, complete pneumonectomy is discouraged at diagnosis and should be discussed in case of persistent unresectable tumor or residual viable cells at second look surgery. Multidisciplinar discussion should then balance irradiation risks with those of total pleuro-pneumonectomy.

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PREOPERATIVE EVALUATION OF PAEDIATRIC ADNEXAL MASSES WITH PAEDIATRIC RISK OF MALIGNANCY INDEX IMPROVES OVARIAN CONSERVATION AND SURGICAL MORBIDITY

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Background/Objectives: To validate the paediatric risk of malignancy index (PRMI), and examine its impact on surgical practices in the management of paediatric adnexal masses.
Design/Methods: Retrospective review of clinical charts and electronic records were performed for girls aged 18 years and under, who were managed for adnexal masses in our institution from January 2004 to December 2014. Surgical approaches adopted for patients managed before and after the introduction of the PRMI were compared.
Results: One hundred and fifteen patients were analysed - 76 were managed before, and 39 after the introduction of the PRMI. A score value of <7 predicted a benign histological diagnosis in children with adnexal masses with a sensitivity of 97.0% and 93.9%, and a positive predictive value of 98.5% and 91.2% in the two groups, respectively (P<0.001, and 0.011). Elevated serum AFP, βHCG, CA-125 and CEA were associated with non-benign pathology (P=0.004, 0.004, <0.001, and 0.002, respectively). Following its introduction, patients with PRMI <7 who had an initial laparoscopic surgical approach increased from 83.1% to 91.2%, and those who had ovarian sparing surgery increased from 72.3% to 97.1%. Patients with PRMI <7 who underwent surgical staging procedures, which included omentectomy, contralateral ovary inspection or biopsy, and lymph node biopsy, decreased from 7.7% to 2.9%.
Conclusion: The PRMI was validated in a post-implementation cohort to be sensitive in predicting benign pathology in paediatric adnexal masses. Since its introduction to our centre, more girls predicted to have benign pathology received an initial laparoscopic approach, ovarian-sparing surgery, and were spared unnecessary surgical staging procedures.

IPSO Session 6: Liver Tumors / Neuroblastoma

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IMAGING-BASED RESPONSE AND EFFECT OF PRE-OPERATIVE CHEMOTHERAPY ON HEPATOBLASTOMAS

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Background/Objectives: To document changes between PRETEXT to POSTEXT on CT scan and correlate with serAFP.
Design/Methods: 18 patients treated between 2010-13 had pairs of pre and post-induction chemotherapy scan on PACS. We documented SIOPEL staging, serAFP levels within 2 weeks of the scans, tumor volume, presence of calcifications, percentage change in volume and serAFP.
Results: The pretext stages were I,II,III and IV in 0,8,7 and 3 patients. Only 1 Stage II patient was down-staged to I. 4 patients with pretext III got down-staged to II, 2 remained stage III and one showed progression to IV. Of 3 stage IV patients, only one shifted to III. Thus only 33.33 % got down-staged. Four patients had portal vein thrombosis, 1 showed resolution of the thrombus while 3 showed reduction in size of thrombus. Of 9 patients with multifocal disease, 4 converted to unifocal disease (F0), 4 remained multifocal and one progressed. All of those with residual F0 disease showed >99% drop in serAFP. 6/11 patients with extra-hepatic extension had reduction in size with no extra-hepatic extension after chemo. 2 patients progressed on chemotherapy. Surgery was performed in 15 patients. Percentage fall in AFP was always more than percentage fall in tumor volume, except in one patient (this patient died of disease). 6 patients developed new calcifications and 2 showed increase in pre-existing calcifications post-chemotherapy. There was no correlation between calcification and response.11/13 are disease free (median follow up of 21/2 year) and 2/13 are alive with recurrent disease. 5 patients died of disease. 9 /11 patients with >90% fall in AFP post induction chemotherapy followed by complete treatment are doing well, the other two are alive with treated recurrence (p value 0.049).
Conclusion: Down-staging doesn't occur commonly after chemotherapy. The response in tumor volume is usually less than the fall in SerAFP.

O-163

HEPATOBLASTOMA: OUTCOMES OF 72 PATIENTS TREATED IN A SINGLE CENTRE

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Background/Objectives: To evaluate the outcomes of hepatoblastoma(HB) patients treated atour centre over last 14 years.
Design/Methods: Prospective study of all patients of hepatoblastoma registered from January 1999 to December 2013. Pretext staging system and risk categorization were used. All were treated with either Cisplatin+Doxorubicin (PLADO) or Cisplatin monotherapy (Mono). Kaplan Meier estimates of overall survival (OS) and event free survival (EFS) was made where death and recurrence of tumor was taken as event.
Results: Of the 72 patients of HB there were 6(8.3%); 35(48.6%); 26(36.1%) and 5(7%) PRETEXT I; II; III and IV respectively. Forty one (57%) were SR and 31(43%) HR. Neoadjuvant chemotherapy was given to 69(95.8%) patients and 3(4.2%) underwent upfront resection. Of the 41SR patients, 38(92.7%) received neoadjuvant chemotherapy (26 PLADO; 11 Mono; 4 Mono+PLADO) and 35(92.1%) had good response to chemotherapy. Of the 31HR patients, all received neoadjuvant PLADO and only 20(64.5%) had good response to chemotherapy. Sixty four (89%) patients [40/41(98%) SR; 24/31 (77%)HR] underwent resection while 8(11%) [1 SR; 7HR] could not be operated [2 lost to FU and 6 preoperative deaths]. Fourteen (19.4%) patients had lung metastasis and of these only 5(35.7%) achieved CR while 5 died, 2 were lost to follow up and 2 had progressive disease. Sixteen of 64 (25%) resected patients [5/40 (13%) among SR; 11/24 (46%) among HR] had recurrence. Overall 20/72 (28%) patients died [6/41 (15%) among SR; 14/31 (45%) among HR]. The 5-year OS was 68.5% (95CI 100-136, mean survival time of 118m) [83.4% for SR; 44.9% for HR(p= 0.0006)] and 5-year EFS was 56.4%(95CI 79-117, mean survival time of 98m) [78.4%for SR and 26.1% for HR(p=0.000)].
Conclusion: Even with neoadjuvant chemotherapy, 11% patients could not be resected. There was significant difference in the 5-yr OS (p=0.0006) and EFS (p=0.000) between SR and HR patients.

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SURVIVAL AFTER COMPLETION OF THERAPY FOR PRIMARY AND METASTATIC LIVER TUMORS IN CHILDREN

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Background/Objectives: To examine the relationship between completion of therapy and outcomes for children with primary and metastatic liver tumors treated at a single program.
Design/Methods: Records of children with primary or metastatic liver tumors treated at our institutions between 1/1/2005 to 12/31/2014 were reviewed. Completion of therapy was defined as no evidence of disease (NED) off chemotherapy.
Results: Thirty five children were treated for 19 hepatoblastomas (HB), 5 hepatocellular carcinomas (HCC), 2 rhabdoid tumors, 1 embryonal sarcoma, 2 metastatic Wilms tumors, 1 metastatic adrenocortical carcinoma (ACC), and 5 benign lesions. Eighteen with HB underwent biopsy with neoadjuvant therapy, and 1(PRETEXT 2 V1P1) underwent primary resection. Two died without resection. Three changed ≥ 1 sector from PRE to POSTTEXT with therapy. Seventeen were resected and achieved NED. Of 16 non-HB patients, 2 with extensive HCC and 1 with metastatic rhabdoid tumor of the liver died without resection. One child underwent two resections 13 months apart. NED status was achieved in 11 of 13.
The 31 resections included 17 conventional, 11 extreme and 3 treated with total hepatectomy and liver transplantation at referral hospitals. Extreme resections included reconstruction of the vena cava (4), hepatic veins (1), bile ducts (2), mesohepatectomy (1), trisectorectomies (7), and hyperthermic intraperitoneal chemotherapy (1). There were no perioperative deaths. Eight patients had Common Terminology Criteria for Adverse Events (CTCAE) grade 3 or 4 postoperative complications. Three patients died of recurrent (rhabdoid) or progressive (HCC, ACC) disease .75, 1.1, and 2.5 years after resection. There have been no late deaths from HB or benign disease. Twenty seven of twenty eight children completing therapy with NED are alive at a median of 2.6 years (range: 0.1-8.8).
Conclusion: Most hepatic tumors in children can be successfully resected or referred for transplantation. Children completing therapy with NED have excellent survival.

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AN APPRAISAL OF MINIMALLY INVASIVE SURGERY FOR THORACIC NEUROGENIC TUMOUR. A MULTICENTER STUDY

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Background/Objectives: To assess the outcome and efficacy of thoracoscopy for children with mediastinal neurogenic tumours.
Design/Methods: Retrospective review from 9 centres between 2000 and 2014 of patients who underwent thoracoscopy for a neurogenic mediastinal tumour. We assessed preoperative data, operative complications, and outcome. Results are expressed in median and range.
Results: We identified 68 patients aged 3 years [5 months-15 years]. The median diameter at diagnosis was 5cm [1.5-15]. INRG stratification was L1: n=41, L2 n= 16, Ms n= 3, M n= 8. Eighteen patients with image defined risk factors (IDRF) had a preoperative chemotherapy which allowed a 12% decrease of the largest diameter in 13 patients. Among them, 7 had still IDRF preoperatively. Median diameter at surgery was 4.7cm [1-12]. Thoracoscopy was performed with insufflation in 19 patients. Tumour spillage occurred in 10 patients and conversion to thoracotomy was necessary in 8 patients: for vascular encasement in 4 and a difficult location or dissection in 4. Median operative time was 2 hours [1-6]. Fifty-seven patients had a chest drain for 2 days [1-11]. Pathology was 32 Neuroblastomas, 17 Intermixed Ganglioneuroblastoma, and 19 Ganglioneuromas). Immediate post-operative adverse events consisted of 3 Horner syndromes, 5 Pneumothorax, 3 chylothorax. Length of hospital stay was 4 days [2-15]. Median follow-up was 23 months [1-109]. Long term complications consisted of 2 more Horner syndromes, 3 scoliosis/back pain, and 1 delayed chylothorax. Forty patients had a residual disease on post-operative imaging, among them 5 (4 were L1 and 1 Mestatatic) had a recurrence at 10 months [2-60]: 1 local, 3 local plus metastatic, 1 pure metatstaic. Two patients died at 9 and 10 months after surgery.
Conclusion: Minimally invasive surgery is safe for thoracic neurogenic tumours without vascular IDRF, however, relapse is mainly local without identified preoperative risk factor.

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RECOVERY OF NEUROLOGICAL DEFICITS IN PATIENTS WITH NEUROBLASTOMA WITH INTRASPINAL EXTENSION: IS SURGICAL DECOMPRESSION REALLY REQUIRED?

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Background/Objectives: To evaluate the outcome of patients with neuroblastoma with intraspinal extension.
Design/Methods: All children of neuroblastoma with intraspinal extension registered from June 1996 through June 2014 were included in the study. INSS was used for staging. All patients were treated with chemotherapy (Cyclophosphamide+Doxorubicin+Etoposide+Cisplatin). Neurological recovery and survival were evaluated.
Results: Of the 264 patients registered in our clinic 29(11%) had intraspinal extension of the tumor. There were 1(3%), 15(52%), 13(44%) patients in Stage 1, 3, 4 respectively. Primary site was abdominal in 13(45%), pelvic 2(7%) and thoracic 14(48%). Twenty (69%) of the patients had neurological symptoms at presentation [13(65%) paraplegia; 2(10%) limping, 1(5%) unstable gait, 2(10%) root pain and 10(50%) neurogenic bladder/bowel]. The history of neurologic symptoms was from 8 weeks to 20 weeks. Of the 20 patients with neurological symptoms 17(85%) received chemotherapy alone and 3(15%) underwent laminectomy and decompression of spinal canal. Neurological recovery was seen in 17/20(85%) patients [10(50%) partial; 7(35%) complete] and in 1(5%) there was no recovery while 2(10%) had progressive disease and discontinued treatment early in the course and so neurological recovery could not be assessed. Among 17 patients who received initial chemotherapy 16 (95%) recovered neurologically

[10(59%) partial; 6(36%) complete] and in 1(6%) there no recovery. All the 3 patients who underwent initial laminectomy recovered neurologically [2(67%) partial and 1(33%) complete]. Of these 29 patients with intraspinal extension 27 were alive (93%) [16(59%) disease free, 9(33%) stable disease and 2(7%) progressive disease] while 2(7%) had died of progressive disease. Of 15 patients with paraplegia 13 were ambulatory [12 without support;1 with calipers] while 1 showed no improvement and 1 could not be assessed.
Conclusion: Even late presenting neurologic deficits, due to intraspinal extension of NB, improves with chemotherapy in a substantial number of patients and surgical decompression may not be required.

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EFFICACY OF THREE-DIMENSIONAL PRINTING MODEL BASED ON PREOPERATIVE CT IMAGES FOR THE SURGERY OF PEDIATRIC MALIGNANCIES

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Background/Objectives: 3-dimensional (3D) printing model based on preoperative computerized tomography (CT) images facilitate visualization of complex structures such as vessels and tumors and it is useful for understanding anatomies of the variety of organs preoperatively. We report our experience with the preoperative surgical simulation using a 3D printing model based on preoperative CT images for pediatric malignancies.
Design/Methods: The multi-detector CT images were transferred to a 3D workstation and 3D volume data were obtained by reconstructing the sections. A 3D model was made with 3D printer using acrylic ultraviolet curable resin. The variety of organs such as the tumor, kidney, liver, spleen, vessels and outer body were selected to fabricate in each case.
Results: We used 3D model for 9 cases with pediatric malignancies (3 neuroblastoma (NB) cases, 2 soft tissue sarcoma cases, one hepatoblastoma case, one mediastinal yolk sac tumor case and 2 cases with local recurrence of Wilms tumor and clear cell sarcoma of kidney). The tumor and vessels can be seen through the translucent body such as liver and we can evaluate patient's anatomies, especially tumor location from all angles using this model. For laparoscopic surgery, 3D model was made it possible to be inserted trocars and the pneumoperitoneum, so that we can discuss the port layout before the operation and to simulate the laparoscopic view and range of forceps movement using 3D model. The laparoscopic view in the 3D model almost completely matched the real laparoscopic view during surgery. All nine cases performed surgical treatment without any complications.
Conclusion: The surgical simulation using 3D printing models based on preoperative CT images for pediatric malignancy was very useful for understanding the patient's anatomy and for planning the surgical strategies.

Nurses - Free Papers Session 1: Nursing Across the Spectrum of Paediatric Oncology Care

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PAEDIATRIC ONCOLOGY SPECIALIZATION IN AFRICA: COLLABORATION BETWEEN CAMEROON AND SOUTH AFRICA

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Background/Objectives: This is a collaboration between Cameroonian and South African nurses on various challenges facing nurses regarding paediatric oncology specialization in Africa. The collaboration resulted from a nursing roundtable during SIOP Africa 2014. Neither country has formal paediatric oncology nursing training in higher education, so both countries participate in twinning programs to try to bridge the gap. We identify the learning needs of nurses caring for children with cancer in each country.
Design/Methods: We explored the experiences of nurses caring for children with cancer at Banso Baptist Hospital and Charlotte Maxeke Johannesburg Academic Hospital. We compared the local nursing challenges and training needs while highlighting the importance of a needs analysis.
Results: In Cameroon, there is a need for specialized paediatric oncology nurses, training in palliative care, counselling techniques and advocacy skills to raise public awareness since in general practice, 26% of nurses were found to have no knowledge of childhood cancer. In South Africa, general nurses lack interest in paediatric oncology nursing believing that these children all die, and those working in the field need further training to support children's compliance with treatment and advocacy skills for awareness as well. There is a critical need for a paediatric oncology nursing certificate in higher education for nurses to truly partner with physicians. The success of any twinning program depends on the directive of the nurses in that low-income country.
Conclusion: African nurses must identify and communicate their learning needs to twinning partners, rather than remain passive recipients of Western/Northern teaching. There is a great need for dissemination of information between African countries as well as from high-income countries. Ownership of the learning process by African nurses will make twinning programs and curriculum development more relevant and beneficial to all parties, including the children and families who come for care.

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BEING HOME AFTER A CHILDS' HEMATOPOETIC STEM CELL TRANSPLANTATION. THE EXPERIENCES AND COMMITMENTS PARENTS FACE, THE INFLUENCING FACTORS AND THEIR NEEDS AS A RESULT

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Background/Objectives: To understand how parents experience the post-transplant period of their child, to get an insight in their commitments and to describe the influencing factors and the needs of the parents in order to improve overall support of the parents during post-transplant hospital visits.
Design/Methods: A descriptive qualitative study was conducted in which semi structured interviews were held with 15 parents. During a two year period at least one parent of all HSCT patients participated. The interviews were transcribed and coded (NVivo7). Constant comparison was used to analyse the data.
Results: Once home, parents face the total responsibility of care of their child. The continuous monitoring implies a great burden and it requires a great of effort to integrate the rules received from the professionals into their daily routine. Not only are the parents confronted with an insecurity in the medical evolution but also with the qualtity of life of their child.
Factors which can influence the experiences to a greater or lesser extent are: the disease progression, the duration of the post transplant period, the relationship with the partner, the family situation, social environment, personal factors, personal background, practical and financial situation, … Parents adjust their lifestyle to take care of their child, prioritizing it over their own needs. Depending on these influencing factors, parents have different needs. A trustful relationship is needed with professionals, and, above all, they need to receive all the information they require. They need psychosocial and practical support, as well as when making decisions. Parentsappreciate help in the education of the siblings. Some of them need a professional life and time for themselves.
Conclusion: Parents face an immense, very complex and extensive commitment when they return home with their child after HSCT.
Results: The results of this study create an awareness in professionals and are a first step towards improved post-transplant consultations.

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NURSING CARE FOR PATIENT WITH RETINOPLASTOMA IN ANGKOR HOSPITAL FOR CHILDREN

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Background/Objectives: Angkor Hospital for Children (AHC) is a pediatric referral hospital in Cambodia which started a new Retinoblastoma treatment program in late 2013. This involved providing chemotherapy agents which had never been used before at AHC. Contrary to many developing countries, nursing at AHC played an essential role in planning and implementing this new initiative and continues to be fundamentally involved in the ongoing oncology activities.
Design/Methods: We provide a detailed description of the role of nursing in a new developing world cancer treatment service.
Results: Nursing was identified early on as a priority for the AHC oncology service and as such, two senior AHC nurses were among the AHC core cancer team leaders during program development. As the program progressed, three more nurses were included and nurses now make up 50% of the cancer team. The role of the nurses includes general clinical nursing, mixing and administering the chemotherapy, and maintaining close communication with the patients/parents in hospital and at home. In addition the oncology nursing team provides cancer related education to the general clinical staff at AHC. The nurses have also taken key roles in providing guidance for patients' pain and palliative management. To date, 21 patients with Retinoblastoma patients have undergone chemotherapy treatment, 6 of whom were for palliative purposes with 4 deaths, and one who abandoned treatment. The remaining are still alive.
Conclusion: Including nursing in the planning and implementation of any new oncology program is essential to the success and survival of such initiatives.

Furthermore, the experience at AHC highlights the value of including nursing in more than just a supportive role. Plans to extend this program to other cancers will continue to emphasize the important role of nursing.

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THREE YEAR EXPERIENCE OF PAKISTAN'S FIRST PEDIATRIC HEMATOLOGY ONCOLOGY INTENSIVE CARE UNIT

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Background/Objectives: Hematology-oncology diseases are becoming a major health care problem in Pakistan. The actual size of the problem is unknown since there is no national population-based hematology-oncology registry. Global statistics depicts rising cases of children suffering through haemoglobin disorders and early childhood cancers as the leading cause of morbidity and mortality worldwide. Looking at these statistics AMTF took initiative in establishing Pakistan's First Pediatric Hematology Oncology ICU (PHOICU) with generous support from Government of Japan. PHOICU project was started in 2011 and was open for services in February 2012. This year PHOICU have completed 3 years of successful running in February 2015. The primary objective of this study is to review clinical data and outcomes of patient with hematology oncology diseases in PHOICU. The article will illustrate organizational and clinical work carried out in 3 year activity of first specialized Pediatric Hematology Oncology ICU in Pakistan.
Design/Methods: Descriptive exploratory study was conducted and retrospective data regarding patient admission was reviewed from patient's chart and ICU record registers from February 2012 to January 2015. Data was obtained regarding patient age, sex, diagnosis, date and reason of ICU admission, comorbidities, length of ICU, and outcome and in case of mortality cause of death.
Results: Total number of admissions were 558, 762 and 652 in year 2012, 2013 and 2014 respectively. The admission trend over the period of three years is 67.1% pediatric oncology and 32.9% hematology in year 1, 49.6% pediatric oncology and 50.4% hematology in year 2, and 60.4% pediatric oncology and 39.5% hematology in year 3. Mean age of patients admitted is 8.26 years. Average length of stay in ICU was of 6.83 days.
Conclusion: More specialized ICU for pediatric patients diagnosed with hematological/oncological diseases are highly required for providing quality care. Pakistan's first hematology/oncology ICU can serve as a model for future projects.

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OUTCOMES FOR CHILDREN WITH NEPHROBLASTOMA IN JOHANNESBURG. NURSING AND MEDICAL PERSPECTIVES FROM A SINGLE CENTRE

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Background/Objectives: Patients with nephroblastoma have excellent survival rates in high income countries. South Africa, as an upper middle income country, has access to most chemotherapy agents, and excellent radiation, paediatric surgical and intensive care services. However, many patients with paediatric malignancies present late and have poor outcomes. This study aimed to characterise a cohort of patients with nephroblastoma in Johannesburg in order to determine nursing priorities.
Design/Methods: A retrospective review was conducted of patients with nephroblastoma treated at Charlotte Maxeke Johannesburg Academic Hospital from January 1999 to December 2009. Descriptive statistical methods were employed.
Results: Records from 65 patients were eligible for inclusion. The male to female ratio was 1.27:1 and the mean age was 3.5 years. The distribution by stage was: 21 Stage I, 8 Stage II, 21 Stage III, 12 Stage IV and 3 Stage V. Patients were treated according to the SIOP 9 nephroblastoma protocol, using vincristine, actinomycin and adriamycin. The crude five year survival rate was 69%. Causes of death included infection (7/15), disease (6/15) and post-operative complications (2/15). Eight patients relapsed, of whom only one was successfully salvaged.
Conclusion: The survival rate in this cohort is encouraging for a middle income country and most likely reflects tumour biology rather than access to care or quality of care. The lack of successful salvage therapies in South Africa dictates that first line therapies be aggressive. Nursing staff should be aware of the high rate of infection and make every effort to prevent infections, and to treat them proactively when they occur. Outreach efforts by nurses should concentrate on malignancies such as nephroblastoma as they are under-diagnosed in South Africa but have a good prognosis.

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PARENTAL CHALLENGES FOR OBTAINING AN ACCURATE DIAGNOSIS FOR THEIR CHILD WITH CANCER AND REACHING AN APPROPRIATE TREATMENT CENTRE IN INDIA

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Background/Objectives: Purpose: In a low - resource country like India, the child and family often stagger from hospital to hospital, city to city before hopefully reaching an appropriate childhood cancer treatment centre. Our objective was to identify delays in recognising cancer symptoms and diagnosis, lack of referral pathways and above all the large vacuum of information and guidance.
Design/Methods: A retrospective study and review of the topic was performed during 2013-2014 with 60 parents of newly diagnosed pediatric cancer patients (all ages, recent diagnosed) in a hospital in Mumbai. Information was obtained from patient files, initial outside consultation records and individual parent interviews.
Results: 90% of our patients were from rural areas and their parents had little education and low economic status. 10% from urban areas, well educated with middle economic status. 100% of the parents interviewed had experienced the following challenges: Did not recognize the signs of cancer; Treated child's on and off fevers locally and child remain undiagnosed; An absence of clear referral pathways; Did not have the resources to get their child to a medical facility; Once at a clinic or hospital, a lack of resources or medical equipment meant a diagnosis was not made. Even when cancer was recognized, a further referral was made; Large vacuum of information and guidance; Parents experienced 5 -6 referrals before reaching our pediatric oncology ward.
Conclusion: One of the huge challenges facing low - income countries, including India, is a timely diagnosis, referral and treatment. Lack of awareness among parents and health professionals hampers timely presentation for cancer treatment. This adversely affects the outcome requiring greater treatment intensity, supportive care, costs, treatment toxicity, treatment abandonment rates and poorer outcomes. Nursing must assume a strong role in improving childhood cancer awareness and advocating for a more streamline referral process.

Nurses - Free Papers Session 2: Training & Supporting the Nursing Workforce

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CAPACITY BUILDING STRATEGIES FOR CRITICAL PEDIATRIC ONCOLOGY NURSING IN A LIMITED RESOURCE SETTING: A REPORT OF CHILDREN CANCER HOSPITAL, KARACHI, PAKISTAN

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Background/Objectives: The High Dependency Unit (HDU) provides intermediate care between the general ward and Intensive Care Unit (ICU) and serves as a step-up or step-down facility. As per critical care standards by the UK Royal College of Paediatrics and Child Health (2014),our HDU is appropriate for level 2 critical care, in which more intricate nursing care is provided to critically ill children who require close monitoring and supervision by more proficient nursing and medical staff with relevant specialized training.
Design/Methods: Due to the needs of pediatric oncology at the Children Cancer Hospital (CCH), the HDU facility was expanded from 2 to 5 beds as of January 2015.Currently, CCH collaborates with an out-sourced ICU to manage patients requiring advanced airway support. But, to provide quality healthcare to patients within the facility and to reduce the cost of the out-sourced ICU, the HDU had to be expanded.To build the capacity of pediatric oncology nurses and technicians working in the HDU, an extensive and thorough one-week critical care course was designed by the Head Nurse and Nursing Education Department and included theory and clinical training. This staff was also recertified for core oncology nursing processes.
Results: Currently, 78% of the HDU nurses and technicians in CCH have been trained to provide quality focused critical nursing care to pediatric oncology patients. The impact of aggressive capacity-building activity of HDU nurses is in the process of being monitored and evaluated. To motivate nursing staff further, an HDU supplemental allowance is given.
Conclusion: CCH has extended their capacity to provide advanced nursing care, optimized resources for providing quality nursing care and increased the skills and knowledge of critical care nurses caring for pediatric oncology patients.

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CHEMOTHERAPY/BIOTHERAPY NURSING EDUCATION IN LATIN AMERICA: AN INITIATIVE OF THE ASSOCIATION OF PEDIATRIC HEMATOLOGY/ONCOLOGY NURSES

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Background/Objectives: Literature has documented a lack of standardized, comprehensive pediatric oncology nursing education in Latin America. The Association of Pediatric Hematology/Oncology Nurses (APHON) has received numerous requests from international nurses to participate in the APHON Chemotherapy/Biotherapy certification course. Recently, the supplementary course text was translated into Spanish and distributed complimentarily to 13 institutions in 9 countries. To increase access to this standardized education/training course, APHON's International Task Force recommended transculturally adapting and offering a Spanish APHON certificate course.
Design/Methods: A 43-item needs assessment in Spanish was created by expert nurse educators and clinicians with relevant international experience. Using a snowball methodology, an online survey was initially sent to 43 stakeholders from 24 hospitals, in 17 countries, to assess: current chemotherapy education, common chemotherapies, and supportive resources. Two bi-lingual Chilean nurse educators will take the English course and provide feedback for cultural adaptation. Final Spanish content will be determined through survey results, expert feedback, and peer-review. The course will be piloted in Chile and then offered across Latin America.
Results: In preliminary survey results from 14 nurses, representing 14 hospitals in 12 countries, one-third reported no chemotherapy education/training for new nurses. Two-thirds offered orientation with variable duration (2-4 weeks) and content. Many existing orientation programs lacked APHON course content that the Latin American nurses also identified as important: biotherapies (75%), cancer genetics (37.5%), drug half-life (44%), late effects (44%), legal and ethical issues (56%), psychosocial issues (44%), and navigating research protocols (87.5%). Fifty-percent lacked chemotherapy continuing education programs. The majority (71%) of nurses prepare chemotherapy. All wished to participate in the APHON course.
Conclusion: Based on preliminary survey results, there is significant demand for a standardized, comprehensive, and transculturally appropriate chemotherapy course for Latin American nurses. APHON's Spanish Chemotherapy/Biotherapy course will offer essential nursing education to enhance safe chemotherapy practices and improve treatment-related outcomes.

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PERCEPTIONS OF PAKISTANI ONCOLOGY NURSES REGARDING THEIR ROLE IN SUPPORTIVE CARE: CHALLENGES AND NEEDS - A PILOT STUDY

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Background/Objectives: Globally, meeting the supportive care needs of children and their families remains a challenge in the continuum of cancer care. Pediatric oncology nurses play a major role in supportive care and several studies have suggested that nursing education contributes to improved patient outcomes, including reduced mortality. In contrast to the extensive supportive care education and clinical training provided to nurses in high-income countries, pediatric oncology nursing education is largely unavailable in Pakistan. This study is designed to determine Pakistani pediatric oncology nurses' perceptions of their role in supportive care; identify challenges; and explore learning needs.
Design/Methods: An experienced pediatric oncology nurse educator interviewed nine nurses in a childhood cancer center in Karachi as a pilot for a planned in-depth study. The center treats APPROX 350 children/year cared for by 49 nurses. The nurses were questioned about their understanding of supportive care and how they saw their ability to provide this care. Phase two of the study will include in-depth interviews with nurses from pediatric oncology units in public and private sector hospitals (face-to-face or via telephone) in Islamabad, Karachi, and Lahore.
Results: Major themes that emerged during the pilot study included knowledge deficits and communication challenges when providing psychosocial support—uncertainty of doctor-nurse boundaries for what can and cannot be communicated to the child and family. Time constraints and staff shortages were challenges and hindered the nurses' psycho-social support versus activity-based clinical care. Nurses also stressed a need for supportive care education to decrease their knowledge gap and build confidence.
Conclusion: This study provides a much needed initial assessment of the gaps in Pakistani nurses' understanding of their role in supportive care and highlights areas that need to be further explored. Study findings from phase two will be used to design a curriculum to address supportive care nursing education needs.

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LOW SELF-REPORTED RATES OF BURNOUT IN JOHANNESBURG NURSES IN ONE PAEDIATRIC ONCOLOGY UNIT

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Background/Objectives: Burnout is a syndrome of emotional exhaustion and depersonalisation which can result in reduced personal accomplishment. In a busy and under-staffed paediatric oncology unit in Johannesburg, a high rate of absenteeism and staff turnover was noted. This population of highly skilled nursing staff had not previously been assessed for signs of burnout. The primary objective of this study was to assess the permanent nursing staff working in the paediatric haematology/ oncology unit at Charlotte Maxeke Johannesburg Academic Hospital to determine the prevalence of signs of burnout, and secondly, to determine if any intervention was required.
Design/Methods: A questionnaire based on the Maslach Burnout Inventory (MBI) was administered to all permanent nursing staff in both the in- and out-patient units by a single researcher. The MBI, validated as a measure of burnout, measures emotional exhaustion, depersonalisation and personal achievement. A high score in the first two sections and a low score in the last section may indicate burnout. Nursing staff completed the questionnaires and the results were scored and interpreted.
Results: The response rate was 25/27 (93%). Eight respondents (32%) fulfilled no criteria for burnout, while the remainder of the participants showed varying levels of emotional exhaustion, depersonalisation and decreased personal achievement, though none met the criteria for full blown burnout. This indicates a population at risk. Senior staff members encourage debriefing and freedom of expression, possibly contributing to the low rate of burnout, although burnt out nurses may leave the unit.
Conclusion: The results of this study do not confirm the hypothesis that nurses in this unit demonstrate high levels of burnout. Nevertheless, nursing staff are susceptible and we recommend that nurses in paediatric oncology units be made aware of the possibility of burnout, be mindful of self-care and access available support services.

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EXPLORING CHALLENGES FACED BY ONCOLOGY NURSES IN A TERTIARY CANCER CARE HOSPITAL IN INDIA

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Background/Objectives: High quality nursing is central to the care of children with cancer. However nurses in India face many challenges while providing nursing care to children. Which are the different challenges they face?
Design/Methods: Exploratory Survey. Structured interview schedule.
Results: Majority of nurses were from age group of 31-40 years(60%) 20% were educated up to Nursing degree, 40% have undergone oncology training and 15% have attended special training of pediatric nursing. Nurse patient ratio is inadequate and absenteeism put the pressure on the nurses to complete the task. Nurses try to complete job with trial and error. 65% agreed lot of time is utilized for non nursing job like controlling relatives, computer work etc.Nurses sometimes face challenges with new equipments (65%). But they (100%) agreed that they were trained with functioning of equipments. Most of them agreed that they do functional assignments especially in evening and night when there is shortage of staffs. They are sometimes (55%) counseled and supported by superiors. They accepted that (75%) they sometimes face difficulty in communicating with superiors, father of child, and subordinates. But never had problem in communicating with mother.60% had fear of unsafe environment: occupational and psychological hazards.70% of them also expressed fear of medico legal issues. As team member are confident to take decisions during emergency but emotionally upset (65%) while dealing with parents of terminally ill child.90% shown concern with family of children who are coming from far distance for treatment and face difficulty with food and residential arrangements.Very few nurses(3) said that they are involved in treatment plans and counseling of parents.
Conclusion: Nurses in pediatric oncology setup in India face lots of challenges which can be cause of stress. We need to identify these factors and prepare them to face these challenges in positive way. Thus they can provide quality care to children with cancer.

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STRATEGIES TO REDUCE BLOOD CULTURE CONTAMINATION IN THE IN-PATIENT AND EMERGENCY DEPARTMENTS OF THE CHILDREN CANCER HOSPITAL, KARACHI-PAKISTAN

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Background/Objectives: Blood culture sampling is an essential tool for patient investigation and treatment plans, but improper technique can lead to false results eventually causing unnecessary patient suffering, morbidity and additional healthcare costs.The rate of blood culture contamination at Children Cancer Hospital in 2011 was 30.5%, 2012 - 27.7%, 2013 - 20.1%, and in 2014 - 19.6%. Although the rate is decreasing, our benchmark for blood culture contamination in healthcare is ≤3% (Clinical and Laboratory Standards Institute, 2007).
Design/Methods: A quality-improvement strategy was designed to reduce blood culture contamination based on earlier findings that when new nurse inductees began working on the unit, the blood culture contamination rate increased. The intervention had two components: 1) planning and implementing an intervention to reduce blood culture contamination in in-patient and Emergency departments and 2) monitoring and evaluating the effectiveness of the intervention. The planning was done through a plan-do-study-act model.The Head Nurse designed and implemented the intervention sessions, an extensive exercise of certifying and re-certifying the nursing staff for blood culture sampling through innovative teaching techniques. The monitoring and evaluation are in process in coordination with the laboratory department by analyzing the rate of contamination and identifying the nursing staff responsible for contamination to reevaluate their practice and take appropriate action.
Results: Since January 2015, 53% of the nursing staff (including registered nurses and technicians)working in the above-mentioned departments have been re-certified for blood culture sampling and the target is to eventually train 100% of the nursing staff.
Conclusion: In the 14 weeks from October 2014 to mid-January 2015, there were 26 contaminated cultures, whereas, after re-certification of 53% of the nursing staff only five blood culture contaminations were reported in February 2015. The trend is expected to further decrease when 100% of the nursing staff is trained.

Nurses - Free Papers Session 3: Innovative Tools in Paediatric Oncology Care

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A SOCIAL NETWORKING TOOL FOR COLLABORATIVE CARE FOR ADOLESCENTS AND YOUNG ADULTS WITH CANCER, CAREGIVERS, AND HEALTH CARE PROFESSIONALS: A USABILITY STUDY

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Background/Objectives: We aimed to develop and test the usability of a secure, cross-setting, cross-institutional, and inter-professional online clinical care collaborative system (LOOP) for adolescents and young adults with cancer, their caregivers and various healthcare professionals (HCP).
Design/Methods: A qualitative approach with semi-structured audiotaped interviews and observation by a trained observer was undertaken. Three iterative cycles (conducted until data saturation) determined the usability of the LOOP interface. A purposive sample of 10 English-speaking adolescents (17.5±3.0 [M±SD]) and 2 young adults (22.8±2.1 years) were recruited from two Canadian tertiary care centers for individual interviews. In addition, a purposive sample of English-speaking HCP specializing in pediatric oncology (n = 7) and pediatric complex medical care (n = 5) were recruited for 2 respective focus groups. Descriptive statistics and simple content analyses were used to organize data into categories that reflected emerging usability themes.
Results: All participants had access to a computer and Internet at home and reported high levels of comfort using each. Overall, participants liked the appearance of LOOP, valued its purpose, and felt it was easy to use, navigate, and understand. Identified usability issues: (1) problematic navigation, (2) needed interface-related changes (format, layout and aesthetics), and (3) necessary additional functionalities. To address these issues the following design solutions were implemented: (1) the message stream was changed to present messages from all users (e.g., HCP, patients) to enhance collaboration between parties, (2) 'new message' notifications were made more obvious, and (3) the search function capacity was enhanced. No new issues were identified following the third cycle of testing.
Conclusion: Usability testing was a crucial first step in refining the clinical collaboration system to meet the various end-users needs. Future work will focus on examining the impact of LOOP on patient and health service utilization outcomes using a randomized controlled trial.

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INFORMATION TECHNOLOGY AS A TOOL TO ENGAGE AND DEMYSTIFY CANCER IN CHILDREN AND ADOLESCENTS

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Background/Objectives: Technological evolution, equipment modernization and internet accessibility are contributing to the increase of Information Technology, especially in the oncology area, where patients and family members are eager for information.However, the exponential growth in the amount of information does not guarantee the quality and responsiveness of it, highlighting the inadequacy and inappropriateness of information as a cause of fear, insecurity and even lack of commitment to treatment.This study aims to inform the current situation of renowned Pediatric Oncology Hospitals websites.
Design/Methods: Ten websites were analyzed in Normative Descriptive Model.The Descriptive Model contemplates the existence and specificity of the areas: Lexi-Visual content, organic search and advanced search. (Yes/No)The Normative Model was based on principles and heuristics proposed by Ergonomics Areas, Human-Computer Interaction and Information Design: information structure, simplicity, clarity, unity, usability and acessibility. (Appropriate/Partially Appropriate/Inappropriate).
Results: Twenty percent of the evaluated websites do not have any information. Twenty-five percent of the websites that have information do not have search. Thirty-five percent of the websites do not comply with usability principles and a hundred percent do not comply with accessibility principles. None of the analyzed sites comply with the adequacy of the Normative Model.
Conclusion: The increase in the search for information is a natural trend of Information Technology advancement. Whereas cancer patients are more likely to be involved in the treatment of other chronic disease groups (The Center for Studying Health System Change, 2010), there is the need to improve the websites of Pediatric Oncology Hospitals.The appropriate production of information facilitates learning, providing greater identification, understanding, and ensuring the message quality. All Information Technology resources should have as its main goal to assist the understanding of treatment, which is assumed to be humanized and effective, meeting the needs, providing relief and improving the patient and family quality of life.

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USABILITY TESTING OF THE PAIN SQUAD+ SMARTPHONE-BASED REAL-TIME CANCER PAIN MANAGEMENT APP FOR ADOLESCENTS WITH CANCER

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Background/Objectives: This study utilized a user-centered design approach to develop and test the usability (acceptable, understandable, easy to navigate, and not prone to error-making) of a smartphone-based real-time cancer pain management app ("Pain Squad+") for adolescents.
Design/Methods: Three iterative cycles of usability testing involving user observation were used to refine the Pain Squad+ app. Sixteen adolescents (14.8±2.0 [M±SD] years) with cancer, and pain in the previous week were recruited from 1 pediatric tertiary care center. A brief app demonstration was provided and the entire usability testing session was audio-recorded. Participants used the app while "thinking aloud" about issues encountered with the interface and content. Two experienced observers recorded difficulties and navigation errors. Participants then answered open-ended questions addressing their experience and recommendations for app improvement. Using a rapid-analysis approach, the observers discussed session content and developed consensus on emerging themes related to app usability and refinements were made. Audio-recordings were referred to as necessary.
Results: Overall, adolescents liked Pain Squad+ aesthetics and content, endorsed its clinically utility, and made few errors. Cycle 1 usability issues related to: (1) streamlining navigation (recommendation for fewer taps to navigate), and (2) improving access to gamification elements (ability to review compliance-encouraging videos). Changes were made to address these recommendations. Cycle 2 issues related to the need to clearly: (1) distinguish the meaning of pain assessment questions, and (2) present information related to the dose and timing of recommended pain advice. Changes were made and no new issues were identified in Cycle 3.
Conclusion: The multifaceted usability approach utilized provided insight into how a real-time pain management app can be made amenable to adolescents with cancer. Next steps will include feasibility testing before testing intervention effectiveness in a

randomized controlled trial. It is expected that an acceptable and usable app will improve pain outcomes for adolescents with cancer.

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RADIATION THERAPY IN LOW- AND MIDDLE-INCOME COUNTRIES: NURSING'S ROLE IN THE FACE OF COMING TECHNOLOGY

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Background/Objectives: An estimated <30% of patients needing radiation therapy (RT) have access in low- and middle-income countries (LMIC) (Samiei 2013). Efforts such as the International Atomic Energy Agency's PACT and AGaRT program and global twinnings are addressing this critical situation. Despite efforts to explore eliminating RT through clinical trials in high-income countries, it remains an essential tool for curing diseases such as retinoblastoma, Hodgkin lymphoma, Ewing's sarcoma and central nervous system tumors, and palliation (particularly relevant in LMIC where children present with late-stage disease).
Design/Methods: Literature from 2009-2015 was reviewed to identify RT currently available in LMIC and nursing's role in this specialized area. Search terms included a combination of key words "radiation therapy", "nursing", "developing countries", and "low- and middle-income countries". Additional articles were identified in article reference lists.
Results: Twenty-six relevant articles were identified: current and historical RT technology and applications (7), state of RT in LMIC (12), support for RT side effects and survivorship (7). Nursing was mentioned in 4/26 articles. Despite significant efforts in LMIC to improve RT, including government equipment purchases and physician and technician training, there is a significant lack of information on nursing's role or training.
Conclusion: Pediatric oncology nurses in LMIC provide many specialist services (e.g., nutritional guidance and psychosocial support), due to the severe shortage of allied professionals. LMIC nurses should have basic knowledge of RT's capabilities and associated risks, because their governments and twinning partners are scaling up RT, children have particular vulnerability to RT, and RT's suitability for palliation. Low public awareness of childhood cancer extends to the myths and fears surrounding RT in LMIC. Whether or not an LMIC unit currently has RT, preparing nurses for the future of RT in LMIC will ensure that children and their families are informed and supported to achieve an optimal outcome during childhood cancer RT.

Nurses - Free Papers Session 4: Exploring the Needs of Parents & Adolescents & the Professional Response

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DEVELOPING AN ONLINE COLLABORATIVE CARE TOOL FOR ADOLESCENTS WITH CANCER, THEIR CAREGIVERS AND HEALTHCARE PROFESSIONALS: A CLINICAL USABILITY TEST

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Background/Objectives: The care of adolescents with cancer, both during and after treatment, requires the collaborative skills and efforts of the adolescent, their caregiver, and various healthcare professionals (HCP), who are often based in different settings. Effective communication between these parties is critical to achieving optimal health outcomes for patients. We have therefore developed a cross-setting and inter-professional online system (LOOP) to support collaborative care between adolescents with cancer, caregivers and HCP. The aim of this study was to test the usability of LOOP in a real-world setting.
Design/Methods: We assembled 3 collaborative teams to each test the clinical usability of LOOP. Teams used LOOP from home and work to consult with each other about the adolescent's care for 4-6 weeks. Individual interviews by a trained interviewer were conducted at the mid-point and end-point of the testing period. Each team member answered open-ended questions related to: (1) overall impressions of the clinical communication system, (2) perceived challenges and benefits of its use, and (3) personal patterns of interaction with the system. Simple content analyses were used to organize data into categories that reflected emerging themes.
Results: The assembled teams included 3 adolescents (mean age: 16.3 years), 3 caregivers, 6 HCP (2 oncologists, 1 oncology fellow, 2 nurses, 1 social worker). All participants had access to a computer at home. Analysis of interview data indicated that participants found LOOP acceptable and would use it if available. Specific endorsements related to LOOP included: (1) ease of use, (2) privacy and security, (3) team composition, and (4) design feedback. HCP raised concerns regarding the integration of LOOP into their daily workflow.
Conclusion: Overall, this research established the clinical usability of the LOOP clinical communication system. Future work will focus on examining the system impact on patient and health service utilization outcomes using a randomized controlled trial.

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DEVELOPMENT OF THE PARENT CARING RESPONSE SCORING SYSTEM (P-CARESS) USING SWANSON'S THEORY OF CARING AND ITS PRELIMINARY RELIABILITY AND VALIDITY

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Background/Objectives: Children with cancer are regularly subjected to procedures that can be distressing and even traumatic for them and their parents. Parents play essential roles in caring physically and emotionally for their children. Parent behaviors can influence child's procedure experiences in both the short- and long-term run. A reliable and valid theory-based coding scheme could provide a means to categorize parent behaviors and inform theory-based nursing interventions that aim to support parents in caring for their child during painful procedures. Existing schema are neither theory-based nor are non-verbal behaviors amply represented. Thus, the purpose of this study is to develop the Parent Caring Response Scoring System (P-CaReSS) based on Swanson's Theory of Caring and to test its preliminary reliability and validity.
Design/Methods: Six video clips showing parents' behaviors with their daughter as she underwent procedures during her visit to an Emergency Room were extracted from the documentary, "The Waiting Room". The video clips were used to inductively generate preliminary observational codes for the P-CaReSS. Parent behavior codes were generated every 20 seconds. Then, these codes were deductively structured into domains consistent with the five caring processes of Swanson's Caring Theory. The inter-rater reliability and criterion validity of P-CaReSS are tested in children during cancer treatment-related port starts.
Results: A 28-item P-CaReSS was developed. Three types of parent behaviors were represented: verbal (13 items), non-verbal (9 items), and emotional indicators (6 items). These behaviors comprised seven domains: Knowing (2 items), Being With (5 items), Doing For (4 items), Enabling (3 items), Maintaining Belief (3 items), Non-Caring (8 items), and Irrelevant (3 items). The validation of P-CaReSS is in the process.
Conclusion: Developing an observational coding scheme to measure parent caring interacting behaviors based on Swanson's Caring Theory is feasible. Future research should test the P-CaReSS in a larger sample of children with cancer.

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EXPLORING THE HEALTH EDUCATIONAL NEEDS AND CONCERNS OF PARENTS OF CHILDREN WITH CANCER AT THE KOMFO ANOKYE TEACHING HOSPITAL, KUMASI

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Background/Objectives: Cancer in children may profoundly affect parents in terms of psychological stress and increased care burden. In spite of the emotional impact that occurs when one's child is diagnosed with cancer, most families receive limited information and support to assist them. Many factors may interfere with the ability of a parent to cope with his or her child's diagnosis. Nurses should be aware of the parents' teaching needs and their concerns during this critical moment.
The purpose of this study was to identify the educational needs and concerns of parents of children with cancer.
Design/Methods: A total of fifteen parents were recruited from the parents association of children with cancer for this study. A focus group discussion was held on clinic days with each group comprising of five participants. The discussions were recorded and later transcribed and analyzed.
Results: The nurses identified a lack of comprehension of the disease process as a principal challenge even though parents are counseled before treatment begins. Also parents had concerns with the high cost of treatment as childhood cancer is not covered under the national health insurance scheme. The distance that parents have to travel to treatment centre is yet another concern raised by parents since there are only two cancer treatment centers in the country-Accra and Kumasi. Coping with changes in body image from treatment, outcome of diagnosis and duration of treatment emerged as the key elements that required further education and support for parents.
Conclusion: Even though the educational needs of parents of children with cancer will not drastically change overnight. Nurses can improve the quality of life of both parents and children with cancer by providing additional psychosocial support and cancer information in our daily interactions with the parents.

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FORCING AND PROTECTING - PARENTS´ LIVED EXPERIENCE DURING THEIR CHILD´S RADIOTHERAPY TREATMENT

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Background/Objectives: Radiotherapy treatment aims to cure or/and relieve symptoms for children with cancer and is a daily treatment, 5 days per week, during a period of 10-35 days. Leaving the child alone in the treatment room and expose them to radiation is a challenging experience for many parents. To gain an understanding of parents lived experience, parents were asked to write a diary during their child's radiotherapy treatment.
Design/Methods: A descriptive inductive design with a hermeneutical phenomenological approach was chosen to analyze the diaries. The parents were asked to write their lived experiences, thoughts and reflections during their child's radiotherapy treatment and could involve e.g. the impact on family, child, sibling or others. Daily notes, both short and long, were desirable.
Results: The parents described the radiotherapy treatment as a twin-pan balance where they constantly were balancing between forcing and protecting their child to increase the child's chances of survival. The parents were fighting for their child and lived through their child's emotions and agonies when they at the same time had to face their own. Meanwhile the parents themselves were struggling with their own despair and feeling of powerless. While protecting their child they experienced a sense of hope and that they gained control.
Conclusion: Parent's daily written reflections are important for clinical practice and give important knowledge. Parents need support when focusing on forcing and protecting their child and they need help with information and to find routines to gain more control over the situation.
Acknowledgements: We would like to express our gratitude to the parents who agreed to share their lived experiences with us and to the Swedish Childhood Cancer Foundation for funding.

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PROFESSIONAL COMPETENCE FOR WORKING WITH TEENAGERS AND YOUNG ADULTS WITH CANCER: CONSENSUS AND DISSENSION REVEALED IN THE BRIGHTLIGHT DELPHI SURVEY

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Background/Objectives: Teenage and young adult medicine is emerging as a distinct speciality, acknowledging the core tasks required to enable a young person to transition successfully to adulthood. The aim was to provide international consensus on the competencies required by healthcare professionals providing specialist cancer care for this population.
Design/Methods: A modified, international e-Delphi survey was conducted over 2 rounds. Experts were defined as professionals having worked in this field of cancer care for more than 12 months. They were identified through publications and invitations via professional organisations. There were 87 closed-ended questions (9-point Likert scale responses) and further open-ended responses to identify skills, knowledge and attitudes. Round 2 contained only items with no consensus in round 1 and additional suggested items of competency. Consensus was defined as a median score ranging from 7-9. Descriptive statistics were used.
Results: A total of 179 registered to be members of the expert panel, with valid responses available for 158 (88%) in round 1 and 136 (86%) for round 2. Most participants were nurses (35%) or doctors (39%) from Europe (55%) or North America (35%). All 87 items in round 1 reached consensus with an additional 15 items identified for round 2. There were significant differences in what doctors, nurses and allied professionals felt were important skills, areas of knowledge and attitude. For example 100% nurses vs. 79% doctors and 74% others agreed providing holistic care was important, whereas 80% doctors vs. 54% nurses and 44% others agreed being able to consent to a clinical trial was important.
Conclusion: Consensus was reached for the competencies required by healthcare professionals caring for this population. There were some notable differences across professional groups. Variation according to profession highlights important distinctions to explore further in pursuit of effective multi-disciplinary team working.

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CONSTRUCT VALIDITY AND RELIABILITY OF A MULTIDIMENSIONAL ELECTRONIC PAIN DIARY FOR SCHOOL-AGED CHILDREN AND ADOLESCENTS WITH CANCER

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Background/Objectives: The aim of this study was to evaluate the construct validity and reliability of a multidimensional smartphone-based electronic pain diary (Pain Squad) in school-aged children and adolescents with cancer.
Design/Methods: Momentary pain data were collected twice daily (morning and evening) for 2-weeks from 99 participants (8-18 years, with various cancer diagnoses, recruited at 4 Canadian pediatric tertiary care centers) using the Pain Squad smartphone diary. The Pain Squad diary is a 22-item measure assessing the multidimensional construct of pain (sensory, affective, and evaluative dimensions). Construct validity was assessed using Pearson's correlations between average weekly pain (intensity, bothersomeness and interference) scores on the Pain Squad diary and scores of: (a) recalled average weekly pain scores (convergent validity); and (b) overall and disease-specific health-related quality of life (HRQL; discriminant validity) for each week. Reliability (internal consistency) was assessed using Cronbach's alpha correlations between average weekly pain intensity, bothersomeness and interference scores for Weeks 1 and 2.
Results: Adolescents reported moderate levels of pain intensity (4.2±2.8[M±SD]/10), pain bothersomeness (5.6±2.9/10), and pain interference (4.4±2.7/10). As hypothesized, the Pain Squad diary displayed correlations between average weekly pain intensity, pain bothersomeness, and pain interference that were: (a) moderate in magnitude and positive in direction ($0.46 \leq r \leq 0.61$) with recalled pain; and (b) low in magnitude and negative in direction with overall HRQL ($r \leq -0.30$ for all) and disease-specific HRQL ($r \leq -0.12$ for all). Regarding the reliability of the tool, as predicted, the correlations for each of average weekly pain intensity, bothersomeness and interference were high (Cronbach's $\alpha \geq 0.88$) for Weeks 1 and 2.
Conclusion: These findings provide evidence of the construct validity and reliability of the Pain Squad smartphone-based diary in adolescents with cancer. Use of real-time data capture approaches should be considered in future studies of self-reported pain in pediatric cancer.

Nurses - Free Papers Session 5: Ethical Issues & Quality of Life in Paediatric Oncology

O-190

HEALTH CARE PROFESSIONALS PERCEPTIONS OF THE PEDIATRIC HOSPITAL ETHICAL CLIMATE IN CHILDHOOD CANCER CARE

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Background/Objectives: The overall aim of this study was to describe perceptions of the paediatric hospital ethical climate among healthcare professionals treating and caring for children with cancer.
Design/Methods: A study-specific questionnaire including a modified version (17 items) of the Hospital Ethical Climate Scale, developed by Olsson, was used to collect data. Descriptive statistics were performed to analyse perceptions. Physicians, nurses and nursing-assistants (n=89) working at three paediatric units, where children with cancer are admitted, participated.
Results: In 6 of the 17 items, less than 25% selected a positive alternative, indicating perceptions of a poor ethical climate. In 5 of the 17 items, more than 75% selected a positive alternative. Nurses rated the ethical climate positively to a lesser extent than physicians in all items. One third of the participants stated that they were able to practice ethically good care and also to a greater extent that nurses and physicians trusted one another and that guardian's wishes were respected. The two-thirds that stated inability to practice ethically good care also to a lower extent stated that they had access to the necessary tools to be able to solve ethical issues/problems; that conflicts concerning ethical issues/problems were openly dealt with and not avoided; and that there was an atmosphere that encouraged them in questioning, learning, and seeking creative responses to ethical problems/issues in treatment/care.
Conclusion: A positive perception of the possibility to practice ethically good care seems to be related to inter-professional trust and listening to guardians/parents. A negative/neutral perception appears to be influenced by a lack of ethical support as well as the experience of ethical conflicts and might be a risk of developing moral stress.

Clinical ethics support needs to be implemented in care where important values are at stake.

O-191

CONSOLIDATING CARE BY CLARIFYING PERSPECTIVES: HEALTH CARE PROFESSIONALS EXPERIENCES OF ETHICS CASE REFLECTION SESSIONS

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Background/Objectives: The purpose of this study was to explore health care professionals' experiences of participating in ethics case reflection (ECR) sessions, in childhood cancer care, in which an ethical concern was reflected on.
Design/Methods: Data were collected by observations and individual interviews/encounters and data analysis followed grounded theory methodology.Health care professionals working at a children's hospital in Sweden participated in ECR sessions in which ethical issues were reflected on, based on clinical cases. A total of 35 health care professionals participated in six ECR sessions that lasted 60-90 minutes and were organized as meetings with an external facilitator. Health care professionals were individually interviewed, formally and/or informally, afterwards (n=10).
Results: When health care professionals participate in ECR sessions with the care team, their main concern is *to consolidate care*. The core category, *clarifying perspectives*, and two related categories explain how care is consolidated. The two related categories were named: deliberating ethics (approaches) and unifying interactions (consequences). Different approaches for deliberating ethics are used during the sessions including *raising values* and *making sense*, leading to *increased understanding, group strengthening* and *decision grounding*.
Conclusion: By implementing ECR sessions, ethical concerns could be eased. Conflicting perspectives can be shifted into unifying interactions in the health care professional team. ECR sessions are furthermore valuable because it allows the discussion of values regarding health care-related issues in childhood cancer care. When the health care team is clarifying perspectives, on the ethical concerns, professionals are enable to reflect on the most sensible and ethically defensible care for the child. A consolidated care approach would be important both for the child and family and the health care professionals because of shared care goals.

O-192

RACIAL AND ETHNIC DISPARITIES IN SURVIVAL OF CHILDREN WITH ACUTE LEUKEMIA

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Background/Objectives: The dramatic increase in survival of children with acute lymphoblastic leukemia (ALL) over the past fifty years is one of the most notable successes in pediatric oncology. While overall survival rates of 85% or higher are documented in contemporary data, significant racial and ethnic disparities in the mortality rate of children with ALL persist for reasons not fully understood. Several large cohort studies illustrate these disparities and propose that variation in survival rates may arise from the complex interaction of economic, social, cultural, biological and pharmacogenetic factors. Pediatric oncology nurses are well positioned to identify patients at risk for poor outcomes and propose strategies for early intervention. Objectives: Summarize the findings of recent cohort studies which describe survival disparities by race in children with ALL; Discuss and analyze factors which may contribute to suboptimal outcomes in children with ALL; Propose strategies for nurses to mitigate risk factors that may interfere with disease-free survival in children with ALL.
Design/Methods: The current literature on disparities in cancer outcomes highlights possible underlying causes of ethnic and racial differences in survival for children with leukemia. A review of the possible reasons for ethic/racial differences in outcomes as they relate to nursing care of children with cancer will be presented.
Results: Socioeconomic and environmental factors correlated with race and ethnicity impact factors such as early diagnosis, access to quality health care, enrollment in clinical trials and treatment compliance. Nurses are present along the entire trajectory of care and are uniquely positioned to recognize patients at risk for poor outcomes due to racial and ethnic factors.
Conclusion: Educating pediatric oncology nurses to identify risk factors that are harbingers of poor outcomes may help to mitigate the racial and ethnic gap in survival rates and promote optimal care for children of all backgrounds.

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QUALITY OF LIFE (QOL) IN CHILDREN DYING OF CANCER: THE STATE OF THE SCIENCE

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Background/Objectives: Approximately 30% of children with cancer die from their disease, with 72% dying in hospital while receiving cancer-directed therapy. They experience impairments in QOL dimensions including pain, fatigue, dyspnea, and uncontrolled anxiety. The purpose of this review is to identify the gaps in the literature addressing QOL in children dying of cancer.
Design/Methods: CINAHL, PubMed and Academic Premier were searched for research findings using the terms: *childhood cancer, end of life, pediatric palliative care, QOL*, *cancer*, and *health-related QOL* published between January 2004 and September 2014 in English language. Exclusion criteria were non-research articles, literature reviews, and participants > 18 years old. Data were extracted from included studies and content analyses were done to synthesize the results of the review.
Results: Sixteen articles met the inclusion criteria. All studies focused on aspects of QOL including physical, psychosocial, social, and spiritual functioning in children who were dying of cancer. However, most studies emphasized physical and psychosocial functioning more than other dimensions. The most commonly negatively correlated QOL domain was physical functioning; specifically fatigue, pain and dyspnea. Children who died due to treatment-related symptoms experienced disproportionate pain, vomiting, sleepiness, weight loss, poor appetite, and physical fatigue than children who died of progressive disease. Children who received more intensive therapies (stem cell transplant) suffered more than those who received less intensive therapies (chemotherapy with surgery, chemotherapy with radiation or chemotherapy alone).
Conclusion: This scoping literature review indicated that children with terminal cancer experienced changes in QOL related to treatment approach. Impairments in two QOL dimensions, physical and psychosocial functioning, were most often associated with decreased QOL. Terminally ill children's adaptation was ineffective, which indicates that QOL was compromised. Strategies facilitating adaptive responses and enhancing QOL are needed.

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IMPACT OF NURSING ON TREATMENT ABANDONMENT IN CHILDREN WITH CANCER

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Background/Objectives: Purpose: A comprehensive nursing program was implemented at a pediatric oncology unit in Central America, to improve the quality of nursing care. Twenty-four new nursing positions were created, decreasing nurse patient ratio from 1:7 to 1:5, and a full-time nurse educator was hired to provide pediatric oncology education. In addition, processes were established to improve 20 nursing quality standards. The purpose of this study was to assess the program's impact on treatment abandonment in children with cancer. Treatment abandonment is a critical problem in developing countries and a leading cause of death for children with cancer.
Design/Methods: Pre-program cumulative incidence (CIN) of treatment abandonment was compared to post-program CIN at the intervention site and to a control site in which no new nursing interventions were implemented during the study period. The sample included 1,936 patients diagnosed with cancer during study period.
Results: Pre-program CIN of treatment abandonment for the intervention site (10.2 ± 1.2) was significantly higher ($p = .045$) than post-program CIN (6.5 ± 1.3). Post-program CIN of treatment abandonment for the intervention site (6.5 ± 1.3) was significantly lower ($p = 0.0003$) than post-program CIN for the control site (14.7 ± 2.7).
Conclusion: Significant improvement in the CIN of treatment abandonment within the intervention site and as compared to the control site was found. Several factors may have contributed to the study's findings. Well educated nurses are better able to provide parents with insight regarding the need to continue therapy, and the improved nurse-patient ratio allowed more time for nurses to provide individualized parent education. In developing countries, abandonment is seen as the primary domain of psychologists and social workers. A combined effort of nursing and psychosocial intervention may be the best option for preventing abandonment.

O-195

A NUTRITION SCREENING TOOL FOR CHILDHOOD CANCER (SCAN)

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Background/Objectives: Nutrition screening is a simple alternative to nutrition assessment for identifying children with cancer who are at risk of malnutrition. A new nutrition screening tool for childhood cancer, SCAN, has been developed. SCAN aims to identify the need for nutritional intervention by identifying patients that are currently undernourished or are at high risk of becoming malnourished. SCAN consists of 6 scored questions, a total score ≥3 identifies patient 'at risk of malnutrition' who should be referred to a dietician or clinician. This study aims to assess SCAN in children and adolescents with cancer.
Design/Methods: SCAN was used to screen 91 children with cancer (n=47 females; n=49 solid tumors), between 0.75 and 17.1 years of age. Subjects were classified as 'at risk of malnutrition' and 'not at risk of malnutrition' according to SCAN. Measures of height, weight, body mass index (BMI), mid upper arm circumference and triceps skinfolds were taken in each subject and measures were compared between the malnutrition risk groups. Survival at 1 year post screening was recorded.
Results: SCAN classified 59% of the subjects as 'at risk of malnutrition'. Subjects who were identified as 'at risk of malnutrition' had significantly lower values for weight Z score ($p<0.001$) BMI Z score ($p<0.001$) and triceps skinfolds ($p<0.01$) than subjects who were 'not at risk of malnutrition'. There were significantly more children with a solid tumor who were classified as 'at risk of malnutrition' ($p=0.01$). The number of patients surviving 1 year after screening was not significantly different between the risk groups ($p=0.85$).
Conclusion: SCAN is a new tool available to screen children with cancer for risk of malnutrition, enabling early identification and treatment of malnutrition. Children screened as 'at risk of malnutrition' have reduced weight and body size and are more likely to be diagnosed with a solid tumor.

Nurses - Free Papers Session 6: Psychosocial Care for Parents, Survivors & Nurses

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TO ASSESS THE LEVEL OF SATISFACTION AMONG PARENTS OF CHILDREN WITH CANCER REGARDING NURSING CARE IN PEDIATRIC WARD

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Background/Objectives: Background: Patient satisfaction has become an important indicator to measure the quality of care rendered to the patients while in hospital. Patient satisfaction surveys can help identify ways of improving nursing and health care services. The study was planned to assess the parent satisfaction with nursing care in selected hospital. *Objective*: To identify level of parent satisfaction in various aspects of nursing care and thereby improve the quality of care and approach. *Set Up*: Pediatric Ward of Tertiary Hospital.
Design/Methods: Design: Descriptive Exploratory study. *Methodology & Data Collection*: The study tool was a questionnaire which had four aspects of nursing care: *communication, physical, psychological and socioeconomical* and assessment biographic data of the parents.
Results: The overall rating scale was 4.5 on an average (on a Likert scale of 1-5 where 1 was poor rating and 5-excellent). The mean score was 93.1. Highest scores (109) was for infection control practices communicated well and timely reinforcement given. Lowest scores (63) was given for explanation during orientation phase and diagnosis, physiology of disease, treatment and prognosis of the child. It is important for the nurses too to improve on their stereotype views and expectations of parents to enhance satisfactory level. There was a trend seen with the patients admitted first time were more satisfied than those admitted more than once. The nurse scored 2.4 mean score (out of 5) for reference given to social help given by hospital and various NGOs.
Conclusion: Nurses are pivotal in communicating and counseling about all aspects of nursing care. Hence this could help to reduce the fear, anxiety and uncertainty among parents and children.

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PERCEIVED CONTROL IN MOTHERS OF CHILDREN WITH CANCER: A LONGITUDINAL STUDY DURING THE FIRST YEAR POST-DIAGNOSIS

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Background/Objectives: Perceived control (i.e. the belief that one is personally able to influence important outcomes in life) is an important stress-coping resource that has been associated with better mental health. Perceived control however, may be undermined by critical life events such as the diagnosis of pediatric cancer. Little is known how (potentially shattered) control beliefs develop over time. The current study aimed to examine the course and adaptive value of perceived control (PC) in mothers of children with cancer during the first year post-diagnosis.
Design/Methods: Mothers (N= 95, 86% response rate) of consecutive newly diagnosed pediatric cancer patients (0–18 years) completed measures of general and domain-specific PC, depressive symptoms, and anxiety at diagnosis, and 3, 6, 12 months thereafter. The data were analyzed by linear mixed model analysis.
Results: General PC, which was relatively high at diagnosis, remained stable during the study period. Likewise, PC over the child's illness, PC over the child's symptoms and PC over one's emotions did not change over time (all p's $>.05$). In contrast, PC over medical care (ß=.04, SE=.02, $t_{240}=2.0$, $p = .05$), PC over relationships (ß=.03, SE=.01, $t_{250}=2.4$, $p = .02$), and PC over daily life (ß=.10, SE=.02, $t_{249}=5.9$, $p < .001$) increased over time. Depressive symptoms and anxiety over time were predicted by general PC and domain-specific PC. Regarding the latter, only PC over one's emotions and PC over daily life were significant in the final equation. The final models explained 38% of the variance in depressive symptoms and 40% in anxiety.
Conclusion: The results confirm previous findings in adult oncology which suggest that individuals maintain perceptions of general PC by feeling efficacious in areas less affected by the disease. The study further supports that PC is an important resource for mothers of children with cancer. Helping mothers to enhance their feelings of control may improve mothers' capacity to adapt.

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ENHANCING THE SELF-EFFICACY OF CHILDHOOD CANCER SURVIVORS TO PERFORM PHYSICAL EXERCISE THROUGH ADVENTURE-BASED TRAINING

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Background/Objectives: Physical activity is of paramount importance to enhance the quality of life of cancer survivors. Nevertheless, there is growing concern about declining levels of physical activity in childhood cancer survivors. The objectives of this study were to examine the effectiveness of an adventure-based training in enhancing the physical activity levels, self-efficacy, and quality of life of childhood cancer survivors.
Design/Methods: A randomized controlled trial, two-group pretest and repeated post-test, between-subjects design was conducted to 69 childhood cancer survivors (9- to 16-year-olds). Participants in the experimental group joined a 4-day integrated adventure-based training and health education program. Control group participants received the same amount of time and attention as the experimental group but not in such a way as to have any specific effect on the outcome measures. Participants' exercise behavior changes, levels of physical activity, self-efficacy, and quality of life were assessed at the time of recruitment, 3, 6, and 9, 12 and 18 months after starting the intervention.
Results: From baseline to 18 months after the intervention, the experimental group reported statistically significant differences in the stages of change in physical activity and higher levels of physical activity, self-efficacy, and quality of life than did the control group.
Conclusion: The adventure-based training was found to be effective in enhancing the physical activity levels, self-efficacy, and quality of life among childhood cancer survivors over at least 18 months. Healthcare professionals should consider adopting such training to promote the regular physical activity among childhood cancer survivors.

O-199

CULTURAL ADAPTATION AND VALIDATION OF THE MORAL DISTRESS SCALE TO THE PEDIATRIC ONCOLOGY CONTEXT

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Background/Objectives: Research has shown that value conflicts can arise in childhood cancer care and contribute to moral stress. The Moral Distress Scale (MDS) has recently been revised (MDS-R) to fit pediatric settings and multiple disciplines. Our objectives were to translate and culturally adapt the MDS-R to the context of Nordic pediatric oncology care.
Design/Methods: The MDS-R was translated by both a certified translator and by specialists in ethics and pediatric oncology. The translated versions were compared and processed in a focus group with experts (n=5). Cognitive interviewing was performed with pediatric oncology nurses (n=6) with ethical competence to test face validity, item relevance and respondent friendliness. Based on these results, modifications were made and thereafter the questionnaire was tested in a focus group with consultant pediatric

oncology nurses (n=14) which led to a few more modifications. All modifications were discussed with a skilled researcher on instrument design and the final version has been translated back to English to ensure equivalence.
Results: The aim was to keep the Swedish version close to the original but some adjustments were necessary. For example, the statement, "Increase the dose of sedatives/opiates …that I believe could hasten the child's death" caused confusion because nurses do not increase the dose without prescription and moreover, associations were made to euthanasia. Another statement included "fears of a lawsuit", which within a Nordic context are unusual while fears of being reported to authorities are more relevant.
Conclusion: Cultural adaptation is time consuming but necessary to ensures a respondent-friendly and relevant instrument. The process has required expertise in pediatric oncology nursing, linguistics, ethics as well as questionnaire design.

Parents/Survivors - Cancer Control Workshop

O-200

THE ROLE OF CHILDHOOD CANCER SUPPORT GROUPS IN IMPROVING CANCER CARE IN SOUTH AFRICA AND ETHIOPIA

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Background/Objectives: The death rate of children with cancer in Africa is far higher than in upper middle income countries. As part of the intervention to decrease the mortality and morbidity of cancer in children, support groups in South Africa and Ethiopia started to collaborate with their national governments, ensuring that childhood cancer be placed on the national government agenda, improving intersectoral collaboration and proper cancer care.
Design/Methods: An assessment was made of the current policies. Stakeholder meetings were attended, ensuring that childhood cancer was part of the national strategy and policy environment. Deficiencies in the system, and potential solutions, were identified to improve cancer care.
Results: The South African national cancer control plan did not address childhood cancer and there is evidence that this situation is similar to other English speaking countries in Africa. Through its contacts in the non-profit sector, CHOC ensured that they represented the interests of the childhood cancer society, including: early and accurate diagnosis, appropriate treatment; and more emphasis on quality survival. In Ethiopia the MWECS seconded a professional consultant to the ministry of health to coordinate the development of the national cancer care control plan through their intervention. The political dynamics in Ethiopia have been dramatically changed in favor of NCD and have contributed to the policy changes at national level.
Conclusion: While it is essential to remain part of the ongoing development of the national cancer control plan, groups in both countries have exerted additional efforts to ensure that it is mandatory that a separate national cancer care management plan for children is devised by the relevant stakeholders and adopted by all departments of health on the Africa continent. This plan should conform to WHO, UICC and international childhood cancer norms. This exercise demonstrates proof positive that joint, multi-sector efforts truly can make a difference.

Parents/ Survivors - Nutrition Workshop

O-201

FOOD AHOY! A PIRATE GAME HELPS CHILDREN ENJOY EATING AGAIN

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Background/Objectives: Cancer and cancer treatment affects children's appetite and disrupts normal eating behavior. The pressure to ensure adequate intake is stressful for parents and child and cause a struggle for control within the family. To date, appropriate interventions that support families are lacking. Therefore, this study aimed to develop an intervention to reduce feeding stress and to support children and families to get a healthier eating behavior.
Design/Methods: Scientists and designers worked together in a so called "participatory design-science" project. Based on qualitative interviews with children and parents and expert sessions with health care providers, designers and students generated ideas for an intervention. Prototypes of the intervention were tested among families, improved by designers, and tested again in an iterative way.
Results: The developed intervention is a Pirate game for children 3-10 years of age. In this explorative story-telling game, children and their families travel around the world guided by a treasure map. Visiting different continents of the world, participants have to fulfill exciting food-related tasks i.e.: "Pirates try to steal your food. Prevent stealing by making a fruit-cactus, so that pirates who try to steal your fruit will prick themselves." By fulfilling tasks, children can earn special rewards. Every continent represents a main group of foods (i.e. dairy products). The game teaches unconsciously that food is fun and stimulates positive food associations. Additionally, the game provides practical tips for parents how to stimulate and reward healthy eating behavior. Pilot tests revealed that families enjoyed the game, children spontaneously tried new foods, and parents felt renewed inspiration to deal with their child's eating behavior. The coming months, the game will be tested by more families.
Conclusion: Preliminary results look promising. The pirate game might be an effective manner to reduce feeding stress and to develop healthy eating behavior among children with cancer.

Parents/ Survivors - Abandonment & Follow-up Care

O-202

PATIENT NAVIGATION AND TRACKING TO REDUCE ABANDONMENT AND ENSURE FOLLOW-UP IN CHILDREN WITH CANCER (PANTRACC) IN INDIA: A PILOT STUDY

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Background/Objectives: Patient navigation and tracking has shown to improve outcomes in adult cancers, HIV and tuberculosis. A similar approach could be helpful in reducing treatment abandonment and ensure follow-up in childhood cancer and we developed a log book for this. The pilot's aim was to test use of log book and a secondary aim was to investigate impact on outcomes.
Design/Methods: 81 patients (73% males, median age 6 years) in four childhood cancer centres in New Delhi, India who contacted Cankids (a national support advocacy group) for assistance were recruited. A specific parent support group member (PSGM) established initial contact with every child shortly after diagnosis and maintained contact at least on a weekly basis for 12 weeks after recruitment. The PSGM kept a record of successful/unsuccessful contacts and treatment status with an algorithm leading to necessary actions (more frequent contact, counselling, financial assistance, etc.).
Results: On a five-point Likert scale, all PSGM strongly agreed that the log book was simple to use, decreased work load, and delivered better patient assistance. Of 986 contact attempts (62% phone, 38% in-person), successful contact was made at first attempt in 88% attempts and in the reminder, on subsequent attempts. In 4 instances, there was dissatisfaction expressed with ongoing treatment and in 1 instance there was a wrong phone number. At end of 12 weeks, 70/81(86.41%) patients are alive and on treatment, 6(7.40%) patients have died, 2(2.46%) were not offered further treatment and 3(3.70%) have abandoned treatment. Of those abandoned, 1 returned subsequently to continue treatment, in 1 carers refused to provide information, and in 1 the contact does not know the status.
Conclusion: The pilot demonstrates that patient navigation and tracking is feasible and acceptable. The potential use of the log book to reduce abandonment rates and ensuring follow-up would be investigated in a larger prospective multi-centre study in India.

O-203

NEURO-ONCOLOGY SURVIVORSHIP PROJECT (NOSP) TO SUPPORT TRANSITION TO HOME, REHABILITATION, EDUCATION AND VOCATIONAL DEVELOPMENT

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Background/Objectives: The NOSP aimed to identify needs and solutions for children, young people and their families moving from the "safety blanket of hospital to home" in order to help rebuild family life.
Design/Methods: Eighteen standardised interviews were conducted with parents or young people (1-14 years post diagnosis) treated previously within EMCYPICS.

Thematic analysis of the interviews was conducted to inform and prioritise the design of interventions to accelerate and support transition.
Results: Thematic analysis identified: a) preparation for discharge, b) learning to live with disability, c) moving to a new normality, d) fostering emotional support, e) accessing educational and vocational support and f) promoting awareness of late effects. These highlighted the need for information and training for families, signposting access to local support services and promoting coping strategies for young people. These needs were addressed through the development of Awareness Day training course(s), Family Support Information Directory and a Local Sport and Activity Directory. Refinements to discharge planning were recommended by early referral to local services. New partnerships between health, psychology and education services were strengthened and knowledge shared to enhance awareness of the patients' needs through a Teacher Training day. "The Way Forward" course has been designed by a multi professional group, which included nurses, allied health professionals, CLIC Sargent social care team, youth workers, parent and patient representatives and voluntary organisations to help young people learn coping strategies and set goals to support them. New partnerships with a local brain injury organisation (Headway) has enhanced access to learning and support for those over 18years.
Conclusion: Collecting evidence from parents and young people living with brain tumours has provided new insights and led to the development of initiatives providing information and targeted support. The assessment of the impact of these interventions will be the focus of future research.

O-204

COMPREHENSIVE REHABILITATION PROGRAM FOR ONCOLOGY PATIENTS NUESTROS HIJOS FOUNDATION

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Background/Objectives: In Chile, such as high income countries, 7 of 10 children survive cancer and 80% of them are going to survive with consequences from treatment and disease itself. Rehabilitation is very important for upcoming quality of life of these children. Chemotherapy, radiation therapy and surgery are priority for survival of patients, and rehabilitation needs are satisfied after treatment. There is no specialized center for the attention of children with consequences in Chile. During September 2014, Nuestros Hijos Foundation create the first Oncology Rehabilitation Center. *Purpose*: To give a comprehensive oncology rehabilitation to children with cancer attended in the public system of health. The center provide assistance in hospitals, houses and outpatient clinics from the first stage of disease and medical treatment.
Design/Methods: The pilot program create an Oncology Center with a team comprised of physiatrist, kinesiology, speech therapist, occupational therapist, psychologist, social workers. They evaluate patients from the oncology service and create an individualized work plan according their needs. The therapy is provided where children are, in the hospital, house or Foundation shelter.
Results: 15 patients have been treated; from 1 to 23 years old; frequent diagnostic is central nervous system tumor (n6) followed by Leukemia (n4); from 2 to 10 weekly sessions according to the specialist. Gait disorders, swallowing and language are the most frequent consequences.
Conclusion: Children survival cancer presenting consequences can be rehabilitated with special programs designed to each patient. Early rehabilitation is essential for the quality of life in the future.

O-205

FOLLOW-UP OF THE IMPROVED FRAMEWORK FOR CHILDHOOD CANCER HOSPITALS, AND A REPORT ON A NEW MOVEMENT FOR ADVANCEMENT OF CLINICAL RESEARCH PROGRAM IN JAPAN

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Background/Objectives: To share information on the latest situation concerning childhood cancer in Japan from the perspective of policy frameworks and clinical research will surely provide fellow parents organizations in CCI with ideas useful for their activities in their respective countries.
Design/Methods: 1. As reported in SIOP-2014 in Toronto, there had been changes/improvements in the framework of childhood cancer hospitals in Japan recently; 2. Coinciding with the improvement of the framework of childhood cancer hospital, a new movement for the advancement of clinical research on childhood cancer in Japan has taken place. In the past, there have been several separate study groups conducting clinical researches. Although all groups have been constantly exchanging information and coordinating research programs, inefficiency is undeniable in terms of human and financial resources.
Results: 1. By the end of March 2015, all actions necessary to activate the new framework have been completed; 2. A new organization called Japan Children's Cancer Group (JCCG) integrating existing clinical research group across Japan was established in Dec. 2014.
Conclusion: 1. Such actions include formation and implementation of regional council to coordinate networks of hospitals treating childhood cancer led by the designated hub hospital in each of the 7 regions, designation of central institution and nomination of advisory board for which the author of the presentation is a member representing parents organizations. The presentation also reports as to how such actions affect the frontline of childhood cancer treatment, and what are the expectations of patients/parents for furtherance of level of medical treatment of childhood cancer in Japan; 2. Medical professionals as well as patients/parents expect that this integration will be a turning point for the advancement of clinical researches of childhood cancer in Japan.

Parents/ Survivors - Psychosocial Support – Mechanisms and Practices

O-206

SIBLINGS – THE SILENT SUFFERERS - A SUPPORT PROGRAMME

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Background/Objectives: Siblings are often referred to as the "silent sufferers" as the diagnosis of childhood cancer or life threatening blood disorders places a tremendous strain on the entire family system including the siblings. Children are perceptive; they can see their parents taking strain and do not want to burden them further; so they rather keep quiet. Parents in turn do not know how to communicate this difficult information and with the intention of protecting them, do not talk to the siblings either. This in turn creates many conflicting emotions for the siblings. On the one hand they feel concern and anxiety for their sick sibling and yet, they also experience anger and resentment.
Design/Methods: The CHOC Psychosocial Support team developed a workbook for siblings of children on treatment. The workbook takes them through all aspects of their journey and the impact of their siblings' illness on the family system. It explores their understanding of the diagnosis, the treatment and its implications and provides a safe space in which they can be with their feelings. It can be used on a one-on-one basis as well as in a group. The programme has also been incorporated in a camp context; combining the group fun element of a camp while working through the workbook. A workbook has also been developed for bereaved siblings.
Results: Parents expressed their gratitude and commented on the change in their children.
Conclusion: Professionally it is humbling to see the transformation in the siblings as they work through the workbook. They learn they are not alone, that it is good for them to express their thoughts and feelings and that they may have fun without feeling guilty about their sick brother or sister.

O-207

VOLUNTEER MANAGEMENT - A DOUBLE-EDGED SWORD – DEVELOPING AND SUSTAINING A VOLUNTEER PROGRAMME

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Background/Objectives: In the NGO world, where keeping within a budget is essential, it is often necessary to seek assistance with non-professional tasks by using volunteers. However, it should be borne in mind, prior to starting a volunteer programme, that the necessary infrastructure should exist within the organisation in order to support the successful management of a volunteer programme.
Design/Methods: There are several key elements to address when developing a volunteer programme: what motivates people to volunteer; identifying and recruiting volunteers, especially in regions where historically the community does not have a high level of volunteering; screening, selection and training; and most importantly, retention and recognition. The management and empowerment of volunteers through providing regular support, supervision and on-going evaluation is essential to protect both the beneficiary and the volunteer.
Results: A well-managed volunteer programme results in a greater retention of volunteers who in turn, can provide essential support to the organisation, patients and families. It is important to recognise that the management of volunteers takes significant resources, and is essential to ensure that there is a net gain to the organisation.
Conclusion: Volunteer mobilisation and coordination should become an essential part of any NGO's strategic planning; however a poorly designed or managed programme can be counterproductive and detrimental to the organisation.

O-208

SURVIVORS AUSTRIA: NOTHING ABOUT US – WITHOUT US

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Background/Objectives: 280 children and young adolescents come down with cancer each year in Austria. Due to a survival rate of over 80% about 235 survive. Some of these former patients have the need to meet people who have made similar experiences and/or want to give something back to patients and families.
Design/Methods: This spirit of some Austrian survivors resulted in the establishment of the Austrian survivors group in 2003. Within the last twelve years the organizational structure as well as the offer for survivors and patients strongly developed.
Results: It is not obvious that former pediatric childhood cancer patients get active, set up a survivors network/group/organization and offer activities for survivors/patients. The Austrian survivors group consists of regional groups and one umbrella group. The regional survivors groups focus on offering meetings on a regular basis for survivors. Especially this offer is adapted to individual needs and for personal exchange. In addition, once a year a big summer party for survivors from all over Austria is organized. On contrary to those fun activities, workshops to all survivors are offered twice a year and this year group members organize the first symposium for survivors about medical late effects. Beside these offers for survivors, mentoring for patients/families is offered in three Austrian hospitals and is coordinated by the regional survivors groups. Moreover, group representatives contribute in a project for long-term after care, in which medical professionals, psychologists and parents organizations are involved. Last but not least individual survivors get the possibility to actively participate on European and international meetings.
Conclusion: One major aim is the recruitment of more survivors and the encouragement to get active members. Furthermore, an additional objective is to expand the offer of seminars and activities for survivors from all over Austria and focus on the special needs of childhood cancer survivors.

Parents/Survivors - Impacts of Childhood Cancer on Families, Siblings & Caregivers

O-209

A NATIONAL COHORT STUDY OF THE EFFECTS OF CHILDHOOD CANCER ON PARENTS' INCOME FROM EMPLOYMENT AND EMPLOYMENT STATUS

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Background/Objectives: There is insufficient knowledge about the economic effects on the family of childhood cancer. The objectives of this study were to investigate the short- and long-term impact of childhood cancer on mothers' and fathers' income from employment and employment status.
Design/Methods: The study included parents of all children (≤ 18 years of age) diagnosed with a primary cancer during 2004-2009 in Sweden (n=3638 parents of 1900 children). Data on income from employment and employment status (employed/not employed) were obtained from the Longitudinal integration database for health insurance and labour market studies. The database integrates data from the labour market, educational and social sectors and is updated each year. Outcomes in the study cohort were compared using regression models with a closely matched reference group of parents (n=35096) sampled from the general population.
Results: Initial analyses confirmed equivalent average starting values (two years before diagnosis) between case- and referent parents for: civil status, parental age, number of children living at home, county of residence, disposable income, and educational level. Parents' income from employment decreased significantly following the child's cancer diagnosis ($P < .001$), and this association was most pronounced for mothers' income. This reduction in income of mothers who had a child with cancer continued for six years post-diagnosis ($P < .05$). Fathers' income was comparable to referent fathers at three years post-diagnosis. Mothers were also more likely to stop working following a child's cancer diagnosis, compared with referent mothers. Importantly, no association with fathers' employment status was identified.
Conclusion: Parents' income from employment and employment status are adversely affected by a child's cancer in Sweden. However, familial socioeconomic consequences of childhood cancers are still not equally distributed between men and women. Fathers' incomes catch up after a few years, while mothers tend to be disadvantaged regarding their professional life for several years after a child's cancer diagnosis.

O-210

CHILD SYMPTOM BURDEN AND DEPRESSIVE SYMPTOMS AMONG CAREGIVERS OF CHILDREN WITH CANCERS

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Background/Objectives: The burden of symptoms among children with cancers evokes various emotional reactions in caregivers that include depressive symptomatology. Given that depression in caregivers can impair their wellbeing and their caregiving roles; this study was set to investigate the relationship between child's symptom burden and depressive symptomatology among caregivers of children with cancers.
Design/Methods: This is a cross-sectional study among 72 consenting caregivers of children with cancers. A designed questionnaire was administered to elicit socio-demographic profile of the children with cancers and their caregivers. Subsequently, the child's symptom was profiled with questions adapted from Memorial Symptom Assessment Scale; while depressive symptomatology in caregivers was elicited using CES-DR. Data were analyzed using SPSS-16.
Results: All the caregivers in this study were all made up of parents with majority (83.7%) being mothers. The mean age of caregivers was 39±2(years). The common symptoms in the children with cancer include pain, feeling drowsy, hair loss and lack of energy among others. More than one third of caregivers (38.2%) had significant depressive symptomatology based on CES-DR interview. Symptom burdens in children with cancers was significantly associated with the experience of depressive symptoms in caregivers ($p<0.05$).
Conclusion: Active management symptoms in children with cancers and psychosocial support services for their caregivers are desirable.

O-211

FROM LANGUISHING TO FLOURISHING: EXPLORING WELL-BEING IN YOUNG ADULTS SURVIVORS OF CHILDHOOD CANCER AND IN THEIR SISTERS AND BROTHERS

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Background/Objectives: One in every sixty hundred and forty young adults is estimated to be a survivor of childhood cancer. Survivors may have long-term side effects which can reduce quality of life. Further, the family's system becomes a 'second-order survivor'. Data on long term psychosocial adjustment specific to this population are lacking and studies that explore simultaneously both patients and their family members were uncommon. The majority of existing researches used an *impairment model* of adjustment (i.e. absence of diagnosed psychological disorders). However, the current psycho-oncology research has directed its attention toward a *multidimensional* and *flourishing model* of well-being (i.e. growth, purpose, realization of personal capacities, life satisfaction). The aim was to explore both adjustment and well-being in a group of thirty-two young adult survivors (five years from the stop therapy) of child-hood leukemia and their forty-three sisters and brothers.
Design/Methods: The measures administrated were: the SCL-90-R, the Psychological Well-being Scale, the Satisfaction with Life Scale and the General Self-efficacy Scale.
Results: T-test analyses showed no difference in all measures between patients and their sisters and brothers. The twelve percent of participants had psychological disorders and symptoms. However the thirty-nine percent had a general self-efficacy below to the twenty percentile. The fifty-five percent showed low-to-moderate levels of self-acceptance and approximately the forty percent exhibited low-to-moderate levels of autonomy, environmental mastery, purpose in life and positive relationship. Only the thirty-nine percent were highly satisfied of their life.
Conclusion: These findings showed the effectiveness of a thriving model of well-being to a deeper understanding of the psychosocial long-term side effects after cancer experience.

O-212

PREPARING CHILDREN AND CAREGIVERS FOR MEDICAL TREATMENT PROCEDURES

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Background/Objectives: Any child undergoing treatment for childhood cancer or a life threatening blood disorder is confronted with a variety of invasive medical treatment procedures. These can result in a vast array of feelings such as fear, anxiety, anger and this is often expressed in obstructive behaviour and resistance in cooperating with treatment procedures.

Design/Methods: Through networking with professionals in the field of child trauma and mental health, the psychosocial team received the necessary training to deal with this situation. Methods used include distraction, sharing of information, play and other therapeutic techniques. The children are also oriented to equipment and treatment facilities.
Results: This preparation gives the children a sense of control over the situation which in turn releases stress and anxiety and helps them to cooperate. The information and choices they are presented with empowers them and aids the treatment and recovery process.
Conclusion: Less trauma is experienced by all involved, especially the child; medical treatment is delivered timeously; and long term scarring is alleviated.

Parents/ Survivors - Palliative Care and Bereavement

O-213

PALLIATIVE CARE SUPPORTING PROGRAM NUESTROS HIJOS FOUNDATION

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Background/Objectives: Each year in Chile, 500 new children are diagnosed with cancer, 75% surviving for five years. Likewise, around 90 children are admitted in the Palliative Care Program of the Public Health Care System. This program subsidizes the costs associated with the use of morphine and other medicines. However, this is not sufficient for all demands of these children and their families in this stage of disease. In 2003, Nuestros Hijos Foundation create a complementary model of care that provides medical, social and spiritual support for children and their families.
Purpose: to contribute with supporting on palliative care (PC) through complementary comprenhensive care for children and their families, with a supplementary role to the Public Health Care.
Design/Methods: Foundation helps through delivery of medicines, loan of medical equipment (electric beds, anti-bedsore mattresses, continuous subcutaneous medicines infusion pump, etc), economic bonus (transportation and special meals), death fee, among others. Besides, Nuestros Hijos Foundation works with the hospital PC group, supporting medical assistance through home visits, 24 hours of telephone service, home improvements, spiritual accompaniment, etc.
Results: From the beginning, 385 children have been helped from 12 national oncology units; Last year, 112 children received some medical care, 23% patients from Exequiel González Cortés Hospital. This program have allowed that 80% of attended patients have died at home.
Conclusion: It is posible to generate a complementary work to public health system, a comprehensive care to children with palliative care. This help children allowing to live with their families until the last day.

O-214

DEBRIEFING PARENTS/CAREGIVERS WITHIN THE WARD COMMUNITY AFTER THE DEATH OF A CHILD

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Background/Objectives: The death of a child within the ward community of a paediatric haematology oncology unit has a significant impact on not just the other parents but also the children. The emotional bond that forms amongst parents while sharing the ordeal of their child being treated for cancer is seriously tested. Conflicting feelings of trauma, grief and sadness, but at the same time relief that it is not their child, create an atmosphere of sombreness and withdrawal. At the same time parents are anxious that their child may be the next to die. As it is difficult to verbalise these feelings, the psychosocial team have created a safe space for the debriefing of this community.
Design/Methods: The parents are grouped together to provide a safe space in which to explore and verbalise their feelings. Through the foundation of non-judgmental listening within the group, these feelings are normalised and resources both internally and externally can be accessed. Different skills and techniques are used to further empower the parents to answer their children's questions around these matters. The sessions close with parents sharing an act of kindness through a gentle physical massage.
Results: The results that have been identified following these debriefing sessions are that parents are calmer and empowered to focus on and be emotionally available for their child.
Conclusion: These debriefing sessions provide the parents with a sense of hope and the confidence to move forward positively.

PODC - Free Papers Session 1

O-215

NURSE-INTERPRETERS IN THE PAEDIATRIC ONCOLOGY UNIT. BAD NEWS OR BAD MEDICINE?

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Background/Objectives: Pronounced economic disparities and the lingering effects of Apartheid continue to hinder effective communication in hospitals in South Africa, a country with 11 official languages. Many caregivers struggle to communicate with medical staff as most doctors do not speak the same first languages as their patients. Paediatric oncology nurses are often required to interpret and assist doctors to deliver bad news, despite a lack of specific training in this task. This study aimed to explore barriers to effective counselling when nurses double as interpreters, identify common feelings experienced by nurses and to ascertain possible areas of improvement in this process.
Design/Methods: Internal audit of nursing staff in the Haematology / Oncology Unit at Charlotte Maxeke Johannesburg Academic Hospital using a structured questionnaire, consisting of 12 "Yes/ No" questions and 7 open-ended questions. Participants were asked to suggest recommendations. Descriptive statistical methods were employed.
Results: The participation rate by permanent nursing staff was 15/20 (75%) and all (100%) had been required to act as interpreters. The majority (11/15) reported discomfort during the process of interpreting and felt inadequately prepared prior to the delivery of bad news. They felt that effective communication between doctors and nurses could improve the process of interpreting. Many felt that there should be more sensitivity towards the feelings of these nurse-interpreters, as they often experience great emotional stress when children are involved. Additional concerns raised were lack of awareness of specific cultures and African family structures.
Conclusion: The interpretation of bad news is more distressing to interpreters than previously recognised. Nurse-interpreters would like doctors to acknowledge the vital role they play in the delivery of bad news. Prior preparation is vital, as are improved communication between medical and nursing staff. Enrichment of the process for health care workers should improve the experience for families and patients.

O-217

EMOTIONAL STRESS AMONG NURSES AT THE PAEDIATRIC ONCOLOGY WARD KORLE BU TEACHING HOSPITAL, ACCRA, GHANA

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Background/Objectives: Emotional stress among nurses on Paediatric Oncology Wards differs from what occurs on other Paediatric wards in many ways, including the fact that nurses come face to face with the death of patients they may have known over a relatively long period of time. The objective of the study was to find out more about emotional stress amongst Paediatric Oncology nurses and make recommendations that would help address this issue effectively.
Design/Methods: This study was undertaken at the Paediatric Oncology ward of the Korle Bu Teaching Hospital in Accra, Ghana. A questionnaire with open-ended questions was distributed to all the nurses currently working on the Paediatric Oncology Ward in February 2015.
Results: Twelve of the fifteen questionnaires were returned completed. All respondents were female. Forty-two percent had over 10 years' experience in nursing, only 17% over 10 years' experience on the oncology ward. Ninety-two percent admitted work related emotional stress. This was mostly due to palliative care and deaths of the children (50%) and financial difficulties of families (33%). Stress led to feelings of helplessness and poor concentration (42%). The main symptoms were headache and palpitations. Most reduced stress by resting or talking to colleagues about it (58%). Most nurses, 75%, were motivated in their work by seeing children improve (33%), being given financial incentives (33%) and appreciation of their services. Sixty-seven percent felt like leaving the ward. Reasons included deaths of children and perceived risks from chemotherapy. Nurses' recommendations to reduce emotional stress included psychological counseling, increasing staff numbers and instituting recreational activities.
Conclusion: Emotional stress is highly prevalent amongst nurses working on the Paediatric Oncology ward in Ghana with serious potential for staff attrition. Strategies to address this should include psychological counseling sessions and increasing staff numbers so as to reduce the work load.

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A COST-EFFECTIVE AND CARE-EFFICIENT BEHAVIORAL CHANGE STRATEGY: HEALTH CARE WORKERS HAND HYGIENE COMPLIANCE IN PEDIATRIC ONCOLOGY CENTER IN LOW MIDDLE INCOME COUNTRY

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Background/Objectives: Improvement in hand hygiene compliance and change in behavior is very difficult task in hospitals. Hands are the most common mode of transmission of infection amongst patients and health care workers. According to Center of Diseases Control and Prevention (CDC) proper hand hygiene is single most effective strategy to reduce Health Care Associated Infections (HAI). The objective was to bring out behavioral change in hand hygiene practices among Health Care Workers (HCW). For that reason, Infection Control Nurse Manager (ICNM) designed and implemented care efficient and cost effective intervention in the pediatric oncology center.
Design/Methods: The intervention planned by ICNM had three components: 1) availability of resources; 2) teaching and training sessions for HCW; and 3) monitoring and evaluation of the applied intervention. To optimize the available resources and realizing the financial constraints ICNM advised to place wall mounted hand rubs on intravenous (IV) stands providing intravenous therapy to keep it on elbow distance, as indicated by WHO. Moreover, the hand washing stations were also placed in every unit to reinforce hand hygiene practices. All the HCW participated in hand hygiene teaching sessions organized by ICNM. And the audits and feedback system was designed to monitor and evaluate the compliance of hand hygiene.
Results: The behavioral change strategy had massive impact and hand hygiene practices increased by 50% amongst HCW after implementing the strategy. Though the strategy had great impact, High Dependency Unit (HDU) had reservation to attach hand rubs on IV stands because in critical care areas already IV poles are occupied with equipments such as infusion and syringe pumps. Alternative strategy was planned to overcome the issue in HDU.
Conclusion: Behavioral modification needs constant reinforcement. Frequent on-going monitoring and evaluation is required to keep this strategy sustainable.

PODC - Free Papers Session 2

O-219

INDIAN PEDIATRIC ONCOLOGY GROUP - AN INITIATIVE OF THE PEDIATRIC HEMATOLOGY ONCOLOGY CHAPTER OF INDIAN ACADEMY OF PEDIATRICS

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Background/Objectives: Formation of co-operative groups has been critical in improving paediatric cancer outcomes. These can be country specific (e.g. COG-USA and CCLG-UK) or disease specific (e.g. SIOPEL for liver tumours) and have research at their core.Similarly, the Indian Paediatric Oncology Group (INPOG) was established in September 2008. The primary objective was promoting regionally relevant paediatric cancer research, including multicentre clinical trials in India (which had so far been limited to ALL) so as to generate evidence in the local population and to improve outcomes.
Design/Methods: INPOG was restructured recently to lend impetus to meeting its objectives including election of a larger executive committee. Several working groups were proposed. All members of the Paediatric Haematology Oncology Chapter of the Indian Academy of Paediatrics were invited to complete a survey in Jan 2015 to express their interest in the activities of INPOG and its working groups, both as contributors of patients in relevant clinical studies, as well as more active participants in the design and conduct of new studies.
Results: Applications were received from 62 members from 46 institutes. From these 21 groups were created including 17 disease specific (e.g. ALL, CNS tumours, etc.) and groups on supportive care, epidemiology, access to care and late effects. Interested individuals were allocated specific groups maintaining a balance of representation from high volume (annual new childhood cancer patients >150) and low volume centres. Each group chose its own chair and has had to invite key relevant allied specialities e.g. radiation oncologists, surgeons, pathologists, etc. The groups then have the task to define research priorities for their respective group and create a roadmap.
Conclusion: An organized effort been made to address the long-standing need of a cooperative paediatric oncology research group in India with involvement of stakeholders from all disciplines and public as well private pediatric cancer units.

O-220

TREATING A WIDE SPECTRUM OF CHILDHOOD MALIGNANCIES DESPITE LIMITATIONS IN DIAGNOSTIC AND THERAPEUTIC RESOURCES IN CENTRAL MALAWI

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Background/Objectives: While most pediatric oncology programs worldwide employ treatment regimens based upon pathology-proven diagnoses, many hospitals in low-income countries struggle to choose protocols due to severe limitations in laboratory, radiology and pathology services. With this scenario in mind, we aim to describe the clinical characteristics and treatment outcomes in central Malawi.
Design/Methods: We retrospectively analyzed records of 271 children with cancer from 12/2011 – 6/2013. Diagnosis was based on cytology/histology in 102 patients. Consistently available chemotherapeutic agents include cyclophosphamide (C), doxorubicin (D, H, or A), vincristine (V or O), bleomycin (B), low-dose methotrexate (M), and prednisone (P). Chemotherapy regimens varied; stage I/II Burkitt lymphoma (BL): COMP, stage III/IV BL and other non-Hodgkin lymphoma (NHL): CHOP, Hodgkin lymphoma (HL): ABV-PC, solid tumors (VDC+surgery), Kaposi sarcoma (KS): BV.
Results: There were 111 females, 160 males. Most common clinical sites of presentation were: abdominal mass 38%, peripheral lymphadenopathy 30%, jaw mass 16%, peri-orbital/orbital mass 15%, central nervous system abnormalities 9%, mediastinal mass 6%, and extremity mass 4%. HIV testing was performed routinely; 49/271 (18%) were HIV-infected (45 KS, 3 BL, 1 NHL).Diagnoses include: BL 28.7%, KS 20.3%, solid tumors of the abdomen 15.5% (Wilms tumor most commonly, then neuroblastoma and germ cell tumors), HL 8.1%, non-Burkitt NHL 7.7%, retinoblastoma 6.6%, rhabdomyosarcoma/soft-tissue sarcomas 4%, bone sarcomas 2.9%, acute leukemias 2.2%, and nasopharyngeal carcinoma 1.5%. Chemotherapy regimens were completed by 55%, while 13% were lost to follow-up. At last evaluation, complete remission (CR) was found in 74 (27%) patients (median follow-up 19 months). Sustained CR rates were highest for children with KS (49%), Wilms tumor (42%), and BL (40%).
Conclusion: The three most common childhood cancers have the highest cure rates. Treatment paradigms focusing on risk stratification can improve outcomes for common diseases and may offer long-term cures to significant numbers despite severe limitations in diagnostic and therapeutic resources.

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ARE ESSENTIAL MEDICINES AVAILABLE, RELIABLE AND AFFORDABLE IN LOW-MIDDLE INCOME COUNTRIES?

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Background/Objectives: A critical challenge for reducing the cancer survival disparity between children living in low- middle income countries (LMICs) and those in high income countries is the lack of consistent supplies of reliable ,effective and affordable essential medicines.
Design/Methods: Using a semi-structured seventeen point questionnaire we sought the perceptions of ten clinical leads from nine LMIC units regarding the availability, importation, efficacy and costs of curative, supportive and palliative medicines within their countries (Cameroon, Ghana, Tanzania, Malawi, Zambia, Bangladesh, Myanmar, Philippines, Colombia).
Results: Collectively they see over 2000 new cases annually of whom a median of 65%(range 5-90%) receive curative intent therapy. No treatment relates to late diagnosis and perceptions of incurability but predominantly to the family cost involved.

Subsequent therapy abandonment ranged from <5% -50%(mean 20%), the lowest in three countries with free drugs and the highest where no subsidy was available. Philanthropic help has reduced abandonment somewhat. Only Bangladesh produces any cyto-toxics and all depend on importation. In three countries the Government directly controls importation, in five the role is delegated to a specific Pharmacy or adult hospital , and in one free market forces operate.All reported inconsistent supplies of key drugs mercaptopurine, methotrexate, cytosine, asparaginase, vincristine, antibiotics and morphine and quality doubts were expressed about Branded generic drugs. The principal sources of these were India (7/9), China, Argentina, Brazil, Korea, Cyprus and Malaysia.
Conclusion: All of the respondents identified that World Health Organisation (WHO) Listed Essential drugs were not consistently being produced, distributed reliably and/or imported into their country. Unless there is state funding of drugs many families can not afford the treatment costs. Internal and external drug subsidies have ameliorated the problem to a degree but are not sustainable in the long term .Only a Global effort by all interested parties including WHO and Pharma can remedy this problem.

O-222

IMPACT MEASUREMENT - A SUSTAINABLE APPROACH

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Background/Objectives: The vast majority of paediatric oncology units in low-middle income countries (LMIC) are underfunded, not prioritised by governments, and frequently rely on outside support. Those making a case for additional support for paediatric oncology units are not often trained fundraisers and so have little experience in securing grants to help them develop their services. Attracting funding becomes difficult when data collection techniques are not established and when the importance of measuring impact and recording overall change is understated.The relationship between donor and the paediatric oncology unit is often 'top down', with little communication regarding monitoring and evaluation (M&E) processes and procedures, often leaving the unit 'muddling through'.
Design/Methods: Donors must realise that it is the paediatric oncology unit which is best placed to develop long-term sustainable project goals, identifying realistic indicators based on both qualitative and quantitative data. They must avoid the temptation to focus solely on quantitative information and encourage local teams to collect a variety of data, enabling a comprehensive picture of overall project effectiveness to be built. It is through this process that paediatric oncology units learn the true importance of measuring impact, whilst donors benefit from a wealth and diversity of data. Accountability and transparency is fundamental to the overall success of securing and maintaining funding. Regular reporting/feedback templates and schedules should be developed in a collaborative process between both parties, with training provided where necessary.
Results: A realistic and sustainable approach to impact measurement will strengthen the overall M&E process, increasing a paediatric oncology unit's chances of securing long-term funding and support. This support will develop the services a unit provides, ultimately resulting in better outcomes for patients.
Conclusion: It can be fairly easy to secure one-off intervention but long-term support requires evidence-based progress to be reported. Sustainability is built through long-term investment and impact measurement.

PPO - Opening Symposium

O-223

UNDERSTANDING CONSENT IN PAEDIATRIC PHASE I/II CLINICAL TRIALS FOR THE PARENTS AND THE CHILDREN

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Background/Objectives: To assess parents and children's comprehension of the information given when seeking for consent to their child's participation to phase I/II clinical oncology trial, and to identify the factors of significant influence on parents' decision making process.
Design/Methods: one hundred nineteen parents who had been approached for enrolling their child in a clinical oncology study were asked to complete an interview. Their understanding was measured by a score which included items required to obtain a valid consent according to French legislation.
Results: Items that were best understood by parents were the risks (88%), the procedures (85%), the potential benefits to other children (76%), the right to withdraw (76%) and the duration of participation (70%). Items that were least understood were the possibility of alternative treatments (48%), the aims of the study (38%), the potential benefits to their child (25%). Seventy parents (59%) reported their decision as evident. Thirty two parents (27 %) declared that they made their decision together with the investigator. Thirty three parents (27%) took the decision on their own. Forty three parents (36%) felt that the level of quantity of information given was satisfactory, even when the level of information quality was up to 69%. Sixteen children (47%) understood that the protocol was a phase I/II clinical trial.
Conclusion: There was a diversity of level of understanding between the evaluated items.

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ENCCA – EUROPEAN ACTIVITIES AND ACHIEVEMENTS WITH POTENTIAL INTEREST OUTSIDE OF EUROPE

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Background/Objectives: The European Network for Cancer research in Children and Adolescents' (ENCCA - funded by the European Union's FP7 program) aims to improve the quality of life of children, teenagers and young adults with cancer by efficiently structuring collaboration within the paediatric oncology community.
Design/Methods: The project was driven by 34 organizations in 11 countries and together with the SIOPE community the following areas of interest were developed: biology, bio-banking, drug development, policy actions to improve the clinical trial framework, population-based cancer registries, special needs of teenager and young adult patients (TYA), innovative statistical methodology, and close collaboration with European Parent and Patient Groups, including ethical aspects in clinical research.
Results: ENCCA established important platforms for Paediatric Oncology: a European Clinical Research Council as a community voice, the CDDF – ITCC- ENCCA- SIOPE platform to facilitate collaborative partnership with Pharma (re-enforcing mode-of-action driven drug developments), a European Parents and Patients Forum, an Ethical Advisory Committee and a TYA network. The new platforms engage successfully in European policy initiatives including new Clinical Trial Regulation (completed) and forthcoming EU Data Protection Regulation. ENCCA designed an "Advanced Biomedical Collaboration Domain", a cloud-based solution for the "European Virtual Institute" and the ENCCA Unified Patient Identity (EUPID), a context–based identity management concept. ENCCA developed a survivorship passport prototype providing long-term guidance to the patients' journey of cancer treatment, an on-line neuro-oncology module in eight languages where patients can enter their outcomes in a standard dataset for future outcome research, a new Syllabus for PHO education and organised several collaborative training courses (including e-learning).ENCCA published 54 research and advocacy papers.
Conclusion: The manifold ENCCA activities have greatly improved the visibility of paediatric oncology in Europe and paved the way towards long-term sustainable research structures in Europe. Lessons learned could benefit other SIOP continents.

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CANKIDS PEDIATRIC PSYCHO-ONCOLOGY PROGRAM: A FAMILY-CENTERED CARE PRACTICE FOR INDIA

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Background/Objectives: The CanKids Pediatric Psycho-oncology Program is an integral part of our objective to improve the quality of life for children with cancer. In India, annually there are 40-50,000 new cases of childhood cancer. The cancer treatment process can be psychologically devastating for children and families and psychological support is an essential component of treatment. Throughout most of India, very few resources are available for psychological support; this lack of emphasis and understanding has often meant that children and families will not receive proper treatment and therefore may have unnecessary fear, anxiety, and confusion, potentially leading to the abandonment of treatment.
Design/Methods: CanKids has initiated a pediatric psycho-oncology program, serving as a low cost model for other cancer institutions and organizations. We operate with a focus on providing family centered care viewing cancer diagnosis as impactful to the whole family. This initiative outlines a set protocol for child friendly wards, explanation/clarification of diagnosis, disease oriented counseling for parents and the child, bereavement support, informational tools for patients and caregivers, capacity building for the social support team and sensitization workshops for healthcare providers.
Results: Measurable results included advanced patient and family support services via the aforementioned protocols, sensitization and increased knowledge for those concerned with pediatric psycho-oncological care and advocacy for an enhanced standard of pediatric psychosocial care in India. Results for the child and family showed higher rates of compliance with treatment and long term psychological and emotional well-being.
Conclusion: The CanKids Pediatric Psycho-oncology model is providing a family centered care approach that works in collaboration and bridges the gap between the psychosocial approach and treatment-centric approach. When uniting these two approaches, the child and family facing cancer is provided with a comprehensive healthcare experience for the best possible outcome.

PPO - Care Issues in the Developing World

O-226

GAPS IN ESSENTIAL RETINOBLASTOMA CARE IN AFRICA

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Background/Objectives: Retinoblastoma is one of the most common childhood cancers with about 25% of the global burden in Sub-Saharan Africa, due to Africa's vast population and high birth rates. An early sign of retinoblastoma can be detected by leukocoria and about 70% can be treated by unilateral enucleation with early detection. However, many barriers in Sub-Saharan Africa prevent children from reaching treatment in a timely manner causing high mortality. This study aims to evaluate the gaps in providing essential care to retinoblastoma patients in 11 VISION2020 Paediatric LINKS across 8 African countries.
Design/Methods: A descriptive cross-sectional study was conducted in Ethiopia, Malawi, Ghana, Nigeria, Uganda, Tanzania, Zambia and Zimbabwe on essential retinoblastoma care. Ophthalmologists were identified through the LINKS and snowballing technique was used to identify oncologists and pathologists totaling 45 participants. Participants answered Internet-based questionnaire addressing comprehensive retinoblastoma care based on Canadian Retinoblastoma Strategy. Ophthalmology participants were followed up with telephone/Skype interviews and fieldwork was conducted in Tanzania and Zimbabwe. Through questionnaire/interview analysis and literature review of retinoblastoma in developing countries, an Africa-based retinoblastoma tool and scoring method was developed including 5 sections, 23 essential components and 66 descriptors. Data collected from each LINK was input into the planning tool and rated using devised scoring method (a rating out of 100% based on availability of each essential component) to determine the gaps in essential retinoblastoma care in each VISION 2020 Paediatric LINK.
Results: An overall gap of 38% across the 11 VISION2020 LINKS was determined using devised scoring method. Zimbabwe had the smallest gap at 18% and Ethiopia the largest with 51%. The main gap was found at the primary health care level with lack of training in detection of retinoblastoma to health care workers.
Conclusion: Further research is required to investigate an association between the essential components and survival rates.

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COMMUNITY PLATELET DONOR DRIVES & ESTABLISHMENT OF A VOLUNTARY DONOR REGISTRY: A NOVEL STRATEGY TO ENHANCE TREATMENT COMPLIANCE & OUTCOMES OF CHILDHOOD CANCERS IN LMIC

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Background/Objectives: Lack of adequate & affordable supply of blood products and psychological as well as financial stress on families to ensure blood products availability by donation from family members or from expensive private blood banks is common in LMIC including India and is an important cause of treatment abandonment. Hence, we started a novel campaign called "Save a Life" to motivate, recruit, and retain voluntary non remunerated blood donors.
Design/Methods: "Save a Life was aimed at identifying target groups, conducting platelet donation drives in community and creating a voluntary donor registry which was first such effort in India. The campaign was initiated in November 2009 by a team consisting of transfusion medicine specialists, pediatric oncologists and 3 NGO (non-government organizations). In 5 years, 17 platelet drives were organized in colleges, and corporate offices in which the audience were motivated through talks on need, impact and process of donations. No incentives were offered but donors were appropriately felicitated in addition to ensuring that donors get a holiday on the day of donation through arrangement with college principals or employers.
Results: A total of 1483 donors were enrolled in registry. Of 1352 eligible donors, 369(27%) donated platelets and 123 of these (33 %) donated more than once. This led to addition of 657 SDP units to hospital inventory in 5 years. The donor numbers increased from 228 in 2009 to 1306 in 2014. Treatment abandonment in the same period reduced from >20% to less than 5% due to multipronged approach including platelet support.
Conclusion: Timely delivery of adequate, safe and free platelets from volunteers through registry had a positive impact in the reduction of treatment abandonment as well as reduction in morbidity & mortality associated with bleeding. This model can be easily adopted in other LMIC with blood products shortage.

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HEALTH-CARE PROVIDERS' PERSPECTIVES ON TRADITIONAL, COMPLEMENTARY AND ALTERNATIVE TREATMENT IN CHILDHOOD CANCER IN KENYA

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Background/Objectives: Our study explores health-care providers' (Hcp) perspectives on TCAM in childhood cancer. Personal experience with TCAM, health beliefs, components of TCAM, recommending or discouraging TCAM, communication between Hcp, parents, and TCAM practitioners and knowledge of TCAM were assessed.
Design/Methods: This cross-sectional study used semi-structured questionnaires. Hcp involved in the care of children with cancer at an academic hospital between July 2014 and October 2014 were interviewed.
Results: Out of total 179 Hcp, 155 Hcp (response rate, 79 %) returned the questionnaire. Hcp describe their view on TCAM as: cautious (39%), skeptic (33%), positive (18%), and undecided (11%). TCAM can cure cancer according to (9%) of the Hcp. More doctors (90%) than other Hcp (56%) think that chemotherapy can cure cancer (P=<0.001). Hcp (97%) think that their patients should inform them if they use TCAM. Only 5% of Hcp always openly discuss the topic TCAM with their patient, Doctors mostly recommend vitamin supplements (66%), self-prayer (58%), and special food intake (58%). Most discouraged forms of TCAM are: witchcraft (85%), scarification (68%) and ritual sacrifice (68%). Communication between doctors and TCAM practitioners is required (91%). Most Hcp feel that their knowledge about the safety and efficacy of CAM is inadequate (71%), Hcp want to learn more about CAM (87%).
Conclusion: A majority of Hcp have a negative attitude towards the use of TCAM. Communication about TCAM between Hcp and parents should be improved so parents feel safe to discuss their interest in TCAM. More attention should be given in updating knowledge of Hcp on safety and efficacy of TCAM in medical training institutions and through continued medical education programs.

PPO - Treatment Abandonment

O-229

TREATMENT ABANDONMENT IN PEDIATRIC CANCER PATIENTS DURING WARTIME IN SYRIA

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Background/Objectives: Treatment abandonment of pediatric cancer patients represents a crucial reason for their low survival rate in limited resources countries. The study aims to discuss this problem and how it is further worsen by fighting acts and war conditions in Syria.
Design/Methods: Syria has three hospitals to treat pediatric patients. Al Bairouni hospital is the specialized center for cancer treatment. Department of pediatric oncology was opened in 2010. Examples of Analyses include: comparison of numbers of newly accepted patients each year before and after the eruption of the conflict, 2011-present time. Statistic of patient's follow-up and medication adherence. Changes in treatment cost during this period and percentage of drug availability. Family residence and transport accessibility to and from hospital location.
Results: Cancer is a national public health problem in Syria with growing incidence, according to the statistics of the cancer registry of the Ministry of Health, already before the Syrian crises in 2011. The number of newly accepted cancer patients decreases. Half of the patients have stopped coming to the hospital to continue their treatment. Decline of available drugs offered. Increase in the treatment cost for each patient.
Conclusion: Deterioration in medical Infrastructure, leakage of doctors and nurses and shortage of affordable low cost therapeutic agents are important causes of treatment abandonment in pediatric cancer patients during wartime in Syria.

O-230

HEALTH-CARE PROVIDERS' PERSPECTIVES ON HEALTH-INSURANCE ACCESS, WAIVING PROCEDURES AND HOSPITAL DETENTION PRACTICES IN KENYA

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Background/Objectives: Patients at Kenyan public hospitals are detained if families cannot pay the medical bills. Access to health-insurance and waiving procedures to prevent detention may be limited. This study explores the perspectives of health-care providers (HCP) on health-insurance access, waiving procedures and hospital detention practices.
Design/Methods: A self-administered structured questionnaire was completed by 104 HCP (response rate 78%) in January and February 2013.
Results: All children with cancer should have health-insurance according to 96% of HCP. After parents apply for health-insurance, it takes too long before treatment costs are covered (67%). Childhood cancer patients without health-insurance have a higher chance to abandon treatment (82%). Hospitals should waive bills of all children with cancer when parents have payment difficulties (69%). Waiving criteria are unclear according to 45% of HCP, and 15% are uncertain. Waiving procedures take too long (75%). Social workers' approach toward pressuring parents to pay is too aggressive according to 44% of HCP, and 19% are uncertain. Parents are scared by waiving procedures and may decide never to return to hospital again (68%). Families' experiences with waiving procedures contribute to high treatment abandonment rates (64%). Poor families delay visiting hospital because they fear hospital detention and first seek alternative sources of treatment instead (92%). When poor families finally come to hospital the disease may be in an advanced stage already (94%). Parents sometimes have to abandon their child in hospital if they cannot pay hospital bills (68%). Children should not be left alone in hospital, if their parents cannot pay hospital bills (84%). Detention of children at hospitals if parents cannot pay medical bills is disapproved by 84% of HCP.
Conclusion: HCP acknowledge that access to health-insurance needs improvement and that waiving procedures contribute to treatment abandonment. Most HCP disapprove of hospital detention practices. These factors warrant urgent attention and adjustment.

O-231

REDUCING ABANDONMENT OF TREATMENT IMPROVES QUALITY OF CARE FOR ALL PATIENTS: THE SALVADORAN EXPERIENCE

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Background/Objectives: When evaluating pediatric cancer in low and middle-income countries, abandonment of treatment is a main cause of treatment failure and death. Beyond cure rates, abandonment reveals complex issues of culture and life conditions across multiple social strata, and speaks to health systems and health teams working in childhood cancer.
Design/Methods: A long-term qualitative research study in El Salvador explored parents' explanations for abandonment revealing relevant specifics of multidisciplinary health care.
Results: During the past decade, each year, approximately 20/200 children diagnosed with cancer abandoned treatment. Despite representing a small proportion of the total number of children on treatment, these families had an impact on the way medical care for paediatric cancer is provided in El Salvador. In the process of attempting to reduce treatment abandonment, the multidisciplinary team optimized resources to provide money for public transportation and meals for patients and parents, reorganized tasks and responsibilities to improve close follow-up of families, and focused most of its energy on refining detection of risk factors in families vulnerable to abandonment. As a result of the various initiatives and dedication, abandonment rates decreased from 13% to approximately 3%. The 'at risk' families became the main force to push the multidisciplinary team to re-examine their care, humanizing their relationships, and improving the quality of care for all patients.
Conclusion: Since it is impossible to identify with absolute certainty in advance which parents will stop bringing their child for treatment, the consequences of the team's efforts in trying to prevent abandonment have had direct benefits on all patients as well as developed the professional and human quality of the multidisciplinary team.

O-232

ABANDONMENT OF TREATMENT: A CALL FOR QUALITATIVE RESEARCH ON CANCER, CULTURE, AND PSYCHOSOCIAL SERVICES

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Background/Objectives: Abandonment of treatment represents a substantial obstacle for curing children with cancer in low-income countries (LIC). Initial research focused on finding measurable factors and cause-effect relationships among quantifiable variables. Socio-economic issues were linked to abandonment, and interventions based on the provision of material resources to parents had a positive impact in reducing the problem. As interventions for reducing abandonment become more effective, qualitative research is needed to understand and solve the minority of cases that continue to defy health team efforts.
Design/Methods: Based on the analysis of the multidisciplinary team interventions and data collected through an ethnographic study on abandonment of treatment in El Salvador, research and clinical practice together offered valuable sources of knowledge for improvement.
Results: The families' experiences of socioeconomic and emotional stress and cultural and religious beliefs, interplay as components of the doctor-parent encounter, and are involved in abandonment of treatment. Equally important, the results show that a committed multidisciplinary team working on individualized approaches to families at risk of abandonment probed to be effective. The data in this study show the value of qualitative research in the medical setting, and the significance of psychosocial teams in oncology. The need for understanding abandonment puts psychosocial teams in the forefront, challenging and promoting their role inside the medical practice and personnel. The same occurs in qualitative research, which is essential for explaining the meanings and relationships like family dynamics, living circumstances, and emotions, involved in the experience of a child's undergoing cancer treatment.
Conclusion: Abandonment of treatment is a cruel reminder for health teams to recognize the impact of socio-cultural meanings in the treatment of cancer and its outcomes. This highlights the need for approaches and practices informed by qualitative research, and mobilizes the enhancement of psychosocial teams.

PPO - Resilience & Social Skills in ALL & Brain Tumours

O-233

RESILIENCY OF CHILDREN AND ADOLESCENTS DURING TREATMENT OF ACUTE LYMPHOBLASTIC LEUKEMIA: THE USE OF 5-HTT AND BDNF POLYMORPHISMS AS BIOMARKERS

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Background/Objectives: Why are some children more likely than others to develop resilience in the face of similar levels of trauma exposure as compared to others who do not. It is increasingly clear that there are critical roles for predisposing genetic and environmental influences in differentially mediating psychological risk. Resilience differs from traditional concepts of risk and protection in its focus on individual variations in response to comparable experiences. Here, we tested the hypothesis that anxiety and depression as well as neural repair and plasticity related polymorphisms may partly account for the difference in resilience observed during treatment for acute lymphoblastic leukemia (ALL).
Design/Methods: Forty-five patients (1-18 yrs old) diagnosed with ALL were enrolled in two centers (protocol AIEOP-BFM-2009) and genotyped for 5HTT and BDNF (val66met). Patients and their family were subjected to a short screening battery, psychosocial testing (PAT2.1) and a specific assessment of their resiliency during treatment. The resiliency scale was composed of three subscales: Sense of Mastery (MAS), Sense of Relatedness (REL), and Emotional Reactivity (REA).
Results: Patients with the SL allele of 5HTTLPR had a more compromised score in some areas of resiliency than patients with the LL allele; the presence of the S allele most affected emotional reactivity REA and sense of mastery MAS. Furthermore, age was an important factor, as younger children displayed a reduced trust and tolerance versus their surroundings. This then contributed importantly to an overall reduction in their overall resiliency. Also, resiliency was reduced one year into therapy while vulnerability was significantly enhanced.
Conclusion: Genes regulating susceptibility to stress, such as 5HTTLPR and BDNF, may help to predict susceptibility towards the development of resiliency in children and adolescents treated for cancer, and may play a critical role as a predisposing factor in differentially dealing efficiently with the emotional risks related to cancer and its treatment.

O-234

IS TUMOUR TYPE A CRITICAL FACTOR IN PEDIATRIC BRAIN TUMOUR PATIENTS' SOCIAL SKILLS AND QUALITY OF LIFE?

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Background/Objectives: Paediatric brain tumour patients (PBTP) treated for medulloblastoma are at increased risk for neurocognitive deficits compared to other PBTP, with radiation doses being a critical factor. Less is known about the effect on their social behaviour and quality of life (QOL) compared to other tumour types. We investigated the differential effect of pediatric brain tumour type/treatment [low grade gliomas (LGG), medulloblastoma (MEDBL), other brain tumours (OBT, including astrocytoma)] on PBTP's social skills and QOL.
Design/Methods: Eighty PBTP (LGG=35, MEDBL=18, OBT=27), ages 8 to 16 years, in stable medical condition, and attending school participated. Parent and Self-reported questionnaires were used to assess social skills (Social Skills Rating System; SSRS), and QOL (PedsQL4.0 generic). PBTPs were on average 5 years post-diagnosis. One way ANOVAs (using diagnosis/treatment type) were conducted for each outcome measure. Alpha levels with Bonferroni correction and effect sizes are reported.
Results: *Social Skills*. There were significant differences between diagnosis type on both Self and Parent-reported Total Social Skills ($p = 0.034, 0.032$; $\eta^2 = 0.08, 0.09$) and Assertion scores ($p = 0.004, 0.001$; $\eta^2 = 0.13, 0.19$); Self-reported Empathy Subscale ($p = 0.009$; $\eta^2 = 0.12$); and Parent-reported Self-Control subscale ($p = 0.045$; $\eta^2 = 0.08$). Parents reported the poorest Self-Control scores for LGG. *QOL*. Parent-reported QOL indicated a significant effect for the Emotional ($p = 0.015$; $\eta^2 = 0.10$) and Social domains ($p = 0.03$; $\eta^2 = 0.09$), with LGG experiencing poorer emotional QOL and MEDBL experiencing poorer social QOL. Self-reports showed no significant effects.
Conclusion: Patients treated for MEDBL may experience more social skills difficulties than other PBTPs, while emotional QOL is a major concern for LGG patients compared to other PBTPs. These findings emphasize the importance of examining in detail what factors of diagnosis/treatment might be critical for these outcomes.
Acknowledgements: The Canadian Cancer Society Research Institute funded this study.

O-235

A RANDOMIZED CONTROL TRIAL OF THE EFFICACY OF A GROUP SOCIAL SKILLS INTERVENTION FOR PAEDIATRIC BRAIN TUMOUR PATIENTS

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Background/Objectives: Paedatric brain tumour patients (PBTP) typically experience social competence deficits and yet, treatment for these deficits has received little attention. The study objective was to assess the efficacy of a manualized group social skills training intervention program (SSIP) for PBTP by evaluating whether the Experimental Group (EG) demonstrated improved social skills when compared to a Control Group (CG).
Design/Methods: A multisite, randomized control trial (RCT) with repeated measures (baseline, post-intervention, six months later) was employed. PBTP aged 8-16 years in stable condition- on or off therapy - and attending school regularly, were block randomized to either the EG or CG. Both groups underwent 8 two-hour weekly sessions. EG ($n = 40$) received manualized social skills training through activities and crafts. CG ($n = 42$) received activities and crafts only. Social skills were assessed using the Social Skills Rating System (SSRS; Parent and Self Reports) – subscales include Cooperation, Assertion, Self-Control, and Problem Behaviours (Externalizing, Internalizing). ANCOVAs controlled for baseline scores.
Results: No significant groups or time effects were found in self-reports. Parental ratings of Total Problem Behaviours and Internalizing subscale yielded a group by time interaction, ($p = 0.032$, $n^2 = 0.06$), suggesting a reduction of Internalizing problems in the EG. Parent reports for both groups indicated a significant time effect ($p = 0.005$, $n^2 = 0.10$) and group effect ($p = 0.013$, $n^2 = 0.08$, $p = 0.015$, $n^2 = 0.07$) in the Cooperation subscale, suggesting improvements within this subscale.
Conclusion: Both groups were offered opportunities for social interactions, but based on parental reports, the SSIP seems to have the added potential for improving PBTP's cooperative behaviour and internalizing changes in social skills. It is unclear whether self-reports reflect true finding or a lack of insight.
Acknowledgements: This study was funded by the Canadian Cancer Society Research Institute.

PPO - Teenagers, Adolescents & Young Adults

O-237

PSYCHOLOGICAL ISSUES IN ADOLESCENTS AND YOUNG ADULTS WITH CANCER REFERRED TO PSYCHO-ONCOLOGY SERVICE IN A TERTIARY CARE CANCER CENTER

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Background/Objectives: Adolescent and young adults (AYA) who are diagnosed with and treated for cancer have distinctive psychosocial concerns that set them apart from pediatric and older adult populations. They have different needs and treatment challenges from children or older adults. There is a dearth of literature in the Indian setting on emotional issues expressed by this population. Our paper studies the psychological concerns in adolescents and young adult cancer patients referred to our psycho-oncology service in a tertiary care cancer hospital.
Design/Methods: A clinical audit of AYA cancer patient referrals to psycho-oncology service was conducted for the period of January to December 2014.Information was collected from prospectively maintained data in the department along with patient charts. Details about diagnosis, treatment, demography, reason for referrals, patients concerns and coping skills were noted. Relevant statistics were used.
Results: 84 out of 553 AYA cancer patients were referred to psycho-oncology service in the study period, a referral rate of about 15%. Out of 84 AYA cancer patients referred, 38 (45%) were from pediatric and 46 (55%) from adult care setting. 55 (65%) were male and 51(61%) were outpatients. Common reasons for referral were counseling and evaluation of mood. The main cancer diagnoses were hematolymphoid (43%) and solid tumors (56%) of which (19%) CNS tumors.Majority of AYA cancer patients had psychological/ emotional issues (anxiety, distress related to physical state, worries about school, missing home) and 75% had multiple concerns (physical, emotional, family, practical, and spiritual). 53 (63%) had adjustment difficulties and mood/ emotional disturbances.
Conclusion: The psychological issues faced by AYA patients referred to our service were related to mood disturbances, distress and adjustment difficulties. More effective monitoring of psychosocial needs of AYA cancer patients is essential to empower them with specialized psycho-therapeutic interventions and to improve their coping and adjustments throughout the cancer treatment and after treatment.

PPO - Measurement of PRO's, Screening & Assessment

O-238

MATCH OF PSYCHOSOCIAL CARE AND PSYCHOSOCIAL RISK IN FAMILIES OF CHILDREN DIAGNOSED WITH CANCER

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Background/Objectives: This study aims to describe psychosocial care provided to families of a child with cancer, and to what extent this care matches with families' psychosocial risk profiles as measured with the Psychosocial Assessment Tool (PAT).
Design/Methods: In this multicenter longitudinal Dutch study, 83 families (response rate 73%) of newly diagnosed children with cancer (0-18 year) participated. The PAT was assessed at diagnosis, and their need for psychosocial care was assessed six months later. Families were considered at low risk (PAT≤0.99), medium risk (PAT1.00-1.95), or high risk (PAT≥1.96) for psychosocial problems. Subsequent matched psychosocial care was defined as child care specialist for all families, social worker for medium risk families, and psychologist for high risk families. When parents wanted help from a psychosocial care specialist, but had not received it, it was defined as an unmet need.
Results: 65% of families had low, 30% medium, and 5% high risk for developing psychosocial problems according to the PAT. Of low-risk families, 17% of the children and 26% of the parents received care by a psychologist, and 49% got help from a social worker. In families with medium risk, 48% of the children and 40% of the parents received psychological care, and 72% got care from a social worker. In high-risk families, 50% of the children and 50% of the parents got psychological care, and 75% received help from a social worker. Unmet needs regarding psychosocial help were highest among families at medium (16%) or high risk (25%) regarding a child psychologist.
Conclusion: Results indicate that psychosocial care is only partly matched to risk profiles. It seems that low risk families tend to get more specialized care than their risk profile would suggest, while families with severe risk get less care than risk profiles suggested. Feedback of the risk profile could optimize this match.

PPO - Patients, Parents & Sibling Subjective Perspectives on the Childhood Cancer Journey

O-239

VOICING MY CHILD CANCER IN SENEGAL: CHALLENGING THE ASSUMPTIONS WE MAKE ABOUT CHILDREN'S PERCEPTION OF THE CANCER EXPERIENCE BY ALLOWING THEM TO NARRATE IT

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Background/Objectives: This qualitative study challenged assumptions made by adults in a culture where silence is supposed to be golden for children.Our purpose was to offer a cathartic space for young cancer patients to describe their experience from diagnosis through remission.
Design/Methods: We've collected data from therapeutic groups in which children hospitalized of the only pediatric oncology unit in Senegal described the treatment process, the hospitalization, and their repercussions on their regular lives. The instruction was to write a letter to a newly diagnosed patient to prepare her for the upcoming cancer experience (original idea from Dr Wiener). We've collected data from 10 hospitalized patients aged between 6 and 15.
Results: Our patients reported a detailed description of the physical explorations necessary for diagnosis; the treatment process including the frequent blood draws; chemotherapy and the "colored" infusions; surgery and its painful aftermath. Young patients have also addressed the bodily changes provoked by the chemotherapy, all their interactions and appreciations of the staff as well as the hospital stay day-by-day. Unexpectedly, they paid special attention to the temperature in the rooms, the quality of food, the distinctions in the quality of care amongst the medical practitioners and depending on the time of day. For their newly diagnosed pair, young patients focused deeply on the painful procedures, the emotional experience of being away from home, having depressive phases during treatment, being stigmatized at school and at home …etc.
Conclusion: In Senegal we assume that children are too fragile to be informed, yet we were surprised of how mindful and aware they were about their cancer experience. Contrarily to popular belief assuming that young patients can't talk about their disease, we've demonstrated that children were at ease in describing their pathology with more details than their parents and with focus on aspects oblivious to the adult eye.

O-240

BEREAVEMENT AND END OF LIFE CARE ISSUES OF CHILDREN WITH CANCER AND THEIR PARENTS

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Background/Objectives: Children Cancer Unit- Indus Hospital, provides free of cost services to children with cancer who come for treatment from all over Pakistan and Afghanistan. Since there is a paucity of human and financial resources, visits could not be made to homes of bereaved families to offer condolences or support. Therefore a protocol was devised which would include offering condolence calls via telephone, to bereaved families and to identify areas of further improvement in end of life care services being offered.
Design/Methods: Sixty-five bereaved families were approached and interviewed by the spiritual counselor and psychotherapists trained in person centered care, over the telephone.
Results: A qualitative analysis was carried out in which the themes that were prevalent in end of life care, were of excruciating pain that children with cancer faced and parents' trauma as well as the post traumatic experiences that the parents faced from seeing the death of their child. Relying on divine will as the reason for the end of suffering through death and the subsequent relief, were also factors that came up. Moreover some parents wanted there to be a way to ease the death of the child. In the bereavement phase the factors that were identified were that the more supportive the families felt health professionals in the Children Cancer Unit, Indus Hospital were, the better their coping mechanisms were with the grief of losing their child. There was gratitude and a sense of calm at getting condolence calls from the counselors, and the ones who showed distress were given grief counseling.
Conclusion: Further research into non pharmacological and pharmacological means of pain alleviation, needs to be carried out to ensure that children with cancer receive effective pain reduction treatment in end of life care. And the distress of the parents whose children have died can be lessened further.

O-241

SIBLINGS' EXPERIENCES OF THE BROTHER'S OR SISTER'S CANCER DEATH: A NATIONWIDE FOLLOW-UP 2-9 YEARS LATER

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Background/Objectives: Even though siblings of a child who dies from cancer live the illness experience with the same intensity as the parents, they often stand outside the spotlight of attention, and until recently, little research has focused on the sibling's situation. The aim of this study was therefore to examine siblings' experiences of their brother's or sister's cancer death and if these experiences influenced levels of anxiety 2-9 years later.
Design/Methods: This nationwide survey was conducted in Sweden 2009. All siblings who had a brother/sister who was diagnosed with cancer before the age of 17 and who died before the age of 25 during 2000-2007 were invited. Of those, 174 siblings participated (participation-rate: 73%). Mixed data from the survey about the siblings' experiences of death were included as well as data from the Hospital Anxiety and Depression Scale. To examine the experiences, descriptive statistics and content analysis were used. Mann-Whitney U-test was conducted to investigate if the experiences influenced anxiety 2-9 years later.
Results: The siblings reported poor knowledge and experienced a lack of communication about their brother's/sister's death, e.g. about the time frame and bodily changes near death. Siblings who reported that no one talked with them about what to expect when the brother/sister was going to die reported higher levels of anxiety 2-9 years after the loss. Seventy percent reported that they witnessed their brother/sister suffering the last hours in life. Stressful situations during end-of-life care and poor communication within the family were described as influencing the siblings' grieving process. Many of those who were not present during the illness trajectory and at the time of death regretted that.
Conclusion: It is important to prepare siblings for their brother's/sister's illness and death in order to prevent anxiety and regrets later on.

O-242

INCORPORATING GOOD PATIENT, PARENT, AND PROVIDER DEFINITIONS TO IMPROVE CARE INTERACTIONS AND PSYCHOSOCIAL OUTCOMES FOR CHILDREN WITH CANCER, THEIR FAMILIES, AND THEIR CARE TEAMS

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Background/Objectives: Understanding how adolescents with cancer define "good patient" and "good child" roles and how parents abide by a "good parent" definition may improve care interactions and decisional approaches for children with cancer.
Design/Methods: The study team engaged in three prospective, face-to-face qualitative interview studies at two pediatric hospitals in the United States. Parents (n=43 in urban PICU setting, n=62 in cancer hospital setting) were asked to describe factors important for parenting their ill child and how clinicians could help them achieve their definition of "being a good parent" to their child. Adolescent-age cancer patients (n=40 in two separate cancer centers) were asked to describe their definition of "being a good patient" and "being a good child" during times of illness. Parent and patient responses were analyzed thematically with strict adherence to consolidated criteria for reporting qualitative research (COREQ) guidelines.
Results: A concept of good child and good patient exists for adolescents undergoing cancer treatment and the ill child is conscious of these in care interactions, family dynamics, and medical decisions. A concept of good parent exists and influences end of life treatment decision-making in at least two different parent groups: parents of children with incurable cancer parents of children in the PICU who may or may not survive. Participants identified key staff interactions that support or hinder these good parent, child, and patient roles.
Conclusion: As the concept of good patient and good child exists for adolescent cancer patients and the concept of good parent exists for their care guardians, the concept of good doctor and good nurse has been reported in the literature as influencing care delivery. A better understanding of the interactions resulting from these concepts and "good role" beliefs may improve medical care, decision support, and psychosocial outcomes in pediatric cancer.

PPO Free Papers Session

O-243

SIOP PODC GLOBAL TASK FORCE ON HOSPITAL DETENTION PRACTICES: COLLABORATING INTERNATIONALLY TO RAISE AWARENESS AND ENCOURAGE ADVOCACY AND ACTION TO END HOSPITAL DETENTION

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Background/Objectives: Data on repeated detention of children with cancer in Kenyan public hospitals presented by Mostert and Njuguna at SIOP Hong Kong and published in *Pediatric Blood and Cancer* and *Psycho-Oncology* led to the 2014 creation of the SIOP PODC Global Task Force on Hospital Detention Practices. The goal is to advocate for awareness and find solutions to end hospital detention practices, where patients are kept in hospital due to families' inability to pay hospital costs.
Design/Methods: Starting with online meetings in existing PODC working groups, the Task Force encompasses 32 members from 12 countries. An online repository was initiated to highlight hospital detention practices in the literature and lay media and to extrapolate lessons from advocacy efforts for patients across diverse settings. Monthly meetings included reports of detention in Africa, Asia, South America and Eastern Europe. Lack of consistent nomenclature was noted to hinder descriptions and comparisons, as did challenges to open reporting by professionals. Outreach to Human Rights Watch and other organizations helped define need for collaborative and creative means to effectively end hospital detention.
Results: The Task Force established use of consistent nomenclature, preferring "hospital detention" to "hospital retention." A Position Statement on Hospital Detention was prepared for publication. Recognition of the Task Force's work led to a Statement of Support from the International Psycho-Oncology Society (IPOS), posted on the IPOS website and reflected in a Presidential Plenary talk at the July 2015 IPOS/APOS Washington meeting. A session hosted by Childhood Cancer International at SIOP/Asia in Jordan in April 2015 was organized to raise awareness and increase international collaboration.
Conclusion: More research and action are needed to document the extent and impact of hospital detention on lowering survival and reducing quality of life for families of cancer patients. International collaboration is essential to finding solutions to end this practice.

O-244

POOR IMPACT OF POST-ABANDONMENT TRACKING AND COUNSELLING PATIENTS WHO DEFAULTED TREATMENT OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA: THE NEED OF PRE-EMPTIVE STRATEGIES

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Background/Objectives: Treatment abandonment is an important hurdle in the optimum outcome of children from low/middle income countries with malignancies. Tracking of patients who abandon therapy is being recongized as a useful interventional tool. We herein describe our experience with post-abandonment tracking and its effect on the outcome of children who abandoned ALL therapy.
Design/Methods: All ALL patients managed at author's institution from 2007-2013 who abandoned therapy were tracked telephonically. Postal communication was used whenever telephone communication failed. The contacted families were called weekly till they returned for treatment or until the child died. During the contact, parents/responders were counselled by the social worker/physician regarding the importance of resuming treatment and urged to return immediately.
Results: 77 of 418 patients abandoned therapy. Telephonic calls were made to 60 of these families, of which 29 could be contacted (give median/mean and range of no of telephone calls).Of those who could not be contacted, 15 telephone-numbers were invalid, calls to 10 went unattended, and 6 were told to be wrong numbers. Letters were sent to48 families, only 10 of which evoked responses.In total 39/77 (50.6%) families could be contacted. Upon contact, 20 patients were reported to have expired and 19 patients were told to be well. Only 8 of these 19 patients returned on repeated counselling and assurance of all possible support (after an average of 6 calls made to each family), 4 with relapse. Recurrent abandonment was seen in 3 patients who returned (1 of them died of relapse, 2 still on treatment).
Conclusion: Tracking patients post-abandonment was unsuccessful in more than half of the patients. Outcome of abandonment remained grim despite our efforts, as post-abandonment counselling failed to ensure compliance in majority of the contacted families. Future efforts will need to be focussed on preemptive strategies.

O-245

MEDICAL AND PSYCHOSOCIAL CORRELATES OF INSOMNIA IN PEDIATRIC BRAIN TUMOR SURVIVORS

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Background/Objectives: Improving survival rates for children diagnosed with brain tumors have resulted in a growing population at risk for medical and psychosocial late effects of treatment. In particular, children treated for a brain tumor commonly report suffering from insomnia. There has been limited literature examining insomnia within the pediatric brain tumor survivor population. We used a clinically significant indicator of insomnia (sleep efficiency) to evaluate insomnia rates, medical and psychosocial correlates, and medical documentation of sleep-related issues during survivorship visits.
Design/Methods: 98 adult survivors of pediatric brain tumors provided self-report data about sleep, psychological distress, and health-related quality of life. Medical records were reviewed for all participants to examine treatment-related information (surgery, chemotherapy, CNS-directed radiation therapy), and for documentation of sleep-related issues if the participant completed study measures on the same day as a survivorship medical visit.
Results: 26% of the sample reported clinically significant insomnia. Insomnia status was associated with a migraine headache history, but not with any other medical or psychosocial outcomes. Approximately 1 in 3 medical providers did not document a discussion about sleep during the survivorship visit.
Conclusion: A sizeable minority of survivors of pediatric brain tumors experience insomnia. With the exception of migraine headaches, there were limited medical or psychosocial risk factors identified. Thus, medical providers must use the survivorship visit as an opportunity to conduct a thorough evaluation of sleep-related issues for this at risk population, and to provide appropriate intervention or referrals.

O-246

REPRODUCTIVE STRATEGIES IN FAMILIES WITH CHILDHOOD CANCER SURVIVORS

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Background/Objectives: The objective is to study reproductive strategies of families with children-cancer survivors and various social, medical and psychological factors contributing to changes in reproductive behavior and family planning.
Design/Methods: Data from the families were collected in 2009-2013 through interviews and questionnaires of 1085 mothers from 78 regions of the Russian Federation; mothers aged 25–49 (average 36.6), with a cancer child aged 5–17, in remission from 1–12 years (average 4.2). The results were compared with the data of the Russian state statistics agency's demographic research of the same period (1118 female respondents of the same age range) – comparable with the population.
Results: The study revealed the gap between our and control group according to the number of children - born, desired and expected. The number of children born per woman increased in our group versus control group: 1 child - 39.7% vs 58.3%; 2 – 48.7% vs 27.8%; 3 – 9.6% vs 3.8%; 4 and more – 2.1% vs 0.7% respectively. The main demographic indices - reproductive attitudes in our group were significantly higher versus control group: average desired number of children – 2.59 vs 2.28; average expected – 2.05 vs 1.72 respectively. This has been linked to changing social and family values in our group. The study proved the higher level of family values in the system of value orientations in our group versus control group. Oncological diseases in children and long-term treatment made considerable impact on family relations: 25.3% - improved; 10.7% - deteriorated; 9% - divorced; 55% - not changed. This data inversely correlated with the level of education of respondents ($P<0.05$) and with nosology of cancer - family relations worse in children with solid tumors versus hemoblastoses ($P<0.05$).
Conclusion: Childhood cancer can change the meanings and life priorities towards pro-family orientation. The families need psychological, social and medical support.

PROS - Free Papers Session

O-247

INTENSIVE TREATMENT OF HIGH-RISK MEDULLOBLASTOMA (HR-MB): HOW TO LEARN FROM TOXICITIES IN A EUROPEAN SETTING OF RADIOTHERAPISTS AND PHYSICISTS OF THE SIOP BRAIN TUMOR WORKING GROUP

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Background/Objectives: Survival of HR-MB has historically been poor despite full-dose CSI and chemotherapy. In 2009, very promising 5-year results were published in JCO concerning an intensive regimen including post-operative sequential high-dose chemotherapy, hyperfractionated-accelerated radiotherapy (HART), 39 Gy CSI plus 60 Gy posterior fossa boost, and two cycles of high-dose tiothepa in case of non-CR before HART. Since then, several Centers in Europe adopted the regimen, not as a GCP protocol, and the HART approach became the backbone to develop a new SIOP study. In 2014, "unexpected" neurotoxicities were reported in different European countries: to address these issues, a meeting was held in Milan in November 2014 during which Radiation Oncologists and Physicists from most European countries collegially reviewed the treatment plans of children showing neurotoxicity after intensive treatment for HR-MB to highlight any possible correlation with radiotherapy technique and dosimetry.
Design/Methods: From 2009, about 240 HR-MBL children were treated according to an HART approach and 27 showed grade 3-4 neurotoxicity as follow: 18 global neuro-functional impairments, 4 myelitis, 5 brainstem/cerebellum radionecrosis. Clinical charts and seventeen treatment plans of children with neurotoxicity were reviewed and discussed in Milan.
Results: Global neurotoxicity occurred in children younger than 10 receiving high-dose thiothepa after HART but no correlation with radiotherapy technique and dosimetry was established. Myelitis was associated with inclusion of upper cervical spine in posterior fossa boost volumes, while brainstem/cerebellum radionecrosis occurred after delivery of an additional 9 Gy boost to posterior fossa residuum not contemplated in the original HART approach.
Conclusion: Global neurotoxicity should be evaluated as a benefit/risk issue in the context of a high risk disease. The joint international discussion and face to face confrontation of radiotherapists and physicists allowed to highlight important clinical and radiotherapy-linked risk factors that will be valuable in developing a new SIOP protocol for HR-MBL and high-standard radiotherapy guidelines.

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LATE TOXICITIES IN CHILDREN WITH NASOPHARYNGEAL CARCINOMA (NPC) TREATED WITH INTENSITY MODULATED RADIOTHERAPY (IMRT): DOSE VOLUME RELATIONSHIPS

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Background/Objectives: Evaluation of late toxicities and their correlation with dose volume relationships in children with NPC treated with IMRT.
Design/Methods: Seventy three children [median age 14 years] treated with IMRT and Cisplatin based chemotherapy from Jan 2004 to Dec 2013 were analysed. Response assessment PETCT was done at 3 months post treatment. Follow up evaluation was done 3 monthly for 2 years and 6 monthly thereafter. Pure tone audiogram and thyroid function tests was done at 3 months, 1 year and thereafter as indicated. Ototoxicity was graded using the SIOP Scale 2012.
Results: At a median follow up of 26.7 months [4-136 months], the overall survival (OS) and disease free survival (DFS) were 89% and 70% respectively. Serial audiometric evaluations revealed Gr II ototoxicity in 63%. ROC analysis showed an increased risk of SNHL with cochlea receiving Dmean $\geq$ 46Gy [p=0.035] or total Cisplatin dose >400 mg [p=0.041]. An improvement in SNHL by at least 2 grades was observed after 2 years. Mandibular remodelling was also significantly affected. A measurable decrease in bigonial and bicondylar width was observed along with absolute halting of mandibular body growth. Significant correlation was found with age at time of radiotherapy [Spearmann's correlation ρ-0.469, p= 0.014], maximum mandibular dose [ρ-0.500, p= 0.008], and V25 [ρ-0.419, p=0.03]. The reduction being greatest in pubertal age group, Dmax > 72Gy, and V25 > 53cc. Subclinical hypothyroidism was seen in 73% after a minimum of 12 months post IMRT. Baseline thyroid gland volume was a significant predictor of hypothyroidism. Children with thyroid dose <30Gy to <2cc volume had a significantly lesser risk of developing hypothyroidism [p= 0.046].
Conclusion: Late radiation toxicities like SNHL, mandibular hypoplasia and hypothyroidism following IMRT for childhood NPC demonstrates a significant dose volume relationship. Appropriate dose constraints should be considered during IMRT planning.

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QUALITY OF LIFE IN TODDLERS TREATED WITH PENCIL BEAM SCANNING PROTON THERAPY FOR PEDIATRIC TUMOURS

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Background/Objectives: Assessment of Quality of Life (QoL) in standard therapies for childhood cancer has become an integral part in many studies. Little is known about QoL in patients treated with proton beam therapy (PT).
Design/Methods: PATIENTS AND METHODS: Longitudinal and cross-sectional QoL data (proxy-assessment) including a baseline-assessment before PT were provided for childhood patients treated at the Paul-Scherrer-Institute (Villingen/CH) during the years 2005-2014. Data of a homogenous sub-sample (n =49) defined by age group and proxy-assessed by the PedsQL (patients aged 2-4) were compared to an age-adapted

reference sample. This represent 71% of all patients treated with PT during this time-period in the according age range.
Results: When compared to the norm (n=256), toddlers with cancer (n=49) had a significant decrease of QoL in all domains except in Emotions before the initiation of PT. During PT, the overall QoL (total mean scores, 26.5 vs. 27.9; p>0.1) did notably increase for these patients. A trend toward statistical significance was observed with decreasing QoL in the Social domain (total mean scores, 84.8 vs. 78.8; p=0.06). One year after PT, a significant increase of the overall QoL was observed (total mean scores, 73.6 vs. 76.6; p=0.05), especially so in the Emotional domain (total mean scores, 67.9 vs. 74.8; p=0.02).
Conclusion: Although QoL of toddlers with cancer is significantly decreased when compared to normative data, PT has no impact on the QoL of these very young patients. One year after therapy, QoL increased significantly in all domains.

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SCOLIOSIS IN CHILDREN RECEIVING CRANIOSPINAL IRRADIATION FOR MEDULLOBLASTOMA

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Background/Objectives: Scoliosis is a recognized complication in children receiving radiotherapy to the hemiabdomen. Care is taken by radiation oncologists to ensure delivery of homogeneous radiation to the width of the vertebra to minimize this complication. In craniospinal irradiation (CSI), the entire width of the vertebra is usually given a homogenous dose. We examined the incidence of scoliosis in our long-term survivors with medulloblastoma.
Design/Methods: Since 1996, 37 children have survived at least 5 years after photon radiotherapy for medulloblastoma at one institution. Twenty-two children had routine spinal X-rays to detect scoliosis and the subject of this report. Seventeen were male, and twelve were ≤ 5 years of age at CSI. All of them were treated using a 3-dimensional photon technique to the craniospinal axis (18 to 39.6 Gy) followed by an IMRT boost to the posterior fossa and/or tumor bed. Patients also received chemotherapy according one of 3 multiinstitutional protocols.
Results: Scoliosis was seen in 15 patients (40.5% of all patients followed for at least 5 years and 68.2% of patients who had routine spine X-rays). Median time to scoliosis was 108 months after CSI (range, 42 to 128 months). Scoliosis was not associated with gender, age at time of CSI, CSI dose, length of follow-up or presence of hemiparesis. Degree of scoliosis was < 10 degrees in 5, 10-19 in 7 and ≥ 20 in 3 patients. Scoliosis involved the thoracolumbar region in 8, thoracic spine only in 3, thoracolumbosacral region in 3 and cervicothoracolumbar region in 1. None of the patients had surgical intervention for the scoliosis.
Conclusion: Scoliosis is an under-reported complication of CSI and was found in more than two-thirds of children treated for medulloblastoma. Despite its high frequency, most are minimal and do not require intervention; however, longer follow-up is needed regarding the significance of this finding.

O-251

PROGRESSIVE TECHNIQUES TO EFFECTIVELY PREPARE CHILDREN FOR RADIOTHERAPY: A SUPPORTIVE FRAMEWORK COMBINING INFORMATIVE FILMS WITH A MINIATURE WORKING MODEL LINAC

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Background/Objectives: The aim of this project is to provide a comprehensive preparation framework that incorporates patient involvement and peer support with the practical facility of a working miniature model LINAC (Linear Accelerator) for therapeutic play. By increasing understanding and familiarity of radiotherapy and its planning procedures prior to commencement of treatment, anxiety levels are lowered, and the need for general anaesthetics may be decreased. Demystifying the process of radiotherapy also increases compliance, which can result in reduced time spent in the treatment room.
Design/Methods: Over an 18 month period 17 children and adolescents, aged 3-16 years, were filmed and interviewed throughout their radiotherapy procedures. These films have been organised into four stages; introduction to radiotherapy, immobilisation, CT planning, and treatment. Downloaded onto the IPad, the films can be taken to the patient at the bedside, into a clinic consultation, to another hospital or on a home visit. The child and family view each step of the radiotherapy process via the preparation film, and can then practice and familiarise themselves with their individual treatment plan on the miniature machine, which has been commissioned within our department.
Results: Feedback from questionnaires for the adolescent film were overwhelmingly positive, with 100% of patients and parents reporting an increase in their understanding of the radiotherapy process. Results are currently being obtained for the paediatric version using age-appropriate questionnaires for children and their parents/carers. The opportunity to view children of similar ages going through the same procedures allows for peer learning and support, while the practical play activities on the miniature LINAC help to normalise the experience.
Conclusion: The supportive framework ensures that all paediatric patients coming for radiotherapy have equal access to tools and equipment that can appropriately and effectively prepare each individual child for their treatment, regardless of language and cultural differences.

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PROTON BEAM THERAPY IN CHILDHOOD - INITIAL RESULTS FROM THE WEST GERMAN PROTON THERAPY CENTER ESSEN (WPE)

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Background/Objectives: Proton beam therapy (PT) has experienced increasing interest over time especially in pediatric malignancies as PT may be able to reduce post-treatment late effects. The West German Proton Therapy Center Essen (WPE) started treatments for pediatric tumors in June 2013. Initial findings are presented.
Design/Methods: Between September 2013 and March 2015, 82 children (40 males, 42 females, aged 1.3-16.8 years (median 5.4 years)) were enrolled into the prospective registry study for children (KiProReg) at WPE. Diagnoses were CNS (n=44), sarcomatous (n=37) and nasopharyngeal tumors (n=1), respectively. Treatment sites were head or neck (n=64), spine (n=9), or pelvis (n=9). In 75.6% of the patients, macroscopic residual disease was present before PT. The median total dose of PT was 54 Gy (range 30.6-74.0 Gy). Only one patient had a mixed beam technique. In 56.1% of the children, concurrent chemotherapy was applied. Side-effects were classified according to Common Terminology Criteria for Adverse Events (CTCAE) V4.0 grading system.
Results: Median follow-up (FU) was 7.0 months (range 0.4-16.0 months). In 76 children (92.7%), no or only mild to moderate acute side-effects (grade 1 or 2) were documented (skin disorders, mucositis). Only 6 children presented with grade 3 treatment-related toxicities (mucositis, fatigue, anorexia); five of them receiving chemotherapy simultaneously. No grade 4 or 5 side-effect was observed. In 50 patients, information on early late effects after at least 3 months (range 3.0-13.5 months) is available. In this group, no toxicities grade 3 or higher were revealed. So far, 12 children failed due to tumor recurrence or progression (local n=7; systemic n=5). Five of them died of disease.
Conclusion: Prospective data from WPE registry suggest good feasibility with only mild or moderate side-effects in the majority of children even when administering high doses at critical sites. Longer FU time is needed to assess late effects and long-term outcomes.

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USE OF HYPNOSIS IN RADIOTHERAPY AS AN ALTERNATIVE TO GENERAL ANESTHESIA IN PEDIATRIC RADIATION ONCOLOGY

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Background/Objectives: Even though general anesthesia (GA) is effective and has proof of safety for the necessary immobilization of patients during radiotherapy (RT) sessions, it stays a timely and costly method on which we know little about the consequences on the long run of repeated use in childhood. The use of rituals and/or hypnosis has been encouraged in multiple fields of medicine, enabling distraction for uncomfortable moments of treatment and it seems children have a natural propensity for it. This observational study which took place in the RT children cancer department (Leon Berard regional center, Lyon, France) aimed to evaluate the place of the alternative of rituals and/or hypnosis in RT.
Design/Methods: Two time periods, before and after 2008 (2003 – 2013) have been compared, the second one introducing accompaniment methods such as hypnosis systematically. 137 children < 5 years benefited from RT in that period and were included (70 pts before 2008, 64 after 2008).
Results: There was no significant difference between the two populations for age, sex and localization of the RT. There was significantly more high-technicity RT in the second period (17% vs 44% p<0.001). There was no significant reduction in the use of GA (57% vs 53%, p = 0.235) globally but the techniques used on the second period were more sophisticated (longer sessions, optimal asset, limited margins …) and GA should have been more frequent. The pts more likely to undergo RT without GA were the oldest and the patients treated for abdominal lesions.

Conclusion: Also globally this study did not find a significant reduction in the use of GA after introduction of extra accompaniment and hypnosis in young children receiving RT, this drug – free technique could limit its logical increasing use in a world where in parallel RT techniques have greatly evolved in precision.

O-254

PROTONTHERAPY IN CHILDREN WITH LOCALIZED INTRACRANIAL GERMINOMA: DOSIMETRIC ADVANTAGE WITH USE OF NEW PENCIL BEAM SCANNING (PBS) IN COMPARISON TO DOUBLE-SCATTERING (DS)

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Background/Objectives: In children with a localized intracranial germinoma, due to the complex clinical target volume, defined as whole ventricle system (WV) and tumor bed, and the excellent long-term survival after induction chemotherapy and radiotherapy, there is a need for the investigation of the dosimetric advantage of new delivery technology such as with pencil-beam scanning (PBS) proton therapy compared with the more common double-scattering (DS) technique.
Design/Methods: Five children with localized intracranial germinoma treated with protons at Hospital of the University of Pennsylvania were retrospectively studied. PBS and DS proton plans were generated for each patient prescribing dose of 23.40Gy to WV, with 21.60Gy boost at primary site (protocol COG ACNS 0232). Dose-volume histogram parameters of clinical organs at risk were compared with Wilcoxon matched-pair signed-rank test. For target coverage assessment, the conformity index and homogeneity coefficient were evaluated.
Results: The V10Gy, V20Gy, V30Gy and integral dose to normal brain tissue of PBS plans showed a significant dose reduction of 22%, 35%, 41% and 4% compared to DS plans ($P<0.05$). There was also a reduction by 14% for the V20Gy and by 8% for mean doses to the temporal lobes ($P<0.05$). No significant differences were found for the mean dose of the hypothalamus and pineal gland ($P>0.05$). For PBS plans the mean doses to the hippocampi and cochlea were also significantly reduced by 6% and 16% ($P<0.05$). The average conformity index was 0.69 for PBS plans, while was 0.62 for DS plans, showing a significant better conformity ($P<0.05$). There was no significant difference in target coverage homogeneity between the two plans ($P>0.05$).
Conclusion: As compared to DS proton therapy for pediatric localized intracranial germinoma, PBS proton delivery technique achieved significantly better target conformity, allowing more dose sparing to normal brain tissue, temporal lobes, hippocampi and cochlea.

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PRINCIPLES AND ADVANCES OF 223-RADIUM AND PROTON PARTICLE THERAPY IN BONE-FORMING TUMORS INCLUDING OSTEOSARCOMA

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Background/Objectives: It is estimated that >2/3 of cancers arise from accumulation of mutations in tissue stem cells. More effective elimination of cancer stem cells can be accomplished using varieties of particle radiation that have high Linear Energy Transfer (LET) values, causing >100x more double-strand DNA breaks which are hard to repair than lower LET radiation (photons or electrons including beta-emitting pharmaceuticals). Radium-223, an alpha particle emitter, is now US FDA and EMA approved for prostate cancer, and improves both pain from bone metastases and prolongs survival.
Design/Methods: We have now successfully reached the dose expansion cohort using Radium-223 for osteosarcoma: 100 kBq/kg monthly x6.
Results: At 2x the standard dose used for prostate cancer, hematologic toxicity has been minor; no significant (grade 2) toxicities were seen. Preliminary imaging data of osteoblastic tumors has shown fluoride-PET/CT to be better than FDG-PET/CT or Tc-99m MDP bone scans in evaluating response. One patient with brain metastases showed Radium-223 can traverse the blood brain barrier. New technology can provide image guided proton beam therapy, with techniques rapidly improving. Also, the cost of building a new proton center with enhanced precision and capabilities is estimated to be a tenth of the cost a decade ago. With improved immobilization and image–guidance, proton therapy is evolving to allow delivery of precision particle therapy with larger fractions. Hypo-fractionated proton plans are currently in development; examples will be shown.
Conclusion: Since relapse at sites of non-osteoblastic metastases continue to be a problem, other means to more specifically target Radium-223 and protons to tumor stem cells is needed. Because of less toxicity, decreased cost, and potential increased efficacy, particle therapy with alpha particles and/or protons will become more widely used in children, adolescents, and adults with malignancies that rely on radiation for durable local control (e.g. axial osteosarcoma, Ewing sarcoma, bone and brain metastases).

Poster Discussion: Acute Lymphoblastic Leukaemia

PD-001

THE NEDD8 ACTIVATING ENZYME INHIBITOR PEVONEDISTAT (MLN4924) INDUCES ER STRESS/UPR-MEDIATED CELL DEATH AND ALTERS THE APOPTOTIC THRESHOLD FAVORING CELL DEATH IN ACUTE LYMPHOBLASTIC LEUKEMIA

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Background/Objectives: Acute lymphoblastic leukemia (ALL) is the main cause of cancer-related death in children and adolescents, and effective treatment strategies for relapsed/refractory ALL remain elusive. In search for novel strategies, we investigated the anti-leukemic activity of the NEDD8-activating enzyme (NAE) inhibitor pevonedistat, an investigational agent that interferes with cullin-RING E3 ligase-(CRL)-dependent protein degradation by preventing CRL neddylation.
Design/Methods: We used pharmacological, molecular, and genetic approaches targeting the NEDD8, UPR, and mTOR pathways in ALL cell lines and primary cells.
Results: Our data showed that pevonedistat induced dose-dependent ER stress/UPR-mediated cell death in ALL cell lines and primary cells, as evidenced by increased expression of UPR markers (GRP78, ATF4, CHOP) and cleaved-PARP. Mechanistically, pevonedistat led to p-eIF2a de-phosphorylation via up-regulation of the PERK inhibitor p58IPK, causing proteotoxic/ER stress from failure to halt protein translation. Pevonedistat also led to up-regulation of mTOR/p70S6K, further increasing protein synthesis and augmenting proteotoxic/ER stress. Additional studies into the mechanism of pevonedistat-induced apoptosis revealed that homeostasis of pro- and anti-apoptotic proteins was rebalanced in favor of cell death through decreased Mcl-1 pro-survival activity, via sequestration by NOXA and BIM. Activation of the MEK/ERK/Mcl-1 pathway following pevonedistat-induced cell death was also noted, possibly as a compensatory mechanism. Further, we demonstrated in vitro synergy between pevonedistat and effective anti-leukemic drugs and showed that NSG mice harboring human ALL cells treated with pevonedistat plus dexamethasone had statistically significant increased survival when compared to single agent therapy, lending support for the clinical investigation of pevonedistat as part of a multi-agent approach.
Conclusion: Our data demonstrate that the NAE inhibitor pevonedistat alters the cells' translational machinery, leading to in vitro and in vivo ER stress/UPR-mediated cell death, and suggest pevonedistat may have a "priming" effect on ALL cells by affecting the apoptotic threshold through modulation of Mcl-1's pro-survival activity.

PD-002

TREATMENT COST FOR CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKAEMIA IN BANGLADESH

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Background/Objectives: Acute Lymphoblastic Leukaemia(ALL), the most common childhood malignancy in Bangladesh, is potentially curable but high rates of treatment refusal and abandonment are seen. The principal reason is the cost burden on families who pay for all drugs. This is the first study performed in Bangladesh to assess the cost of having a child with ALL.
Design/Methods: A cross-sectional study of costs incurred by 50 families of a child with ALL at the BSMMU hospital was conducted over a six month period. 10 parents were requested to keep and submit receipts for all costs of drugs, transport, food and accommodation at each of five treatment phases: initial investigation, remission induction, intensification, consolidation and maintenance. All the children were treated on the same modified UK Medical Research Council ALLX1 protocol.
Results: The mean age of the boys was 6yrs and 7.8yrs for girls. The identified mean basic cost of all therapy was $ 4443(range $3234-$7672).49%of costs were for cytotoxic drugs,9% for investigations,2.5% for procedures, 0.6% for blood and blood products,12.9% for general treatment and 26% for other aspects including transport ,food and parental lodging. On average each episode of febrile neutropenia added $1200 and for this cohort the mean number of episodes was three .With refractory fever

requiring changes in antibiotics a further $1740 was required. This mean cost in local currency was BDT 311028(226400-537040 BDT). 33%of Bangladeshi families live on<5000BDT per month and 51% between 5000 and 20,000 BDT per month.
Conclusion: Although the costs reported are considerably less than in high income countries they remain prohibitively high for most families in Bangladesh leading to treatment abandonment in 15-20% of cases. Internal and external philanthropic subsidies have ameliorated the problem to some extent but long term solutions to the cost of treatment both in Bangladesh and worldwide are required.

PD-003

IMPACT OF ASPARAGINE-DEPLETION ON TREATMENT OF RELAPSED CHILDHOOD ALL: RESULTS OF THE ALL-REZ BFM 2002 TRIAL

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Background/Objectives: About 15-20% of patients with childhood acute lymphoblastic leukemia (ALL) suffer from relapse after frontline therapy. The significance of asparaginase treatment during frontline therapy is well known. We here describe the impact of asparagine depletion (using native E.coli-, PEGylated E.coli, or Erwinia asparaginase) on outcome of patients with relapsed childhood ALL treated according the ALL-REZ BFM 2002 trial.
Design/Methods: We retrospectively analysed the outcome of patients who were treated according to ALL-REZ BFM 2002 trial from January 2002 until December 2014. Only patients with first relapse were included in the analysis. From a total of 908 patients registered within the ALL-REZ 2002 trial, sufficient data on type and extend of treatment with asparaginase were available for 789 patients.
Results: Asparagine depletion at the first induction cycle of relapse treatment was performed using native E.coli, PEG- and Erwinia asparaginase in 51%, 38%, and 7% respectively. In 30% of patients type of asparaginase was changed due to allergic reactions or silent inactivation. Recurrent severe allergic reactions precluded continuation of asparaginase treatment in 17% of patients. Substitution of native E.coli by PEG- or Erwinia asparaginase did not result in reduced 5y-EFS (56% ± 3% vs. 55% ± 2%). In contrast, univariate analysis revealed discontinuation of asparaginase treatment as risk factor for poor outcome (5y-EFS 46% ± 4% vs. 57% ± 2%, p=0.05). During induction therapy, asparaginase treatment was of particular significance. Incomplete asparaginase application was associated with poor morphological response after induction (rate of morphological remission: 34% vs. 65%, p<0.001) as well as poor outcome (5y-EFS 41% ± 7% vs. 56% ± 2%, p=0.01).
Conclusion: Asparagine depletion is an important component of treatment of relapsed childhood ALL according to the ALL-REF BFM 2002 trial. The type of asparaginase used has no impact on outcome, but sustained asparaginase treatment during the complete relapse therapy is required.

PD-004

A REVIEW OF NEW AGENTS TESTED BY THE PEDIATRIC PRECLINICAL TESTING PROGRAM AGAINST ACUTE LYMPHOBLASTIC LEUKEMIA XENOGRAFTS

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Background/Objectives: While the overall cure rate for pediatric acute lymphoblastic leukemia (ALL) is approximately 90%, patients with high-risk subtypes remain relatively intractable and new treatments are required. The objective of the Pediatric Preclinical Testing Program (PPTP) is to utilize panels of patient-derived xenografts (PDXs) to prioritize new agents for clinical evaluation in pediatric malignancies.
Design/Methods: PDXs were established from biopsies of pediatric patients with ALL by direct transplantation into immune-deficient mice. PDX panels represent the heterogeneity of pediatric ALL and high-risk subtypes. Drugs are selected based on demonstrated activity against adult cancers, as well as rationale for efficacy against pediatric ALL. *In vivo* testing is conducted in a blinded fashion against panels (n=8) of PDXs, with responses evaluated by event-free survival (T/C) measurements and stringent objective response criteria modeled after the clinical setting.
Results: Over 70 new agents/combinations have been evaluated, including small molecules, antibodies, and antibody-drug conjugates. Less than 25% of the new agents tested elicited objective responses in ≥ 50% of PDXs, despite several drug classes being represented by multiple agents. For example, 6 agents representing the PI3K/AKT/mTOR pathway were completely ineffective. The antimitotic agent eribulin, the kinesin spindle protein inhibitor ispinesib, and the Aurora Kinase A inhibitor alisertib (MLN8237) were highly effective. The most consistently active drug class was MDM2 inhibitors, with MK-8242 and RG7112 inducing objective responses in 6/7 and 7/8 ALL PDXs, respectively.
Conclusion: *In vivo* efficacy testing of novel drugs against panels of pediatric ALL xenografts has identified several candidates for clinical evaluation. Moreover, reporting of all PPTP testing results has highlighted numerous drugs that are unlikely to be active in the clinical setting. The p53/MDM2 axis appears to be of particular interest as a target for the development of novel treatment strategies in pediatric ALL. Supported by NCI NO1CM91001 and NO1CM42216.

PD-005

ACUTE LYMPHOBLASTIC LEUKEMIA OF THE CENTRAL NERVOUS SYSTEM IS MEDIATED BY VASCULAR ENDOTHELIAL GROWTH FACTOR INDICATING A NOVEL TARGET FOR COMPARTMENT-SPECIFIC THERAPY

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Background/Objectives: Involvement of the central nervous system (CNS) in acute lymphoblastic leukemia (ALL) is associated with adverse prognosis. CNS directed therapy is indispensable in all ALL patients, indicating subclinical CNS manifestation in many patients. Therefore, we aimed to characterize mechanisms mediating CNS leukemia and to identify targets for directed treatment.
Design/Methods: Primary B-cell precursor ALL cells were xenografted into NOD/SCID mice. At onset of disease, leukemia cells were isolated from bone marrow (BM) and CNS and analyzed by transcriptome profiling. ALL cells with VEGF knockdown, overexpression and in response to VEGF or an antagonizing antibody were further analyzed.
Results: In a subset of patient-derived xenograft ALL samples we observed leukemia manifestation in BM, spleen, and peripheral blood along with meningeal infiltration in contrast to absent CNS manifestation despite high infiltration in BM, spleen, and blood. In line, meningeal enhancement was detected by magnetic resonance imaging. Expression profiling comparing CNS to BM-derived ALL cells identified *vascular endothelial growth factor A* (*VEGF*) to be significantly upregulated in CNS-ALL cells. Interestingly, increased levels of VEGF known to mediate vascular permeability and trans-endothelial migration have been reported in cerebrospinal fluid of CNS-positive acute leukemia patients. VEGF overexpression, down-regulation, or exposure of leukemia cells to VEGF or the anti-VEGF antibody bevacizumab did not affect cellular proliferation and survival. In brain endothelial cells, VEGF induced signaling activity mediating endothelial permeability. Interestingly, in a trans-well model of brain endothelial cells VEGF-dependent trans-endothelial leukemia cell migration was observed. Moreover, in an *in vivo* model of CNS-positive ALL anti-VEGF treatment significantly reduced leukemia load in the CNS but not in other organ compartments.
Conclusion: In summary, we identified VEGF as a mediator of CNS manifestation in ALL. Importantly, *in vivo* VEGF inhibition significantly decreased involvement of CNS ALL indicating a novel therapeutic strategy to control CNS leukemia.

PD-006

RAPID LUNG MRI: PARADIGM SHIFT IN EVALUATION OF FEBRILE NEUTROPENIA IN CHILDREN WITH LEUKEMIA

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Background/Objectives: Immunocompromised children with hematological malignancies are at increased risk of developing potentially fatal pulmonary infections. Early detection and prompt treatment is critical to combat morbidity and mortality in these children. Computed tomography (CT) scan has inherent radiation risks, which are more harmful in children. We performed this study to determine the technical feasibility and sensitivity of a new rapid magnetic resonance imaging (MRI) protocol compared with high resolution computed tomography for the detection of pulmonary findings in febrile neutropenic children with leukemia.
Design/Methods: Twenty Six children with leukemia (age range: 5-13 years) presenting with fever and neutropenia were included in this prospective study, which was approved by the institutional ethics committee. All patients underwent CT scan and MRI of the chest on the same day. The findings were recorded as nodules, consolidations and ground glass opacity areas. The findings of CT scan and MRI were compared, with CT as the standard of reference.
Results: For the detection of nodules and consolidations, MRI had100% sensitivity, specificity, PPV and NPV, when compared with CT scan.
For the detection of ground glass opacity, MRI had sensitivity, specificity, PPV and NPV of 66.67%, 100%, 100% and 90.91% respectively. There was perfect agreement between MRI and CT examination findings by kappa test (κ=1). No significant difference was observed between the two modalities by the McNemar test (p >0.05).

Conclusion: Rapid lung MRI is technically feasible; has a high correlation, sensitivity and specificity to CT scan; and can emerge as the first line modality for the detection of pulmonary nodules in children with leukemia and persistent febrile neutropenia.These children shall be thus saved from unnecessary radiation involved with CT scans.

PD-007

GENOMIC DNA BREAKPOINTS IN *MLL* GENE AND TREATMENT OUTCOME IN INFANTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA ENROLLED INTO MLL-BABY TRIAL

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Background/Objectives: Acute lymphoblastic leukemia (ALL) in infants is characterized by high incidence of *MLL* gene rearrangements. The purpose of this work was to evaluate the relation between genomic DNA breakpoints in *MLL* gene and treatment outcome in infant ALL treated according to MLL-Baby multicenter trial.
Design/Methods: 62 infants (22 boys and 40 girls with median age of 4.4 mo) with *MLL*-rearranged ALL were included in the current study. Genomic DNA breakpoint detection in *MLL* gene was performed by long-distance inverse PCR. Exon-intron numbering of *MLL* gene was done according to I. Nilson et al, 1996. Among our cohort there were 35 patients with *MLL-AF4* fusion gene (56%), 14 ones with *MLL-MLLT1* (23%), 8 with *MLL-MLLT3* (13%), 4 with *MLL-EPS*15 (6%), 1 with *MLL-AFF3* (2%).
Results: The most common breakpoint location within *MLL* gene was intron 11, detected in 31 cases (50%), less frequently breakpoints in intron 10 (n=13;21%), intron 9 (n=8;13%) and others (n=10;16%) were found. We estimated prognostic significance of *MLL* breakpoint locations in 46 cases homogenously treated by MLL-Baby protocol. 5-year event-free survival was significantly lower in patients with breakpoints in intron 11 (n=29) in comparison to patients with breakpoint localized from intron 7 to exon 11 (n=17) (0.16±0.07 vs 0.38±0.14 p=0.035). While cumulative incidence of relapse was remarkably higher in the first group of patients (0.80±0.33 vs 0.56±0.20 p=0.020). However in Cox regression model including breakpoint location in intron 11 together with age, immunophenotype, initial WBC count, initial CNS involvement, type of *MLL* rearrangement, absolute blast number at day 8 of dexamethasone profase, minimal residual disease (MRD) at time point 4 (TP4) of MLL-Baby protocol, the only significant covariate associated with unfavorable outcome was the presence of MRD at TP4 (HR 5.994, 95% CI 2.209-16.263, p<0.001).
Conclusion: Our data provide additional information of molecular genetic features of *MLL*-rearranged infant ALL.

PD-008

PREVALENCE OF INVASIVE FUNGAL INFECTIONS (IFI) IN CHILDREN WITH FEBRILE NEUTROPENIA BETWEEN 1- 12 YEARS TREATED FOR ACUTE LEUKEMIA- A PROSPECTIVE STUDY

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Background/Objectives: The objective of our study was to ascertain the prevalence, determinants, etiological species of invasive fungal infections (IFI) and outcome (discharge/ death) during febrile neutropenia episodes in children with acute leukemia between 1-12 years age group during chemotherapy.
Design/Methods: Episodes of febrile neutropenia of duration ≥96 hrs were enrolled and investigated for fungal infection. Blood investigations including Galactomannan antigen, aspergillus serology, Bactac fungal culture and radiological investigations were done. Serial monitoring of Galactomannan Ag was done to assess treatment response. Revised definitions of IFI from the European Organization for Research and Treatment of Cancer (EORTC) were used for analysis.
Results: Total 319 febrile neutropenic episodes were screened and 74 patients fulfilled the enrollment criteria. Out of 74, seventeen (23%) had IFI. As per EORTC criteria's out of seventeen, three (17%) classified as proven, eleven (65%) probable and three (17%) possible. Seven (9.5 %) patients died during same admission. Commonest fungal isolate was Aspergillus (79%) followed by Candida. Radiological findings suggestive of IFI were present in fourteen patients; well circumscribed nodules in lungs were most consistent finding. On multivariate analysis clinical sinusitis and abnormal chest X -ray at admission were significant predictors of IFI.
Conclusion: IFI's are associated with significant morbidity and mortality in leukemia. We found clinical sinusitis and abnormal chest radiograph as significant predictor of IFI in leukemia. Aspergillus was most common fungus causing IFI. Galactomannan Ag was found to be useful in early diagnosis and monitoring of response to antifungals. Sputum for Aspergillosis, Chest tomograph and Galactomannan antigen test strongly correlate with each other. EORTC guidelines has limitations; as children with nasal/Oral swab or urine culture showing fungal growth, Tomograph showing fungal ball in solid organs(Kidney) with positive Galactomannan Ag test also benefited with antifungal therapy suggesting likely systemic fungal infection although these were not included in criteria of IFI.

Poster Discussion: Bone Tumours

PD-009

PREDICTORS OF SURVIVAL IN PEDIATRIC PATIENTS WITH METASTATIC OSTEOSARCOMA TO THE LUNGS

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Background/Objectives: Surgical resection of lung metastases is a treatment option for select pediatric patients with metastatic osteosarcoma. We aim to describe outcomes following pulmonary metastasectomy in patients with metastatic osteosarcoma and to determine which factors contribute to improved survival.
Design/Methods: Between 2002 and 2012, 30 patients (≤ 21 years old) underwent pulmonary resection for metastatic osteosarcoma at the Mayo Clinic Rochester. Demographics, survival, metastasis location, primary tumor size, number of nodules, unilateral versus bilateral disease, and tumor histology were evaluated. Survival was calculated using Kaplan-Meier estimates, and Cox proportional-hazards regression analysis was used to compare differences in survival between various groups.
Results: The mean age of our sample was 14 years (60% male). Of these patients, 27 (90%) underwent wedge resections and 3 (10%) underwent lobectomy or pneumonectomy. There were no deaths from surgery. The median overall survival was 2.2 years. Survival at 1 and 5 years was 68% and 48%, respectively. Patients' risk of death was 5.8 times greater if they had central or central and peripheral disease compared to patients with peripheral disease alone (p=0.01, 95% CI: 1.52-22.5). Tumor size, number of nodules, unilateral versus bilateral disease, and tumor histology did not have a significant effect on overall survival. Median recurrence-free survival was 10.3 months. Recurrence of pulmonary metastases at 1 and 5 years was 49% and 77%, respectively. There was not a significant difference in recurrence-free survival between patients with central or central and peripheral disease compared to patients with peripheral disease alone (p=0.48).
Conclusion: Pulmonary metastasectomy in select patients with metastatic osteosarcoma can be associated with improved survival. The location of lung nodule is significant for overall survival but not for recurrence-free survival.

PD-010

NON-HIGH-DOSE-METHOTREXATE (HD-MTX) BASED DOSE-DENSE (DD)CHEMOTHERAPY(CT) IN OSTEOSARCOMA: IS IT EFFECTIVE, ECONOMIC AND EASY?

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Background/Objectives: There is still no worldwide consensus on a standard chemotherapy approach in osteosarcoma.Concept of dose-density has proven effectiveness in breast cancer.Considering, mandatory complex pharmacokinetic monitoring (labor-intensive & costly) and unpredictable toxicity of HD-MTX, Non-HDMTX based DD,CT merits exploration.
Design/Methods: This prospective study evaluated OGS-12 regimen comprising DD-CT with Doxorubicin, Ifosfamide, & Cisplatin. Neoadjuvant-chemotherapy (NACT) response was evaluated with histological-necrosis (HN) grading; wherein, ≥90% HN defined good-responders (GR). Baseline tumor-burden and nutritional parameters were correlated with outcomes and toxicity. Survival analysis was performed using the Kaplan–Meier method and compared with Log-rank test.
Results: There were 325 patients enrolled from 2011-2014, of which 26% were metastatic. At presentation, 74% were malnourished, 38% anemic, and 57% were iron and vitamin-B12 deficient.Mean lesion size was 11cm, all had high LDH and 37% had high SAP.Among 239 nonmetastaic patients 190 completed NACT and underwent surgery at the analysis. 60% were GR. At a mean follow-up of 15(3-38) months, median disease-free-survival (DFS) and overall-survival (OS) is not reached .Estimated 2-year DFS is 79 % and OS is 98%. Incidence of grade III/IV chemo-toxicities were febrile-neutropenia (FN)(30%), thrombocytopenia (18%), GI-toxicity (6%), and

Cardiac-toxicity (4.7%),however none toxic death occured. In uni-variate analysis, age (>12yrs), LDH (>500U/L), SAP (>500 U/L), Thrombocytopenia, and cardiotoxicity were found as poor prognostic variables; however in multivariate analysis only cardiotoxicity was identified as independent variable for DFS. For OS, LDH and SAP were found as poor prognostic markers. SAP, LDH and Albumin were found as predictors for GI toxicity, and SAP alone for thrombocytopenia.
Conclusion: Non-HD MTX based OGS-12 regimen was proven as Effective, Economic and Easy to manage, even in nutritionally challenged and high tumor- burden osteosarcomas. LDH, SAP and Albumin are identified as non-conventional potential prognostic markers for toxicity prediction at baseline, and cardiotoxicty was identified as novel marker for DFS and merits further exploration.

PD-011

THE CHALLENGE OF GENOMIC CANCER THERAPY: COPING WITH TUMOR DIVERSITY AND T CELL PROMISCUITY

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Background/Objectives: High throughput genomics technologies generated great hopes of targeted therapies (TT). Targeting by tumor specific T cells was particularly looked-for to overcome resistance and avoid side effects due to its specificity. So far, TT have widely failed in cancer of childhood. They seem to prime for resistance. T cell therapy is not specific since one T cell receptor (TCR) has to recognize many peptides. An exception to the TT prime for resistance rule is targeting oncogene addiction. However, many addiction targets such as mutated P53 or EWS-FLI1 are not actionable by drug based TT.
Design/Methods: We have assessed gene ontology (GO) annotated expression as well as pathway activation by gene set enrichment analysis (GSEA) under selective pressure of expression based TT yielding resistance. In addition, we assessed specificity and cytotoxicity of HLA-A2 allorestricted T cells against those oncogene addiction targets, identified by expression profiling and validated in vivo by knock down in refractory sarcoma, specifically Ewing sarcoma (ES).
Results: Upon simultaneous targeting of both the EWS/FLI1 dependent catalytic sunbunit polycomb repressor complex 2 enhancer of zeste homologue 2 (EZH2) and reactive oxygen species (ROS) independent pathways with Vorinostat, Paclitaxel and Vincristin, we found a loss of expression of EWS/FLI1 target genes and up regulation of ROS dependent (i.e. STEAP1) signaling. Moreover, we discovered up regulation of oncogenic pathways from 10 to 18 pathways. (NomP >0.70 vs. 0.40, FDR q value >0.80 vs. 0.40; both for NES 1.0). Finally, A2 allorestricted T cells against oncogene addiction targets displayed cytolytic functionality against STEAP1. STEAP1 A2 allorestricted TCR transgenic T cell clones displayed also significant off-target reactivity.
Conclusion: Intratumoral heterogeneity in pediatric malignancy may require strategies capable of generating synergy between expression based molecular precision chemotherapy and T cells restricted to addiction gene products in an parental HLA diversity context by individualized longitudinal profiling.

PD-012

GENOMICS AND ALLORESTRICTION BASED IMMUNOTHERAPY: COPING WITH T CELL PROMISCUITY …

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Background/Objectives: EWS/ETS dependent genes (EDG) are not actionable by targeted drug therapies, but potentially by T cells. Though perceived as specific, chimeric antigen receptor T cells (CARs) are rather increasing the therapeutic index, while bypassing evolutionary safety features, restricting recognition of surface-molecules to immuoglobulins. Accepted CAR expenses are unwanted activation of innate immunity and agammaglobulinemia.
Design/Methods: We employed allorestricted T-cell receptor (TCR) transgenic T-cells (ATRs) from donor parents recognizing peptides presented by the non-inherited human leukocyte antigen (HLA)-disparate haplotype (Vigor of Defense against Non-Self, Burdach & Kolb 2013). ATRs recognize intracellular targets; their target-pool is unlimited. T-cell activation and deregulation of innate immunity are low, while off-targets effects are more frequent. Most important, ATRs target antigens essential for survival. Regulatory authorities tweak science, requiring specificity of ATRs but not of CARs: TCR promiscuity is imperative, given that 10^{11} human TCRs have to recognize 10^{20} peptides.
Results: Functionality of ATR targets, identified by genomics, as addiction oncogenes in Ewing Sarcoma (ES) was verified by RNA interference in vivo, including EDG EZH2 (Histone methyltransferase) and ChM1 (osteochondrous differentiation regulator): ChM1 specific ATRs are capable of killing ES in vivo, without target down modulation in bulky tumors, whereas EZH2 specific ATRs killed in vitro, but not in vivo. STEAP1 (ROS signaling receptor) specific humanized ATR clones showed off-target reactivity as assessed by alanine/threonin scan, while killing ES efficaciously (Schirmer 2015). ADRB2 (adrenergic receptor) specific ATRs committed fratricide (Kirschner 2015). Last not least, EDG ATRs killed ES irrespective of donor source (Thiel 2015). Autologous T cells are not inferior to allogeneic in HLA-disparity based killing, making haplodisparate transplants dispensable.
Conclusion: Taken together, some addiction oncogene peptides are actionable by ATRs, whereas fratricide may be a cause why others are not. Specificity is not required. Epitope spreading and evolutionary conserved strength of alloreactivity may help to overcome resistance.

PD-013

IMPACT OF ZOLEDRONIC ACID ON CHILDREN GROWTH: RESULTS OF THE OS2006 RANDOMISED TRIAL

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Background/Objectives: Evaluation of Zoledronic acid (ZA) efficacy is ongoing in children and adult with Ewing sarcoma. Concerns were raised from preclinical data about a possible impact of ZA on children growth. This question was evaluated within the OS2006 randomised trial in osteosarcoma patients.
Design/Methods: The OS2006 trial recruited patients from 5 to 50 years, with a newly diagnosed osteosarcoma, from 2007 to 2014. We selected for the current study patients <18 years at study entry, recruited >1 year ago, alive free of disease ≥1 year after inclusion. Patients received methotrexate-etoposide-ifosfamide chemotherapy, + doxorubicin-platinum post-operatively if poor histological response, +/- 10 ZA-injections according to randomisation. Height was normalised by age and gender using WHO growth curves, and transformed into Z-score. Repeated Z-scores over time were modelled using mixed models considering time during treatment and follow-up time separately. Covariables included treatment (ZA+ versus ZA-), initial Z-score, age and pubertal status.
Results: The current study is focused on 161 patients; mean initial z-score =+0.45, significantly higher than 0 ($p<0.0001$). After a mean follow-up duration of 3.1 years, the mean height increase was 6.9 cm, lower than expected, leading to a mean decrease in Z-score of -0.40, with no significant difference between randomised groups (-0.33 in ZA+ versus -0.46 in ZA-,$p=0.18$). In multivariable model, Z-scores significantly decreased over time, even after the end of treatment although the slope was less steep than during treatment (slope= -0.661/year during treatment and -0.342/year during follow-up, interaction test, $p<0.0001$). Decrease was significantly more important in younger patients ($p<0.0001$) and in patients with a high Z-score at study entry ($p=0.0001$). We did not observe any significant impact of ZA on patient growth (interaction between treatment and time, $p=0.21$).
Conclusion: Patients with osteosarcoma may be taller than healthy peers. Osteosarcoma and its treatment appear to impact children growth, regardless of zoledronic acid.

PD-014

NATURAL KILLER CELL TARGET OSTEOSARCOMA TUMOR INITIATING CELLS USING NKG2D-NKG2DL INTERACTIONS

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Background/Objectives: Tumor-initiating cells (TICs) have been described in osteosarcoma, and are responsible for drug resistance, recurrence and metastasis. Current therapies fail to cure recurrent or metastatic osteosarcoma and to target this compartment. Natural Killer (NK) cells are lymphocytes with cytotoxic activity toward virus-infected or malignant cells. In this study we have explored the ability and the pathways involved in the NK cell elimination of osteosarcoma TICs.
Design/Methods: TICs in osteosarcoma cell lines 531MII, 654M and MG-63 were identified phenotypically by the expression of c-kit and CXCR4 markers using Flow Cytometry (FCM) and functionally by Sphere Formation Assays (SFA). NK cells capacity to reduce TICs was assayed by co-culture of MG-63, 654M and 531MII and NK cells for 4 and 24 hours and FCM analysis. To evaluate if NK cells could impair OS

cells ability to grow as spheres, MG-63 GFP$^+$ cells were co-cultured with NK cells for 4 and 24 hours, GFP$^+$ live cells were then sorted and re-plated for SFA. One week later spheres were counted using an inverted Nikon Ti microscope (Tokyo, Japan). The role of NKG2D receptor and its ligands interactions was assayed using NK cells treated with an NKG2D blocking antibody.
Results: We found osteosarcoma cells have a TICs compartment with expression of c-kit and CXCR4, and ability to grow as spheres. Co-culture with NK cells showed to reduce TICs subset. Specific antibody blockade showed NKG2D receptor and its ligands interactions have a role in the elimination of osteosarcoma TICs by NK cells.
Conclusion: TICs can be identified in osteosarcoma cell lines. NK cells show ability to reduce this compartment both in phenotype and in function. NKG2D and NKG2DL have a role in the NK cell elimination of osteosarcoma TICs. Our data suggest osteosarcoma patients could benefit from NK cells based therapies.

PD-015

CO-AMPLIFICATION OF MYC/PVT1 AND HOMOZYGOUS DELETION OF NLRP1 LOCUS ARE THE FREQUENT GENETICS CHANGES IN MOUSE OSTEOSARCOMA

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Background/Objectives: High-grade osteosarcomas (OS) are characterized by high levels of genomic instability compared to almost any other cancer. To gain insights into the genomic instability and its contribution towards understanding the genetic basis of osteosarcoma, we characterized 19 primary and 13 metastatic mouse tumors in a genetically engineered novel mouse model of osteosarcoma by a combination of genomic techniques.
Design/Methods: We established two osteosarcoma-susceptible lines of genetically engineered mice (GEMM) utilizing osteoblast-specific Cre allele crossed with floxed p53 or LSL-p53 R172H alleles to generate localized or metastatic OS. Subsequent tumors were isolated and established tumor cell lines from primary bone and/or distal metastatic lesions, e.g. lung and liver. Several genomic techniques such as SKY, CGH, array CGH, FISH and qRT-PCR were employed to characterize the complex chromosomal aberrations in OS.
Results: Based on SKY/G-Banding analysis, genomic instability (GI) score was estimated for each tumor and similar to human osteosarcoma, a wide spectrum of GI was found, with some tumors displaying few changes (~2) and others displaying > 40 chromosomal aberrations. We identified frequent amplification of 15D1 and loss of 11B4 by SKY/CGH and subsequent array CGH, FISH and qRT PCR analysis demonstrated co-amplification and overexpression of *Myc*/*Pvt1* transcripts from the 15D1 amplicon and loss and decreased expression of the *Nlrp1* from 11B4. Both 15D1 and 11B4 has homology with human chromosomal bands 8q24 and 17p13, respectively.
Conclusion: We have shown a compelling homology between the genomic changes identified in mouse tumors and several human cancers. This study also demonstrated the co-amplification and overexpression of *Myc* and*Pvt1* genes and regulation of high Myc protein levels through the *Pvt1* non-coding micro RNAs may provide considerable therapeutic targets in Myc-driven Osteosarcoma. In addition, we identified novel tumor suppressor gene *Nlrp1* with proapopotic properties and the functional significance of this gene needs to be ascertained in OS.

Poster Discussion: Brain Tumours

PD-016

CLINICAL AND MOLECULAR RESULTS OF THE GERMAN PHASE II STUDY HIT-HGG-CILMETRO: CILENGITIDE AND METRONOMIC TEMOZOLOMIDE FOR RELAPSED/REFRACTORY HIGH GRADE GLIOMAS/DIPG IN CHILDREN AND ADOLESCENTS

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Background/Objectives: Relapsed high-grade gliomas (HGG) in pediatric patients like glioblastoma multiforme (GBM), anaplastic astrocytoma (AA), diffuse intrinsic pontine glioma (DIPG) represent a dismal prognosis group currently without standard salvage therapy. In this population, a combined protocol was investigated: Cilengitide 1800 mg/m^2 twice weekly; temozolomide 75 mg/m^2/d for 6 weeks with one week rest, given for one year.
Design/Methods: Between 02/2012-03/2013 28 patients were recruited (3 AA, 9 GBM, 15 DIPG, one anaplastic oligoastrocytoma), 27 after first-line temozolomide radiochemotherapy.
Results: 3/28 patients completed the full 52 weeks of treatment without signs of active disease (all GBM); one of these patients died due to pneumonia without clinical tumor progression 20 months after relapse; the two other patients are alive and progression-free (follow-up 23/34 months). The following serious adverse events (SAE) were observed: Intracranial hemorrhage (n=4); neurological deterioration (n=4), seizures (n=3), pneumonia (n=2); and edema, severe obstipation, pain, cellulitis (each n=1). No suspected unexpected serious adverse reaction (SUSAR) occurred. Recruitment was prematurely stopped due to an altered risk assessment after negative clinical data employing cilengitide in HGG. Survival was compared to historical relapse patients from our database treated individually (n=417). Median overall survival in HIT-HGG-CilMetro was 0.397 (0.181-0.613) vs. 0.507 (0.451-0.562) years (not significant). Since our three GBM longterm survivors might represent true responders, molecular analyses were done. The therapeutic targets (i.e. beta-5 integrins) were expressed on all GBMs without a difference between survivors and the others. Most interestingly, all CilMetro responders demonstrated an unmethylated MGMT promoter status. Other molecular analyses including EGFR, PDGFRA, p53, H3F3AK27 status, ATRX, IDH1, BRAFV600, CDKN2A, and MYCN-amplification, were inconclusive.
Conclusion: HIT-HGG-CilMetro offered a feasible salvage treatment approach with tolerable toxicity for pediatric patients with relapsed HGG and might induce an increased progression-free survival in a GBM subgroup, potentially with unmeythylated MGMT promoter status.

PD-017

SURVIVAL AND PROGNOSTIC FACTORS IN 211 INTRACRANIAL EPENDYMOMAS - 13 YEARS EXPERIENCE OF CHILD'S CANCER FRENCH SOCIETY

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Background/Objectives: To analyze the outcome and assess the prognostic impact of clinical characteristics for pediatric patients with localized ependymoma in a French muticentric cohort.
Design/Methods: 211 patients with newly diagnosed intracranial ependymoma were treated with adjuvant radiation therapy (RT) in the 13 French major radiation oncology centers between January 2000 and December 2013. Clinical data were retrospectively gathered on a web-based national database until January 2015. Median age was 5 (range1;23). Location was posterior fossa in 74%, supratentorial in 26%, with anaplastic features in 63%. The extent of resection was gross-total in 86%. The median delivered dose was 58.7 Gy. Sixty-six patients received pre-RT chemotherapy. RT was 3D conformal in 121 patients, intensity-modulated (IMRT) in 71 (13 tomotherapy) and protontherapy in 17. With a median follow up time of 43.7 months, the estimation of cumulative incidence of local relapse at 3 years was 24.7%. Recurrences were mainly local (strictly local in 66% of recurrences, local and distant in 23% and strictly distant in 11%). The estimated 3-year overall survival (OS) and event-free survival (EFS) rates were respectively 86 % and 62% for patients who received a dose > 54Gy vs 77% and 53% with dose ≤54 Gy (both p= 0.03). Three-year OS and EFS were respectively 87 and 65% for patients older than 3 years at the initiation of RT and 72 and 47% for children less than 3 years (p=0.009 and p=0.002). Three-year OS was better after gross-total resection (85 vs 68%; p=0.02).
Conclusion: In this large multicentric French cohort, children with a localized intracranial ependymoma had a significant better survival with a dose > 54 Gy. Age younger than 3 years at initiation of RT and incomplete surgery were significant prognostic factors of worse outcome.

PD-018

RE-IRRADIATION IN PATIENTS WITH DIFFUSE INTRINSIC PONTINE GLIOMAS. THE CANADIAN EXPERIENCE

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Background/Objectives: More than 90% of the children diagnosed with diffuse intrinsic pontine gliomas (DIPG) will succumb within two-years of diagnosis. Clinical-trials over the last four decades failed to demonstrate a survival benefit of adjuvant chemotherapy. Radiotherapy is the only effective treatment thus far but of limited duration. The aim of this study is to determine the safety and efficacy of re-irradiation.
Design/Methods: Since September 2013, patients with DIPG showing clinical and radiological progression were considered for re-irradiation. We retrospectively reviewed demographic, clinical and radiation data of all patients with DIPG treated in Canada with re-irradiation.
Results: Since September 2013, 10 patients with progressive DIPG received re-irradiation in Canada. Median age at diagnosis was 4.9 years (range, 2.2-13y). Median time from diagnosis to progression was 12 months (range, 4-37m). Re-irradiation total dose varied between institutions from 21.6 Gy (2 patients), 30.6 Gy (6 patients), and 36 Gy (2 patients), in 1.8 Gy daily fractions. Re-radiation was focal except in two patients who received whole-brain irradiation due to distant/disseminated relapse. One patient received a third course of focal radiation (21.6 Gy) 6 months after re-radiation. Re-irradiation was very well tolerated by all children. Dexamethasone was avoided where feasible but necessary in 4 patients. Four patients had transient tiredness and decrease of appetite during treatment. All but one showed neurological improvement, with 4 patients showing full-recovery. With a median follow-up from diagnosis of 19.5 months (range, 9-45m), seven patients died, with a median time from re-irradiation to death of 9 months (range, 5-13m). When compared to an historic cohort of 46 patients, median time from progression to death was 91.5 days in the non re-irradiated patients, vs. 171 days in the re-irradiated ones ($p<0.05$).
Conclusion: In this limited experience re-irradiation was safe and feasible in patients with progressive DIPG, providing neurological recovery and a prolonged life span.

PD-019

UK NATIONAL AUDIT REVEALS UNEXPECTED NEUROTOXICITY OF CHILDREN WITH STPNET TREATED WITH INTENSIVE CHEMOTHERAPY, HYPER FRACTIONATED RADIOTHERAPY (HART) AND TANDEM HIGH DOSE THIOTEPA CONSOLIDATION

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Background/Objectives: Supratentoral Primitive Neuroectodermal Tumour (StPNET) is rare in children. Prognosis is poor with various series reporting 20-40% survival. The Milan group published improved outcomes with intensive chemotherapy, HART followed by tandem high dose thiotepa consolidation in 2006 and 2013. The 5-year PFS, EFS, and OS rates were 62%, 53%, and 52%. UK CCLG adapted this treatment as recommended strategy for all patients with stPNET in 2009.
Design/Methods: A national audit was undertaken in the UK in 2014 to evaluate the outcome and the toxicity of this treatment. Information collected included details of the diagnosis, treatment, outcome and toxicity. All patients with StPNET, metastatic pineoblastoma, above the age of 36 months at diagnosis, treated as per the recommendation between Jan 2009 to May 2014 were included.
Results: A total of 19 patients (2 Pineal and 17 non-Pineal PNETs) were identified. Mean age was 9.81 (range 5-16.5) and M:F ratio was 2:1(M13). All patients received recommended induction chemotherapy and radiotherapy. 14 patients received the 1st thiotepa consolidation and 9 of them received the 2nd dose thiotepa consolidation. 7 (36%) patients had died by the end of study period with a follow up ranging from 8-56 months (mean 9.81):6 from progressive disease, 1 from toxicity of treatment. Grade 3/4 neurotoxicity was noted in 8 patients. 7 of these developed fairly rapid onset global neural deterioration with bulbar dysfunction. All these patients were neurologically intact before the thiotepa consolidation. MRI brain showed varying degree of leucoencephalopathy changes in these patients.
Conclusion: This audit shows severe unexpected neurotoxicity with the use of intensive chemotherapy, HART and high dose thiotepa consolidation. The treatment strategy was discontinued in the UK immediately following the audit. Further research is urgently needed to improve outcomes in this enigmatic disease.

PD-020

A METRONOMIC ANTIANGIOGENIC COMBINATION THERAPY APPEARS TO BE SUPERIOR TO HIGH-DOSE CHEMOTHERAPY IN RECURRENT MEDULLOBLASTOMA AND ATYPICAL TERATOID RHABDOID TUMOR

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Background/Objectives: Prognosis of patients with recurrent medulloblastoma and atypical teratoid rhabdoid tumor (ATRT) is dismal despite intensive therapy including high-dose chemotherapy with stem cell rescue. An evolving alternative approach to conventional chemotherapy is to target neovascularisation by interfering with tumor angiogenesis at various levels. We report on 20 patients with recurrent medulloblastoma and ATRT treated with an antiangiogenic combination therapy.
Design/Methods: From 11/2006 to 09/2014, 20 patients were diagnosed with recurrent embryonal tumors, 13 with a recurrent medulloblastoma (8 first, 5 multiple recurrences) and seven with recurrent ATRT (4 first, 3 multiple), three had germ line mutations. Treatment consisted of an antiangiogenic multidrug-regime including IV bevacizumab, oral thalidomide, celecoxib, fenofibrate, and etoposide alternating with cyclophosphamide, and augmented with intraventricular therapy (etoposide and liposomal cytarabine). Median age at start of antiangiogenic therapy was 13 (1-24) years for medulloblastoma and 4 (1-13) years for ATRT.
Results: As of 03/2015, 7/13 patients with medulloblastoma are alive at a median of 48 (5 to 78) months after their last recurrence. 6/13 surviving patients are currently in CR for 78, 75, 74, 48, 9, and 7 months, four off therapy for 60, 43, 39 and 18 months, one has stable disease after 5 months. 3-year and 5-year-OS is 57.1±14.8%. One patient died of an accident in CR 23 months after initiation of antiangiogenic therapy. 3/7 patients with ATRT are in CR, one in PR. Follow-up since last recurrence is 42, 41, 8 and 5 months, two are off therapy for 36 and 32 months. Therapy was generally well tolerated and toxicities were manageable.
Conclusion: The proposed antiangiogenic regimen is currently being evaluated for medulloblastomas in a formal international phase II protocol (MEMMAT; ClinicalTrials.gov Identifier: NCT01356290). The same approach seems to be also efficacious in recurrent ATRTs and warrants further evaluation.

PD-021

DISPOSITION OF HIGH-DOSE METHOTREXATE IN VERY YOUNG INFANTS WITH MALIGNANT BRAIN TUMORS

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Background/Objectives: Little is known about the use of high-dose methotrexate (HDMTX) in very young infants (< 1 year) with malignant brain tumors who have immature renal function by virtue of their age alone. Developmental changes in renal function likely introduce inter- and intra-patient variability with drug therapy, and in the absence of any data, no specific dosing guidelines or supportive care measures have been proposed or optimized for this patient population.
Design/Methods: We investigated MTX pharmacokinetics in a clinical trial evaluating risk-adapted therapy for infants and young children with brain tumors (NCT00602667). During induction therapy, all patients received HDMTX as a 24-hour infusion of 5 g/m^2 and we empirically decreased the dosage to 2.5 g/m^2 for infants ≤ 31 days of age on the first day of each 28 day cycle. Serial pharmacokinetic sampling was obtained after HDMTX infusion, and MTX concentrations were measured by a fluorescence polarization immunoassay. Population parameters for a two-compartment pharmacokinetic model were estimated by nonlinear-mixed effects modeling (NONMEM).
Results: Thirty-eight patients with a median age of 7.3 months (range: 0.2 - 11.6 months) contributed 817 MTX pharmacokinetic samples to the data set. The population MTX clearance estimate (CL_t) in the base structural model was 68.2 ml/min/m^2 with inter-individual variability (IIV) of 23.3% (R^2=0.32). MTX Cl_t appears to increase linearly during the first year of life, paralleling the physiological maturation in renal function that occurs during infancy. Future studies will include a full covariate analysis for the prediction of MTX CL_t, including age, gender, race, total body weight, body surface area, and estimated GFR.
Conclusion: This preliminary analysis suggests incorporation of a maturation function on clearance will improve the dosing of MTX in infants and young children with malignant brain tumors.

PD-022

IMPACT OF INDUCTION CHEMOTHERAPY, HYPERFRACTIONATED ACCELERATED RADIOTHERAPY AND HIGH DOSE THIOTEPA ON BRAIN VOLUME LOSS AND FUNCTIONAL STATUS OF CHILDREN WITH PRIMITIVE NEUROECTODERMAL TUMOUR (PNET)

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Background/Objectives: Aggressive chemo-radiation treatments have been introduced to improve the dismal prognosis of high risk PNETs. There is increasing concern that combination therapies may result in neurotoxicity, but the clinical impact of these findings remains to be determined. The aim of this analysis was to investigate the relationship between brain volume loss and functional status in children treated with sequential chemotherapy, hyperfractionated accelerated radiotherapy (HART) and high-dose thiotepa with autologous stem-cell rescue.
Design/Methods: We retrospectively reviewed clinico-radiological data of children with primitive neuroectodermal tumours (including supratentorial PNET, high risk medulloblastoma and pineoblastoma) treated at our national referral centre between 2009-2013 according to the Milan Cancer Centre protocol published by Gandola et al. (J Clin Oncol 2009 Feb 1;27(4):566-71). Serial MRI scans from presentation until the end of treatment were qualitatively analysed by two board certified neuroradiologists assessing for brain volume loss and signal abnormality. A quantitative brain volume analysis was undertaken using FSL's Sienax toolkit. Functional status was determined using the Lansky Performance Scale.
Results: Thirteen of 14 children developed generalised brain volume loss with moderate or severe volume loss in 7 of 14 children. Of 11 children who received thiotepa, 7 suffered moderate to severe brain volume loss. Mean brain volume loss of all subjects was 8.9% (4.2-17.4%) averaged over 2 years from presentation. Two children developed transverse myelitis and 1 patient suffered peripheral neuropathy, urinary incontinence and seizures. Performance status was severely restricted in 4 of 14 children (Lansky score 10-40). Mild to moderate impairment was noted in 7 of 14 children (Lansky score 50-70).
Conclusion: Substantial brain volume loss was evident in our cohort of children following treatment. Of 14 children 4 had severe and 7 mild to moderate impairment of clinical performance status. The presence of imaging changes was associated with a greater performance decline at the end of therapy.

Poster Discussion: Epidemiology

PD-023

UTILIZATION OF THE WHO MODEL LIST OF ESSENTIAL MEDICINES (EML) FOR ANTI-NEOPLASTIC DRUGS IN LOW AND MIDDLE INCOME COUNTRIES (LMICS)

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Background/Objectives: The lower survival rates in children with cancer in LMICs, by comparison with those in high income countries, is related in part to limited availability, access and affordability with respect to anti-neoplastic drugs. The objective of this study was to determine alignment of national Essential Medicines Lists (NEMLs) with the panel of essential and ancillary anti-neoplastic medicines recommended by the SIOP Working Group on Essential Medicines.
Design/Methods: NEMLs are available on the WHO website http://www.who.int/selection_medicines/country_lists/en The number of the medicines included on NEMLs available on the website in 2015 was correlated with three indices – gross national income per capita (A), average government expenditure on health care per capita (B), and the number of physicians per million population (C); indices obtainable from WHO and World Bank websites.
Results: Information was available for 116 LMICs. Availability of individual essential non-steroidal anti-neoplastic drugs – X n=18) ranged from 25.0% for thioguanine to 86.2% for methotrexate (also listed in EMLs for non-cancer purposes). The median number of drugs available was 11.6, range 0-18. In the ancillary list - Y (n=8) the median was 1, range 0-7. For the variables A, B and C the medians and ranges are US $3735, $123-$25,000 (A); $113, $1.7-$1423 (B); 650, 8-4236 (C) respectively. Remarkable exceptions notwithstanding, the Pearson correlations (r) were as follows: X v A 0.19, p=0.0411; Y v A 0.36, p<0.0001; X v B 0.03, p=0.7492; Y v B 0.26, p=0.0048; X v C 0.20, p=0.0314; Y v C 0.43, p<0.00001 (p values are two-tailed).
Conclusion: The availability of anti-neoplastic drugs for children with cancer in LMICs is highly variable and generally limited. While there are correlations between listing as essential medicines and variables A, B and C, the strongest is between ancillary (non-essential) drugs and the number of physicians per million people.

PD-024

CHILDHOOD LYMPHOMA INCIDENCE IN THAILAND FROM 1990-2011

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Background/Objectives: While lymphoma is one of the most common childhood malignancies, the incidence overall and by subtype varies significantly worldwide. This variability may be due to differences in both genetics and environmental factors. However, more work is needed to elucidate patterns of childhood lymphoma in developing countries. Therefore, we analyzed childhood lymphoma incidence trends from 1990 to 2011 in Thailand and compared these results to United States (US) data. We evaluated the following childhood lymphoma subtypes: Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL).
Design/Methods: We used population-based cancer registry data from five provinces in Thailand (n=402). Data from the US were obtained from the Surveillance, Epidemiology, and End Results program (n=3,948). We computed age-standardized incidence rates (ASIR) using the WHO 2000 standard population. We evaluated temporal changes in incidence by year of diagnosis using joinpoint regression and reported the annual percent changes (APC).
Results: The ASIR of lymphoma was 1.1 and 2.4 cases per 100,000 in Thailand and the US, respectively. The proportion of NHL and HL in Thailand was 52.5% and 20.4%, respectively, vs. 35.6% and 50.1% in the US (p<0.001). In Thailand, the mean age at diagnosis was younger compared to the US (11.5 vs. 13.4 years, p<0.001). The incidence of HL increased by 4.1% per year (p=0.006) in Thailand while it remained stable in the US (APC=-0.24%, p=0.589). While the incidence of NHL increased in the US by 1.9% per year (p<0.001), it increased in Thailand by 3.5% per year (p <0.001).
Conclusion: Our findings suggest that while lymphoma incidence is lower in Thailand than the US, NHL and HL incidences are more rapidly increasing and the proportion of these subtypes differs significantly when compared to the US. These patterns warrant comparing these results to the Asian population within the US and investigating novel risk factors within Thailand and Southeast Asia.

PD-025

NON COMPLIANCE OF CHILDREN CANCER PATIENTS WITH THERAPY: A SINGLE CENTER EXPERIENCE IN A DEVELOPING COUNTRY

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Background/Objectives: To evaluate risk factors affecting compliance of childhood cancer patients with therapy.
Design/Methods: The following data were collected by retrospective reviewing of reports of all patients who were diagnosed and started treatment between 2006 and 2010 in the pediatric oncology department, South Egypt Cancer Institute (SECI): Age, sex, diagnosis, duration of travel from patient's home to SECI, time lag between first symptom till first visit to SECI and between first visit till start of treatment, first evaluation after initial course of therapy, compliance with therapy. Non-compliance with therapy was defined when patients missed their determined appointment for therapy for 1 week or more, or who refused or escaped therapy.
Results: About 15% (n=75) of the included patients (N=502) were non-compliant. As 40 patients missed their determined appointment for therapy; 7 refused; and 28 escaped further therapy. There was not a significant difference between non-compliant patients vs. compliant patients in the following factors: the travel time from home to SECI, 1.35 (0.28 - 6.8) vs. 0.85 (0.17 – 9) hours; from first symptom till first presentation, 4 (0.43 – 96) vs. 4 (0.14 – 96) weeks; and from first presentation till start of treatment 5 (0 – 60) vs. 5 (0 – 210) days, respectively. Although 14% of patients who were not in complete remission at time of first evaluation after initial therapy, and 13.5% of patients who suffered severe complications were non-compliant with the further therapy, these differences were not significant. In addition, within the excluded patients, 2.4% (n=17) escaped from the hospital just after initial suspicion of cancer; 0.8% (n=6) refused chemotherapy after reaching a final diagnosis of cancer; and 0.3% (n=2) escaped after doing initial surgeries as a primary step in therapy.
Conclusion: Treatment refusal and abandonment are still big problems facing cancer management in developing countries.

PD-026

RECURRENCE OF GRAM-NEGATIVE INFECTIONS AMONG PATIENTS WITH PEDIATRIC CANCER

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Background/Objectives: Gram-negative pathogens are a widespread concern because of their potential for developing antibiotic resistance. Prior studies of Gram-negative infections among patients with pediatric cancer have focused on the risk of first infection. The paucity of data about recurrent Gram-negative infections limits understanding the continuum of infection risk. Therefore, we aimed to estimate the risk of recurrent Gram-negative infections among patients with pediatric cancer.
Design/Methods: Individuals eligible for our longitudinal cohort study were aged <20 years and treated for a malignancy at Hospital de Niños Sor Maria Ludovica (La Plata, Argentina) between January 2011 and June 2013. Patients contributed person-time to the cohort until end of therapy, death, loss to follow-up, or end of study. We estimated the incidence rate (IR) of microbiologically-documented Gram-negative infections and corresponding 95% jackknife confidence limits (CL) to account for within-patient clustering. The IR was subsequently used to estimate the risk of recurrent Gram-negative infections, assuming a random Poisson distribution.
Results: Our study population comprised 159 patients with pediatric cancer. We observed 35 Gram-negative infections during 47,245 person-days at risk (IR per 1,000 person days=0.74, 95% CL: 0.50, 1.1). The overall estimated risks of having one, two, or three Gram-negative infections during a one-year period were 21%, 2.8%, and 0.25%, respectively. The risk of recurrence differed by subgroups. In particular, patients with pediatric acute myeloid leukemia (AML) had the highest estimated risks of having one, two, or three Gram-negative infections during a one-year period, which were 34%, 11%, and 2.3%, respectively.
Conclusion: Our results suggest considerable risk of recurrent Gram-negative infections among patients with pediatric cancer, particularly among patients with pediatric AML. Our findings may be useful for promoting discussion about antimicrobial stewardship strategies for subgroups with high risks of recurrent Gram-negative infections and repeated exposures to antibiotic therapy.

PD-027

CAREGIVERS WHO MISS APPOINTMENTS TO THE PEDIATRIC CANCER CLINIC OF A TEACHING HOSPITAL IN GHANA

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Background/Objectives: At Komfo Anokye Teaching Hospital (KATH), Kumasi, Ghana, over one-third of caregivers of children with cancer miss their children's scheduled clinic appointments. Our goal was to describe the demographic and socioeconomic characteristics of caregivers who had missed their clinic appointments.
Design/Methods: This is a prospective cross-sectional survey of caregivers attending the paediatric cancer clinic who had a history of previously missing clinic visits. Respondents completed a questionnaire of closed and open-ended questions. Data was collected over a 3 months period (1st November, 2014 to 31st January, 2015) and analyzed using STATA IC 12.0® software.
Results: Twenty-five respondents had previously missed clinic visits; 72% females and 28% males. Sixty percent were married, 16% were divorced and 12% cohabiting. Christians constituted 80% while 20% were Moslems. There was an average of 3 children per household with a mean age of 7 years. Overall, 72% had Primary and/or Junior High School education and 28% had Senior High School education/higher. Most, 68% were self-employed traders and farmers, 24% were unemployed and 8% were government employees. Majority (72%) reside outside Kumasi. The mean travel time to the Clinic was 2 hours, 8 minutes and 60% required at least 2 vehicles to reach the Clinic. Reasons for missed appointments included lack of money for investigations and/or treatment as given by 24% of respondents, with 20% reporting an inability to afford transportation cost. While 12% were absent due to miscommunication of dates, 8% forgot their appointment dates.
Conclusion: Most of the respondents were females of low socioeconomic status, resident outside the city and requiring an average of 2 hours and at least two vehicles to reach the Clinic for appointments. Majority attributed their absence to lack of money for transportation and clinical care, and others to miscommunication and forgetfulness.

PD-028

ENVIRONMENTAL RADON EXPOSURE AND INCIDENCE OF PEDIATRIC LYMPHOMA IN TEXAS, 1995-2011

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Background/Objectives: There is consistent and growing interest in assessing the association between environmental exposure to radon and the risk of childhood cancer. However, previous studies have been largely equivocal. Therefore, we sought to evaluate the association between indoor radon exposure and the incidence of pediatric lymphoma in Texas, a state characterized by a large population-based cancer registry and variable concentrations of radon.
Design/Methods: Information on childhood lymphoma cases was obtained from the Texas Cancer Registry (n=2,147) for the period 1995-2011. Denominator data were obtained from the 2000 United States Census. Exposure to radon was estimated using data from the Texas Indoor Radon Survey. Specifically, arithmetic mean radon concentrations (picoCuries/liter; pCi/l) were obtained from 13 geologic regions in the state and linked to the residence at diagnosis. Exposure was assessed both on a continuous scale and dichotomously ($<90^{th}$ percentile [low exposure] vs. $\geq 90^{th}$ percentile [high exposure]). Poisson regression was used to generate incidence rate ratios (IRR) and 95% confidence intervals (CI) adjusted for sex, race/ethnicity, and area-level poverty. We evaluated the following lymphoma outcomes: Hodgkin (HD; n=1,248), Burkitt Lymphoma (BL; n=241), and Non-Hodgkin excluding Burkitt Lymphoma (non-BL NHL; n=658).
Results: The mean radon concentration across regions was 1.24 pCi/l (range: 0.25-3.30). For every one pCi/l increase in radon exposure, there was a modest, but non-significant, increase in the incidence of non-BL NHL (IRR [95% CI]: 1.07 [0.93-1.24]). Additionally, areas with high radon concentrations had a 26% higher incidence of non-BL NHL (95% CI: 0.88-1.81) compared with areas of low radon concentrations. Associations were not detected for HD or BL.
Conclusion: Overall, there was little evidence to suggest radon is strongly associated with childhood lymphoma incidence. However, the incidence of non-BL NHL was modestly increased in areas of the highest concentrations.

PD-029

DELAYS IN CANCER DIAGNOSIS AND TREATMENT AMONG CHILDREN WITH CANCER COMPARATIVE STUDY BETWEEN EGYPTIAN AND SAUDI CENTERS

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Background/Objectives: Childhood cancer outcome is greatly affected by delay in diagnosis. Our objective was to explore factors underlying delay in diagnosis as an important step to establish control measures.
Design/Methods: We carried out retrospective study on 300 children suffering from different types of malignancies from two Arab countries; Egypt and Saudi Arabia. One-hundred-fifty children were enrolled from Egyptian oncology centers and another 150 children from Saudi Arabian oncology centers. They were studied for different possible factors influencing timing of diagnosis which were categorized as patient related factors, disease related factors and health care related factors. Correlations between all possible factors and total delay time to final diagnosis were carried.
Results: The median total diagnosis delay period was longer in Saudi Arabia than in Egypt; 59 versus 42 days respectively. In both countries, health care related factors significantly contributed to delay in diagnosis. Patients'/ parents' related factors (child age, parental age, education, socioeconomic status, maternal work) caused 3 times more delay in Saudi patients as compared to Egyptian patients with obvious significant negative effect of different factors during patient pathway till final diagnosis is obtained. Disease related factors including; disease type, presenting symptoms and stage of malignancy at the time of presentation, also played an important role.
Conclusion: Significant correlations were detected between delay in childhood cancer diagnosis and patients' factors and disease related factors. Health care related factors were the most delaying factor in both countries. Efforts should be carried to raise awareness of parents, improve health care providers' skills and health care centers facilities to achieve early diagnosis and best outcomes for childhood cancers.

PD-030

FACTORS ASSOCIATED WITH TIME TO DIAGNOSIS OF CHILDHOOD CANCER: A RETROSPECTIVE COHORT STUDY

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Background/Objectives: Time to diagnosis (TD) or "lag time" is the time between a patient's first symptom recognition to a diagnosis of cancer. Delayed TD allows tumor progression and poor outcome in childhood cancer in many studies, although it remains controversial. In our country, high rate of metastatic presentation and poor survival has been described. The aim of this study was to define clinical and socio-demographic factors associated to TD, which includes "Parents delay" (PD) and "Medical delay" (MD) in children and adolescents diagnosed with cancer in Lima, Peru.
Design/Methods: A total of 314 patients younger than 18 years of age diagnosed with lymphoma and solid tumors between January 2012 and December 2014 were retrospectively evaluated. Clinical and demographic variables such as type of diagnosis, clinical stage, sex, age and parental characteristics were analyzed to evaluate their effects on TD, PD and MD.
Results: The TD ranged between 1 week and 26 months (median, 9.75 weeks), with a median of PD and MD of 2 and 5.5 weeks, respectively. Among type of disease, we found significant differences in TD (longer in patients with Hodgkin disease and osteosarcoma and shorter in patients with Wilms tumor and hepatoblastoma). A greater TD was found in children first diagnosed by a general physician or surgeon than by a pediatrician ($p=0.004$). Advanced parental age ($p=0.035$), low mother´s level of education ($p=0.013$) and older children ($p<0.01$) was significantly associated with delayed TD. Children of divorced or separated couples ($p=0.008$) had longer TD than their counterparts. Metastatic disease, clinical stage and sex did not affect significantly TD.
Conclusion: In our country, median TD was comparable to described in developing countries, where index of suspicion of childhood cancer remains low. It is necessary to establish strategies for optimizing early diagnosis based on associated factors.

Poster Discussion: Late Effects

PD-031

HEALTH-RELATED QUALITY OF LIFE IN LONG-TERM SURVIVORS OF BRAIN TUMOURS IN CHILDHOOD AND ADOLESCENCE: A SERIAL STUDY SPANNING A DECADE

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Background/Objectives: Survivors of brain tumours in childhood experience adverse sequelae from their disease and its treatment that are greater in prevalence and severity than those encountered by survivors of all other forms of cancer in early life. This is reflected in burdens of morbidity reported by cross-sectional surveys using instruments measuring health-related quality of life (HRQL). However, there are few studies of change in HRQL over time in such populations; the objective of this study.
Design/Methods: Patients 5 years of age or older, at least two years from completion of therapy and able to communicate in English were eligible for survey by the generic, preference-based multi-attribute Health Utilities Index Mark 2 (HUI2) and 3 (HUI3) at study initiation (T1) and again 5 (T2) and 10 (T3) years later. HUI provides utility scores of single-attribute (domain/dimension) morbidity and multi-attribute HRQL. HRQL scores are on a scale such that 0.00=dead, 1.00=perfect health and negative scores represent states of health considered worse than being dead. Responses were collected from patients and their proxies.
Results: An initial cohort of 40 patients decreased to 37 and 25 at T2 and T3 respectively, though only one death occurred during the study period. Overall HRQL, derived from the responses of patients, showed a progressive and clinically important size decline over the decade. Median HRQL scores at T1, T2 and T3 respectively for HUI2 were 0.93, 0.90 and 0.88; and for HUI3 were 0.88, 0.85 and 0.77. Cognition was the attribute compromised most often (T1=67%, T2=62% and T3=60%). Pain was also reported frequently (T1=35%, T2=25% and T3=52%).
Conclusion: Decreased HRQL in survivors of brain tumours in childhood is multifaceted. Cognitive deficits and pain are prominent problems. Pain represents an unexpected burden of morbidity. Further studies should be undertaken to explore problems with pain and potential therapeutic intervention.

PD-032

ECONOMIC INDEPENDENCE IN ADULTHOOD AMONG SURVIVORS OF CANCER IN YOUNG AGE

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Background/Objectives: Several studies demonstrate that survivors of cancer in young age have a variety of long term challenges, both medical and social. We wanted to study whether a cancer diagnosis in young age affected future earnings and need for short-term financial assistance from the government.
Design/Methods: By linking national registries (the Norwegian Cancer Registry, the Central Population Registry, the Medical Birth Registry, the Norwegian Labour and Welfare Administration and Statistics Norway) we defined a cohort of all live births in Norway from 1965-1985 followed up through 2007. The cancer group and the non-cancer group were compared using logistic regression models for outcomes of high- and low-income (defined as 80^{th}- and 20^{th} income percentile (sex specific) per year of birth), as well as need for financial assistance.
Results: After excluding individuals with a disability pension and those who died or emigrated, our final cohort consisted of 1,054,375 individuals, of whom 3,617 had been diagnosed with cancer before the age of 25. Men surviving a cancer diagnosis in young age had no altered likelihood of being in either the high income, OR=0.92 (95% CI 0.82-1.03), or the low income, OR=1.09 (0.98-1.2), category. For women in the cancer group, there was a 25% increased risk of being in the low income category, OR=1.25 (1.11-1.41), and no altered risk for being in the high income category, OR=0.95 (0.83-1.08), compared with the non-cancer group. Men with cancer had a reduced risk of receiving financial assistance from the government, OR=0.87 (0.79-0.96), whereas there were no differences for women with cancer, OR=1.00 (0.90-1.12), compared with the non-cancer group.
Conclusion: In this population-based cohort, we demonstrated an economic disadvantage for women surviving cancer in young age, whereas no such association was found for male cancer survivors.

PD-033

TREATMENT AND OUTCOMES OF RADIATION INDUCED MENINGIOMAS (RIM) FOR CHILDHOOD CANCER SURVIVORS RECEIVING CRANIAL IRRADIATION

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Background/Objectives: Secondary meningiomas after the treatment of central nervous system (CNS) with radiotherapy (RT) are serious complications and therapeutic strategies are complex. We reviewed our institutional experience of treatment and outcomes for patients with RIM.
Design/Methods: A review of all patients followed in the Childhood Cancer Survivor Program showed 17 patients developed RIM after cranial irradiation for non-CNS tumors. We reviewed demographics, histology, tumor location, treatment, latency interval, time to first intervention and time to subsequent interventions.
Results: Of 17 patients diagnosed with RIM, 58.8% were female. All patients received ≥ 20 Gy PCI and systemic chemotherapy and 88.2% received intrathecal methotrexate. Demographics revealed that RIM was solitary in 58.8% and multiple in 41.2%.The meningiomas were WHO grade 1 in 73.3% and 26.7% grade 2, skull base in 35.3%, 35.3% convexity, 17.6% parasagittal and 11.8% multiple locations. Median latency to development of RIM was 25.6 yrs (95%CI=20.5-27.6yrs). Sixteen patients had symptoms prior to diagnosis; headache in 88.2% and cranial nerve deficits in 35.3%. Fifteen patients had surgery, 46.7% gross total resection (GTR) of all lesions, 33.3% GTR of some lesions, and 20.0% with subtotal resection (STR) and 2 patients had no intervention. Median time to first intervention was 25.6 yrs (95%CI=19.2-27.8yrs). Ten patients (58.8%) required further intervention with median time to second intervention was 2.7 yrs (95%CI=1.0-5.8yrs). All patients with STR recurred. Eight patients received further surgical resection and 2 patients were treated with RT alone. Four patients had further progressive disease.
Conclusion: RIM is a significant complication for pediatric patients receiving cranial irradiation. Multiple interventions were required in 58.8% patients. RIM reviewed had a higher proportion of being multiple, grade 2, and skull base than seen in the literature for spontaneous meningiomas. These factors may impact treatment of RIM, although further study is required.

PD-034

PROSPECTIVE ANALYSIS OF LONG-TERM RENAL FUNCTION IN SURVIVORS OF CHILDHOOD WILMS TUMOR (NEPHROBLASTOMA)

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Background/Objectives: Wilms tumor (WT) is the most common renal malignoma in childhood. Considering improved outcome, a better understanding of late effects in WT survivors (WT-S) is needed. The aim of this study was to evaluate renal function and to determine the prevalence of subclinical renal impairment in a cohort of WT-S using a clinical, sonographic and biomarker approach.
Design/Methods: Fourty-nine former WT-S were enrolled in this prospective single center study. Glomerular filtration rate (GFR) was measured by creatinine clearance and estimated using creatinine-based and Cystatin-C-based approximations. In addition, urinary excretion of total protein, albumin, α1-microglobulin and neutrophil gelatinase-associated lipocalin (NGAL) were assessed. Clinical examination included kidney sonomorphology and blood pressure measurement.
Results: All examined WT-S (mean age 23.8 years, range 1.68-48.8 years; mean follow-up 18.3 years) were treated with a combination of surgery (total/partial nephrectomy) and chemotherapy; 57% received adjuvant radiotherapy. A creatinine clearance below age norm was detected in 32% of WT-S. Moreover, applying age-adjusted Cystatin-C-based GFR-estimation, a GFR below age norm was identified in 56% of the WT-S studied. In 7 patients with low GRF, glomerular selective proteinuria (micro- or macroalbuminuria) was identified. Pathological urinary NGAL excretion as a marker of renal tubulary dysfunction was detected in 13%. Ultrasound revealed a compensatory contralateral renal hypertrophy > 95th percentile in 81% of the patients. Fifteen (31%) WT-S presented with hypertension and 6 (12%) with high-normal blood pressure (according to WHO definition).
Conclusion: Even though it is believed that WT-S have a low risk for end stage renal disease, in this study a remarkable part of former WT-S presents with previously unidentified subclinical signs of renal function impairment and secondary morbidity with no ceiling of the cumulative incidence after WT-therapy over time. Further studies are needed to define optimal long-term follow-up of WT-S, especially with regard to subclinical disease and risk stratification.

PD-035

SKELETAL LATE EFFECTS IN CHILDHOOD CANCER SURVIVORS

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Background/Objectives: A significant number of childhood cancer survivors develop treatment related health problems that manifest early to years after completion of cancer treatment. The purpose of this study was to assess the risk and spectrum of skeletal late effects in childhood cancer survivors.
Design/Methods: A cohort of 19.970 one-year cancer survivors diagnosed before 20 year of age was identified in the national cancer registries of Denmark, Iceland and Sweden and a cohort of 123.680 population controls was selected from the respective national population registries. By linking study participants to national hospital registries the observed numbers of first-time hospital contacts for acquired skeletal disorders were compared with the expected numbers in the population cohort. Standardized hospitalization rate ratios (SHRRs) and absolute excess risks per 100.000 person-years (AERs) were calculated from the observed and expected numbers among the study participants.
Results: In total, 1457 childhood cancer survivors (7.3%) were diagnosed with skeletal disorders, yielding a SHRR of 1.30 (95% CI, 1.23-1.37) and an overall AER of 114 (88-141). We observed an increased risk among the survivors for osteonecrosis SHRR 14.6 (8.9-24.3), osteoporosis 3.6 (2.5-5.2), osteochondropathies 1.6 (1.2-2.0), osteoarthritis 1.3 (1.1-1.6) and fractures 1.2 (1.16-1.31), especially osteoporotic fractures 1.5 (1.4-1.7). The risk and pattern of skeletal disorders varied between different cancer groups and age groups but the increased risk continued throughout life.
Conclusion: Childhood cancer survivors have a lifelong increased risk of skeletal disorders. To decrease the burden of late effects in childhood cancer survivors, assessment of skeletal health is important both during treatment and in the long-term follow-up.

PD-036

CHILDHOOD CANCER SURVIVORSHIP CLINIC ATTENDANCE IN A REGIONAL SAMPLE: PATTERNS AND PREDICTORS

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Background/Objectives: Even when specialty survivorship clinics are available, many childhood cancer survivors do not receive recommended surveillance for late effects of treatment. We sought to characterize clinic attendance in a regional sample and identify predictive factors.
Design/Methods: Using the Connecticut Tumor Registry and Yale hospital records, we identified all patients diagnosed with cancer at age ≤18 years from 3/1/1998-3/1/2008, still in follow-up 5 years post-diagnosis, and living <100 miles from Yale. Survivorship clinic attendance, demographics, disease characteristics, and treatment exposures were ascertained from medical records. Vital status was confirmed using the National Death Index. Kaplan-Meier curves and hazard ratios were calculated for survivorship clinic attendance; patients were censored upon attending clinic, death, or 3/1/2013.
Results: 489 eligible survivors were diagnosed at a mean age of 9.1±5.8 years with leukemias/lymphomas (47.2%), brain tumors (16.4%), sarcomas (11.2%), thyroid cancers or melanomas (7.8%), other solid tumors (17.4%). The Kaplan-Meier estimated 5- and 10-year post-diagnosis clinic attendance probabilities were 27.8% (SE=2.3%) and 35.5% (SE=3.1%) respectively. The attendance probabilities were 36.9% (SE=4.4%) after radiation and 40.8% (SE=3.8%) after anthracycline therapy at five years. After adjusting for age at diagnosis, gender, and insurance, patients treated with anthracyclines (HR=3.047;p<0.0001) and radiation (HR=1.902;p=0.0004) were significantly *more likely* to attend clinic. Patients with a history of brain tumors (HR=0.298 compared to leukemia; p=0.0008), surgery without radiation or chemotherapy (HR=0.023 compared to chemotherapy only; p=0.0002), no insurance (HR=0.345;p<0.0001), and no primary care physician (HR=0.060;p<0.0001) were significantly *less likely* to attend clinic. Income, travel time to clinic, clinical trial enrollment, and race were not significant predictors.
Conclusion: The majority of childhood cancer survivors in our regional sample, including high-risk groups who received radiation or anthracyclines, had not attended survivorship clinic. Factors related to health care access, including having a primary care physician and insurance, were important predictors of clinic attendance.

Poster Discussion: Liver Tumours

PD-037

GENOME-WIDE ANALYSIS OF DNA METHYLATION IN HEPATOBLASTOMA TISSUES

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Background/Objectives: DNA methylation has a crucial role in cancer biology. We performed a genome-wide analysis of DNA methylation in hepatoblastoma (HB) tissues to verify differential methylation levels between HB and normal tissues. As alpha-fetoprotein (AFP) has a critical role in HB, we also detected AFP methylation levels, using pyrosequencing.
Design/Methods: Normal and HB liver tissue samples were obtained from patients with HB. Genome-wide analysis of DNA methylation in these tissues was performed using an Infinium HumanMethylation 450 BeadChip, and results confirmed with quantitative RT-PCR (q-PCR).
Results: The Infinium HumanMethylation 450 BeadChip showed distinctively less methylation in HB tissues than in non-tumor tissues. We also found methylation enrichment in positions near the transcription start site of AFP, which exhibited lower methylation levels in HB tissue than in non-tumor liver tissues. Lastly, we found a significant negative correlation between AFP mRNA expression and DNA methylation percentage, using linear Pearson's R correlation coefficients.
Conclusion: Our results demonstrate differential methylation levels between HB and normal tissues, and imply that aberrant methylation of AFP in HB could reflect HB development. Expansion of these findings could provide useful insight into HB biology.

PD-038

THE ANALYSIS OF THE FACTORS AFFECTING THE RESULT OF THE HEPATOBLASTOMA TREATMENT IN CHINA - ONE SINGLE CENTER EXPERIENCE

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Background/Objectives: The mortality of hepatoblastoma remains worse in developing country. This study aims to introduce the experience and outcome of hepatoblastoma at a local children's medical center in China.
Design/Methods: The study was a retrospective analysis of 98 children with hepatoblastoma between January 2006 and December 2014 in one center. The standard treatment of hepatoblastoma is composed of PLADO or C5V chemotherapy and surgery. Patients who were not sensitive to primary regimen, the other regimen could be changed to alternatively.
Results: Two-year/5-year overall survival (OS) of this study was 68.8%/65.7%, respectively, while patients with PRETEXT stage I~III were 83.3%/83.3%, 100%/92.9%, 68.8%/66.1%, respectively. The 3-year OS of stage IV was 10.3%. 18 patients (23.1%) recurrenced after surgery. PRETEXT III/IV, vascular invasion and resection margin <5mm are three high risk factors of recurrence with univariate analysis (P<.05). Age >5 years old, vasulcar invasion, tumors resection, PRETEXT stage are four prognostic factors of survival with univariate analysis (P<.05). Tumor resection is the only one prognostic factors with multivariate analysis (p<.001, HR=0.049, 95%Cl (0.013, 0.175).
Conclusion: Surgery plays the central role of the treatment. The survival of stage IV and unresectable tumor with stage III is lower than those reported in developed country. The restriction of liver transplantation is the main reason for this difference. Although PLADO and C5V had similar efficiency, when patients who were not sensitive to one regimen, the other regimen is could be effective.

PD-039

MICELLAR CURCUMIN EFFECTIVELY REDUCES AFP AND TUMOR GROWTH IN AN ORTHOTOPIC MURINE MODEL OF PEDIATRIC HEPATOCELLULAR CARCINOMA

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Background/Objectives: In children with hepatocellular carcinoma (pHCC) the 5-year overall survival rate is poor. Effects of cytostatic therapies such as cisplatin (CDDP) and doxorubicin are limited due to chemoresistance and tumor relapse. In adult HCC several antitumor properties are described in *in vitro* models for the use of curcumin. Curcumin is one of the best investigated phytochemicals in complementary oncology without relevant side effects, but its use is limited by the low bioavailability.
Design/Methods: Orthotopic growth of the pediatric hepatocellular carcinoma cell line HC-AWF1 in NOD/LtSz-scid/IL-2Rgamma(null)mice was induced by intrasplenic cell injection and splenectomy. By the increase serum alpha fetoprotein AFP >5 U/mL mice were randomly assigned to one of four groups: control (no treatment); curcumin (micellar curcumin, 60 mg/Kg body weight 3 weeks); Cisplatin (CDDP, 1 mg/Kg bodyweight on days 1 and 2), and micellar curcumin + CDDP (combination therapy CDDP + curcumin micelles). Curcuminoid levels in serum and organ lysates as well as AFP serum levels were investigated.
Results: Tumor uptake was 91.5%. Serum curcumin decreased from 3514 ± 2792 nmol/L two hours after administration to 770 ± 449 nmol/L after five hours. Curcumin concentrations significantly differed between organs (p=0.000) and the highest concentrations were observed in the lungs 11.33 ± 9.17 nmol/Kg and the lowest in the brain 0.16 ± 0.24 nmol/Kg. The concentrations in the tumor tissue (2.57 ± 1.49 nmol/Kg) were higher than in the liver (1.77 ± 1.50 nmol/Kg). The combination therapy (micellar curcumin + CDDP) significantly reduced AFP concentrations compared to control group (week 3: 1.04 ± 0.67 vs. 2.73 ± 0.64, p = 0.004; week 4: 2.05 ± 1.01 vs. 3.35 ± 0.43, respectively, p = 0.02).
Conclusion: These data prove the potential of micellar curcumin as a complementary agent in pediatric oncology to enhance the overall survival of patients with pediatric liver tumors.

PD-040

LOW EXPRESSION OF N-MYC DOWNSTREAM-REGULATED GENE 2 (NDRG2) CORRELATES WITH POOR PROGNOSIS IN HEPATOBLASTOMA

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Background/Objectives: Besides mutation of the beta-catenin gene epigenetic alterations are heavily discussed to play a major role in the development of hepatoblastoma (HB). Here, we investigated whether epigenetic silencing of the N-myc downstream-regulated gene 2 (*NDRG2*) may contribute to HB development.
Design/Methods: The methylation status and mRNA expression level of 38 human HB and normal liver tissue samples was evaluated by pyrosequencing and real-time PCR, respectively. Subsequently, we analyzed whether *NDRG2* promoter methylation and expression are clinically relevant by correlating the molecular findings with clinical data obtained from the German Liver Tumor Registry.
Results: Downregulation of *NDRG2* is a common event in HB (28/38 cases) and *NDRG2* transcription is potentially down-regulated through promoter hypermethylation. *NDRG2* expression was significantly lower in patients with metastatic disease and *NDRG2* downregulation significantly correlated with poor prognosis.
Conclusion: Our findings suggest that *NDRG2* expression may be an important factor for maintenance of normal condition of infantile liver tissue. Its epigenetic silencing could contribute to HB formation and its downregulation might be used as a marker for poor prognosis.

PD-041

CONGENITAL HEPATOBLASTOMA IN JPLT-2 STUDY

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Background/Objectives: Congenital hepatoblastoma was previously thought to have poor prognosis and different characteristics compared to hepatoblastoma in children beyond neonatal period. However, recent reports demonstrated it could have similar prognosis by standard therapeutic strategy consisted of hepatectomy and chemotherapy.
Design/Methods: We analyzed the clinical characteristics and outcome of the neonatal patients with hepatoblastoma enrolled to a protocol of the Japanese Study Group for Pediatric Liver Tumor, JPLT-2 study, which enrolled a total of 279 children with malignant liver tumors. In this study, primary chemotherapy consisted of cisplatin and pirarubicin (CITA), and for unresectable or unresponsive disease, the combination of ifosphamide, pirarubicin, etoposide, and carboplatin (ITEC) was used.
Results: Seven (2.5%) developed hepatoblastoma in the neonatal period (6 males, 1 females). All patients were born with normal birth weight and no associated congenital abnormalities. Tumors were classified as PRETEXT II (5), III (2). All had no metastatic disease. The median α-fetoprotein level was 462,700 ng/ml (range, 182,490 to 1,390,000 ng/ml). Two of the three patients who underwent primary resection received adjuvant chemotherapy. Four patients underwent partial hepatectomy after neoadjuvant chemotherapy followed by postoperative chemotherapy. In all patients who received chemotherapy, it consisted of cisplatin and pirarubicin (CITA) with 30 to 50% dose reduction. No patients received the salvage regimen ITEC. Grade 3 to 4 neutropenia was documented in three patients, and cardiac dysfunction (ejection fraction 60%) occurred in one patient. One patient who underwent primary resection without adjuvant chemotherapy had metastatic recurrence in the lungs after five months from diagnosis and died after brain metastasis. All other patients were alive without evidence of disease with median follow-up of 36 months (range, 14 to 159 months).
Conclusion: Congenital hepatoblastoma could be successfully treated by surgical resection and standard cisplatin-based chemotherapy with dose reduction.

Poster Discussion: Lymphomas & Histiocytosis

PD-042

RESULTS OF TREATMENT OF LYMPHOBLASTIC LYMPHOMA AT THE CHILDREN CANCER HOSPITAL EGYPT- A SINGLE CENTER EXPERIENCE

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Background/Objectives: Lymphoblastic lymphoma (LL) and acute lymphoblastic leukemia (ALL) and are neoplasms of immature B or T-cell precursors. They are considered as a unique biological entity in the 2008 World Health Organization Classification of Hematologic Neoplasm. Treatment of LL has evolved over time from conventional high-grade NHL schedules to ALL- derived protocols. The aim of this work is to estimate the EFS, OS, and common chemotherapy toxicities of LL patients treated at the Children Cancer Hospital Egypt during 5.5 years period.
Design/Methods: A Retrospective review of patients charts diagnosed and treated as LL during the period between July 2007 till end of December 2012 was done. Patients were treated according to St. Jude Children Research Hospital ALL Total Therapy XV protocol, standard risk arm.
Results: This study included 77 patients. T- cell LL patients were 87%, while and B-cell were 13%. The median age was 9 years (range 1–17 years). The majority were males (70.1%). Stage III was the most common at presentation (74%). Complete remission post induction chemotherapy was seen in 25.3% of the patients, partial remission in 72%. Progressive disease was the event in 6.6%, while 5.3% suffered from a disease recurrence. The most common chemotherapy toxicities were cerebral venous thrombosis (20%), followed by bone infarcts ((10.6%), and avascular necrosis of head of femur (9.3%). Disease recurrence was local in 4% and systemic in 5% of the patients. By the end of the study, 84% of the patients were alive in CR, 16% were dead. Mean duration of follow up was 48.6 months (range 1-89 months). The 4 years overall survival was 82.7% while event free survival was 82.2%.
Conclusion: Disease progression and chemotherapy related toxicity are the main causes of death in pediatric LL patients. While cerebral vascular thrombosis and steroids induced musculoskletal complications are the major chemotherapeutic adverse events.

PD-043

CHANGE TO OEPA/COPDAC AND PET-CT BASED STRATEGY FROM FORMER ABVD/COPP FOR TREATING HODGKIN LYMPHOMA: LESSONS LEARNT FROM CHANDIGARH, INDIA

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Background/Objectives: Reduced anthracycline/alkylating-agent, non-bleomycin and PET-CT response based protocols are being evaluated to reduce long-term toxicity in Hodgkin lymphoma (HL). Aim was to analyze short-term outcome of patients with HL treated with Euronet-PHL-C1 based strategy as 'off-study' from 2010-14. A comparison was performed with institute's earlier published study using chemotherapy (ABVD, ABVD/COPP/MOPP) alone, non-radiotherapy, non-PET based approach. In the older strategy, the mean number of cycles administered in early and late-stage were 5 and 6.5, respectively.
Design/Methods: Retrospective study.
Results: Forty-nine patients were treated. The mean age was 7.7±2.4 years (range: 2-12). The number of patients in TG-1, 2 and 3 were 18, 15 and 16, respectively. A PET-CT was performed at diagnosis and following OEPA-2. Two/four courses of COPDAC were administered in treatment-groups (TG) 2/3, respectively. Radiotherapy was indicated for inadequate PET-response. The mean duration of follow-up was 25.6±14 months (range: 0.3-52). An inadequate PET-response was observed in 23 (46.9%) patients. Radiotherapy was administered to 8. Radiotherapy was 'replaced' by 2 courses of COPDAC in 9 patients, due to physician preference. In the remaining 6 patients, radiotherapy or additional chemotherapy was not administered due to misinterpretation of PET.There were 17 episodes of febrile neutropenia: 2 (4%) patients died. Two patients relapsed. One had progressive disease and another had secondary-AML. The 4-year-EFS and OS were 86.4% and 95.9%, respectively. It is comparable to the 5-year-EFS (77.7%) and OS (92.7%) of the institute's previous study. The 4-year-EFS in TG-1, 2 and 3 was 88.9%, 100% and 72.7%, respectively. The relatively lower EFS in TG-3 was probably contributed in part by misinterpretation of PET in the early period of the study.
Conclusion: Chemotherapy with OEPA/COPDAC and decision for radiotherapy based on re-evaluation PET-CT, permits reduction of therapy with excellent short-term outcome. Efforts should be made to adopt risk-stratification and response based therapy in developing countries as well.

PD-044

ANTHRACYCLINE-BASED THERAPY AMONG CHILDREN WITH ENDEMIC BURKITT LYMPHOMA IN LILONGWE, MALAWI

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Background/Objectives: Endemic Burkitt lymphoma (eBL) is highly curable in resource-rich settings with anthracycline-based chemotherapy, but such approaches have not been widely adopted in sub-Saharan Africa (SSA) due to toxicity concerns.
Design/Methods: We describe children ≤18 years with eBL enrolled June 2013-December 2014 in a prospective observational cohort. Due to frequent relapses historically with less intense regimens, children were uniformly treated during this period with an institutional protocol involving COP prephase followed by CHOP for 6 cycles as tolerated. Patient monitoring and supportive care were standardized. We summarize treatment course and toxicities for this approach.
Results: Sixty-two children with eBL [median age 8.6 years, 41 (67%) male, 46 (74%) stage III/IV] received first-line CHOP. As of December 31, 2014, 24 (40%) were alive after completing treatment, 8 (13%) were alive while receiving CHOP, 29 (47%) had died, and one patient was lost to follow-up. Median follow-up was 10.8 months among children still alive. For the cohort overall, median absolute neutrophil count remained $>1.5 \times 10^9$/L, absolute lymphocyte count $>1.5 \times 10^9$/L, hemoglobin >8 g/dL, and platelets $>300 \times 10^9$/L throughout treatment. Excluding 8 children still receiving first-line CHOP at censoring, significant neutropenia occurred in 11/54 (20%, 7 grade 3, 4 grade 4) and anemia in 25/54 (44%, 21 grade 3, 4 grade 4). Chemotherapy delay >7 days occurred in 33/54 children (61%) mostly due to incomplete blood count recovery prior to scheduled treatment. Of 29 deaths, 15 were attributed to disease, 10 to treatment, and 4 to unknown causes.
Conclusion: CHOP for predominantly advanced-stage eBL in Lilongwe resulted in overall similar outcomes compared to historical experience using less intensive regimens. CHOP may be appropriate for some children, and many deaths were from disease rather than therapy. Better risk-adapted, response-guided strategies can help optimize treatment for individual children with eBL in SSA.

PD-045

PRIMARY BONE LYMPHOMAS IN HIV- INFECTED CHILDREN

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Background/Objectives: Background Diffuse Large B- Cell and Burkitts Lymphoma which account for 90% of lymphomas in the HIV- infected patient are aggressive cancers with a high morbidity and mortality. Primary Bone Lymphoma (PBL) is a rare disease and accounts for 3-5% of all pediatric lymphomas.
Design/Methods: This is a retrospective review of the presentation, results, treatment and outcome of four HIV-infected children who presented with PBL.
Results: There were two males and the mean age was 11.5 years. All presented with lymphadenopathy, one had scalp lumps, one had a mass in the left hip and one had a swelling of the left face. All were stunted and wasted with HFA and WFA between -2 and -3 SD. The laboratory investigations: a mean Hb= 10.8g/dl, WCC= 5.2×10^9/l, PLT= 446×10^9/l and LDH=639 u/L. The mean CD4 number was 364×10^6/l and the CD4% was 13.4%. None had metastatic disease to the bone marrow or CSF, but radiology and bone scans revealed extensive bulky disease. The immunophenotypic analysis: two CD20+, CD79a +, BCL2 +, BCL6 +, MMI +; and one CD10 +, all strongly positive for K167, negative for TdT and CD3. All were stage 3, risk group 4 and treated with the NHL-BFM 1998 protocol and ARVs. All four patients completed therapy successfully.
Conclusion: PBL is a rare tumour. NHL in the HIV-infected, ARV naïve group of patients is associated with a high morbidity and mortality due to disease progression, relapsed disease, infectious complications and poor compliance. We describe a group of ARV naive patients with advanced disease with a good outcome. The numbers are limited to draw conclusions, but may represent a group of patients in whom we could dose-reduce treatment to minimise chemotherapy related toxicity.

PD-046

SUPERIOR OUTCOMES AT A LOWER COST WITH COG BASED PROTOCOL FOR ANAPLASTIC LARGE CELL LYMPHOMA: EXPERIENCE FROM INDIA

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Background/Objectives: Anaplastic large cell lymphoma has excellent treatment outcomes in children. We discuss the treatment outcome in resource limited setting, using BFM and COG based protocols.
Design/Methods: This is a retrospective descriptive study in patients diagnosed to have Anaplastic large cell lymphoma treated with BFM protocol or COG protocol between 2002 and 2014 in two cancer centres.
Results: Out of a total of 30 patients, 19 patients received treatment as per BFM –NHL 90 protocol .The mean age was 8.7 years (range 1.5 to 16 years). Patients in high risk group 70%, standard risk 26% and 4% were in low risk group. Thirteen patients are in complete remission, three died of infection during treatment, 3 had progressive disease of which one achieved remission after second line treatment. The mean febrile neutropenic episode in this group was 1.8 (ranged 0-5).Twenty six percentage of these patients developed septicaemia. Severe mucositis and hospitalisation needed for 10% of patients. Mean duration of follow up of those in CR is 25.4 months (range 3-56 months). Three (16%) patients had relapse with the mean time to relapse was 36.6 months. Eleven patients were treated with COG ALCL protocol with mean age 9.3(range 2to 16). Patients in high risk group 77% and 23% were standard risk. The mean duration of follow up is 2.6 months (range 1- 4 months). There have been no deaths and no documented relapses till date. No documented bacteraemia or severe mucositis in this group.
Conclusion: Patients from developing countries fared better with a COG based protocol for Anaplastic Large Cell Lymphoma. We would recommend this outpatient based protocol including treatment over 15 months requiring less supportive care and superior outcome due to lack of regimen related toxicity to all cancer centres in our country based on our pilot study.

PD-047

EVENT FREE SURVIVAL OF PATIENTS WITH MULTISYSTEM-RISK LANGERHANS CELL HISTIOCYTOSIS IS SUBOPTIMAL WITH LCH-III PROTOCOL: 8-YEARS CHANDIGARH, INDIA EXPERIENCE

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Background/Objectives: Langerhans cell histiocytosis (LCH) III trial recruited patients worldwide from 2001-08. Experience with LCH-III, with patients enrolled as 'off-study' is presented from a pediatric oncology unit in India.
Design/Methods: Retrospective (2006-2013) chart review was performed. Patients in group-1 (Multisystem-risk) received initial treatment of 6-12 weeks, followed by continuation treatment to complete 12-months. Drugs included, vinblastine, prednisolone and 6-MP. Patients in group-2 (Multisystem-low-risk) received similar treatment, except 6-MP. Group-3 (Single-system/multifocal-bone-disease) patients were treated for 6 months. An event was defined as relapse, progressive disease or death. No patient received a liver or hematopoietic transplant due to limited accessibility.
Results: Forty-nine patients were diagnosed in the 8-year-period: 24 (49%), 14 (29%) and 11 (22%) in Group 1, 2 and 3, respectively. The mean age was 31.6±28.4 months (range: 4-120). Patients in Group-1 were younger (p=0.001). The median follow-up duration was 25 months (range: 0.5-120). Five patients abandoned treatment. There were 7 deaths (all in Group-1), at a median duration of 22 days (range: 14-213) from treatment; from progressive disease (4), febrile neutropenia (2) or meningoencephalitis (1). All patients who died had partial response or progressive disease following induction (p<0.001). Disease relapsed in 12 (24.5%) patients, at a mean duration of 17.2±7.6 months. Incidence of relapse was similar in 3 groups (p=0.83).There was no increase in deaths in patients with respiratory involvement (22.2% vs. 12.5%, p=0.45). Sclerosing cholangitis was an independent predictor of mortality (OR: 85.8, p=0.01). Five-year-EFS was 34.5±11.3%, 63.5±15% and 77.9±14.1% in groups 1, 2 and 3, respectively (p=0.027). Five-year-OS was 68.9±9.8% and 100% in Group 1 and 2/3, respectively (p=0.01).
Conclusion: Majority (49%) of patients presented with multisystem-risk disease. Partial response and progressive disease is a major concern in patients with multisystem-risk disease, resulting in a suboptimal five-year-EFS of 34.5±11.3%. The 5-year-OS of patients with multisystem low-risk and multifocal bone disease is 100%.

PD-048

COMBINED BIOMODULATORY THERAPY TARGETING THE TUMORS´ BIOLOGY AS AN ALTERNATIVE TREATMENT IN CHEMOREFRACTORY PAEDIATRIC MULTISYSTEM LANGERHANS CELL HISTIOCYTOSIS

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Background/Objectives: Nearly half of the patients with systemic Langerhans´cell histiocytosis (LCH) relapse, mostly within 2 years from diagnosis (Minkov et al, 2008). For patients failing to achieve stable remission under conventional chemotherapy according to the LCH III protocol we applied a multi-targeted therapeutic approach simultaneously directed at tumor metabolism, inflammation, angiogenesis and immune response.
Design/Methods: An 18 months old girl presented with LCH of the skin, bones and spleen. She started on vinblastine and prednisone according to the LCH III protocol. After recurrence of skin and bone lesions during treatment the relapse was treated with vincristine, cytarabine and prednisone. Due to severe adverse effects the chemotherapy was interrupted. An 11 months old boy presented with LCH of the skin, liver and small bowels. He also was treated according to the LCH III protocol. With refractory disease he received a salvage therapy with prednisolone, cytarabine and cladribine. In maintenance therapy with indomethacin he again relapsed with multiple bone lesions. As for increasing liver failure (cirrhosis) a third line conventional chemotherapy was unfeasible.
Both patients were started on a metronomic biomodulatory therapy approach in analogy to an adult melanoma trial, consisting of low dose trofosfamide, a PPAR alpha/gamma agonist (pioglitazone), a COX-2 inhibitor (etoricoxib) and low-dose dexamethasone.
Results: Both patients treated with a combined biomodulatory therapy in a compassionate use approach responded to the treatment as determined clinically, by MRI scans and biopsies and are still in stable remission after one and two years respectively. So far the liver cirrhosis of the boy came to a halt.
Conclusion: A combination of anti-inflammatory and angiostatic drugs is a well-tolerated and feasible treatment option for children with refractory systemic LCH. Confirmation of efficacy should be evaluated prospectively in patients who fail to stably respond to conventional therapy.

Poster Discussion: Myeloid Leukemias, Myelodysplastic & Myeloproliferative Syndromes

PD-049

BENZENE EXPOSURE FROM A BP REFINERY FLARING INCIDENT INCREASES THE RISK OF DEVELOPING HEMATOLOGICAL MALIGNANCIES IN CHILDREN

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Background/Objectives: Benzene is a recognized environmental carcinogen and causes serious adverse hematological effects. Especially, benzene exposure increases the risk of developing lleukemias and lymphomas. Children are highly vulnerable to the toxic effects of benzene exposure. The objective of this study was to evaluate the health consequences of benzene exposure among children from a flaring incident that occurred at the British petroleum (BP) refinery in Texas City, Texas, USA.
Design/Methods: The study included both children aged <17 years who had been exposed and unexposed to benzene. Using medical charts, clinical data including white blood cell (WBC) counts, platelets counts, hemoglobin, hematocrit, blood urea nitrogen (BUN,) creatinine, alkaline phosphatase (ALP), aspartate amino transferase (AST), and alanine amino transferase (ALT) were reviewed and analyzed.
Results: A total of 899 children (benzene exposed, n=641 and unexposed, n=258) were included. Hematological analysis indicated that WBC (X 10^3 per μL) counts were significantly decreased in the benzene exposed children compared with the unexposed children (7.1±2.2 versus 7.6±2.1, P=0.001). Similarly, the mean hemoglobin (g/dL) levels were decreased significantly in the benzene exposed group compared with the unexposed group (12.7±1.3 versus 13.1±1.5, P=0.001). Conversely, platelet (X 10^3 per μL) counts were increased significantly in the benzene exposed group compared with the unexposed group (318.6 ± 79.8 versus 266.9 ± 58.8, P=0.001). Similarly, benzene exposed children had significantly higher levels of ALP (264.6 ± 64.6 versus 192.1±55.1 IU/L, P=0.001), AST (28.2±9.5 versus 22.9±14.6 IU/L, P=0.001) and ALT (20.9±7.4 versus 16.2±6.5 IU/L, P=0.001) compared with the unexposed children.

Conclusion: Children exposed to benzene had significant alterations in their hematological and liver functions indicating that these children are at a higher risk of developing both soft tissue and bone marrow related malignant disorders.

PD-050

EFFECT OF SEVEN ANTIFUNGAL AGENTS AGAINST CANDIDA SPP. ISOLATED FROM ORAL CAVITY OF PEDIATRIC PATIENTS WITH LEUKEMIA

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Background/Objectives: Oropharyngeal candidiasis is a frequent problem in patients with leukemia, associated with different clinical presentations including pseudomembranous and erythematous forms. Nevertheless, azole antifungal drugs are frequently prescribed for the treatment of these infections. The aim of this study was the analysis of susceptibility pattern of *Candida* spp., isolated from oral cavity of pediatric patients with leukemia, against seven antifungal agents.
Design/Methods: A total of 88 *Candida* strains were obtained from oral cavity of pediatric patients with leukemia. Samples were plated on Sabouraud dextrose agar and incubated at 24°C for 10 days. The identification of *Candida* strains was performed using carbohydrate assimilation reactions on the API 20 C AUX system. *Candida parapsilosis* ATCC 22019 was used as control. The minimum inhibitory concentrations (MICs) against amphotericin B, fluconazole, ketoconazole, voriconazole, itraconazole, caspofungin, and posaconazole were analyzed by E-test method.
Results: Among the *Candida* (C) strains, *C. albicans* (60%) was the most prevalent *Candida* spp. followed by *C. dubliniensis* (6.8%), *C. tropicalis* (6.8%), *C. krusei* (6.8%), *C. parabsilosis* (6.8%), Other *Candida* spp. (12.5%). Most of the patients had acute leukemia including acute lymphoblastic leukemia and acute *myeloid* leukemia, and underwent chemotherapy and/or hospitalizations. Many of patients had a history of antifungal prophylaxis administration. *Candida Krusei* was the most resistant isolated yeast, which was 40% resistant to fluconazole and 30% to itraconazole, 11% to ketoconazole, and 1% to amphotericin B. All the tested species were mostly sensitive to caspofungin.
Conclusion: Knowledge about the susceptibility patterns of *Candida* spp., colonized in oral cavities of high risk patients can help more effective management and treatment of the conditions. In this study, caspofungin and amphotericin B were revealed as the most potent agents against the colonized Candida spp.

PD-051

DNMT3A MUTATION IN CHINESE CHILDHOOD ACUTE MYELOID LEUKEMIA

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Background/Objectives: DNMT3A mutation has been found in approximately 20% of adult AML patients and in 0~1.4% childhood AML. The prognosis of adult patients with *DNMT3A* mutation is worse, however, the prognosis of *DNMT3A* mutation in childhood AML is still dismal. Here, we tried to determine the incidence and prognostic significance of *DNMT3A* mutation in Chinese childhood AML.
Design/Methods: We detected the mutation in *DNMT3A* exon 23 by PCR and direct sequencing in 343 children with AML (range: 0~16 years old, M1:4, M2:143, M3:75, M4:43, M5:33, M6:11, M7:30, unclassified: four patients) from January in 2005 to June in 2013, treated on BCH-2003AML protocol. Details regarding the clinical characteristics, fusion gene, and other molecular characteristics (*FLT3-ITD*, *NPM1*, *C-KIT* and *WT1*) of the study cohort were analyzed.
Results: *DNMT3A* mutations were detected in 1.17% (4/343) of patients. Of them with *DNMT3A* mutated, Pt 1. (M/6, M4) harbored a S892S mutation was diagnosed leukemic infiltration of the gastrointestinal tract, and gave up after 38 days; Pt 2. (F/12, M3) harbored a V912A mutation and *PML-RARA* fusion gene got continuous complete remission for 60 months; Pt 3. (M/1, M5) harbored a R885G mutation and two inrtonic mutations (c.2598-15C>T and c.2739+55A>C) was newly diagnosed myeloid sarcoma and was combined with testicular leukemia and CNS leukemia after 2 months. After 10 months, he undertook the BM Transplant but got relapsed in testicular after 39 days and then died after 8 months; Pt 4. (F/2, M3) harbored a Q886R mutation was found to be *PML-RARA* and *FLT3-ITD* positive, and dead of retionic acid syndrome after 22 days.
Conclusion: *DNMT3A* mutation can be found in 1.17% Chinese childhood AML. The mutation positions were different from the hotspots reported in dult AML. We supposed that *DNMT3A* mutations may have adverse prognostic impact at earlier ages in childhood AML.

PD-052

DOES HDARA-C IMPROVE THE OUTCOME OF DOWN SYNDROME PATIENTS WITH ACUTE MYELOID LEUKEMIA?

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Background/Objectives: Patients of Down syndrome with AML have an overall good outcome but are at increased risk to chemotherapy related toxicities.
Design/Methods: Medical records of 27 DS AML patients who received chemotherapy on two different protocols between 1998 and 2013 were reviewed. Data extracted included those related to clinical characteristics of patients and their outcome.
Results: 20 patients were males (74%). Median age at diagnosis was 24 months (range 1.31-152.98). Four patients were below the age of 12 months (14.81%).7 were FAB M7. Mean WBC count was 32.73(range 1.80-219.96). Six patients had trisomies in addition to ct21. Fifteen patients received Japanese protocol (No HDAra-C)JAP (55.55%), 10 POG (Containing HDAr-C) (27%) and 1(3.7%) other protocol.14 patients (93%) on JAP achieved remission at the completion of induction, 3 relapsed (2 in BM and 1 in BM+CNS) with a median relapse free time of 4.2 months (range1.92 -16.08). 3 died (2 due to Progressive disease and one to infection). 3(20%) patients admitted in PICU. 8 patients (80%) on POG achieved remission at the completion of chemotherapy. 3(30%) relapsed in bone marrow with a median relapse free time of 3.96 months (range 01.8-4.44). Three patients (30%) expired due to progressive disease. 2(20%) patients needed PICU admission. There were more post induction infectious toxicities in the POG group compare to JAP (F/N episodes 9 vs 2, Invasive Fungal Infection 6 vs 0, Bacterial 4 vs 2, Viral 1 vs 0 and mucositis 1 vs 0). Statistically there was no significant difference in the OS (JAP 75.4% vs POG 70%, p-value= 0.262) and EFS (JAP 65.5% vs POG 70%, p-value = 0.412) between the two protocols.
Conclusion: The use of HDAra-C in treatment of DS-AML patients did not improve outcome and is associated with higher infectious complications.

PD-053

ACUTE MYELOID LEUKEMIA: TREATMENT RELATED MORTALITY IS A BANE IN A DEVELOPING COUNTRY

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Background/Objectives: To determine the outcome of children treated for Acute Myeloid Leukemia (AML) in a university hospital in India.
Design/Methods: Hundred children were treated for AML (Non M3) from January 2004 to December 2013. AML MRC X protocol was followed before 2007 & AML MRC XII subsequently. Baseline characteristics, response rate and complications were analyzed from case records.
Results: The mean age was 7.3±3.6years. There were 76 boys and 24 girls. FAB subtype: M0: 2; M1: 12; M2: 46; M4: 17; M5: 14; M6: 3; M7: 6. Cytogenetics were not available. Seven patients had gum hypertrophy and 14 granulocytic sarcoma. Median TLC: 26,500 /mcL (8,200-67,000); Platelets 30,000/mcL (13,500 -69,700). Eight patients had central nervous system (CNS) involvement.Remission: Bone marrow in 75 patients after course 1: 64% in remission (M1), 76% : <15% blasts. Five children had refractory AML. Three defaulted therapy. Treatment related mortality (TRM): Forty eight children died. Twenty five (53%) deaths occurred during course 1, with 8, 7 & 8 deaths after course 2, 3 & 4. Cause of death: 25(52.1%) severe sepsis; 13(27.1%) bacterial culture positive sepsis, 6(12.5%) probable fungal infection, 3(6.3%) proven fungal infection, 1(2.3%) leukostasis related. Relapses: Twenty patients relapsed; ¾ being early relapses. . Survival: The overall survival is a dismal 27.2% (665.47± 130.24). Disease free survival (DFS) is 34.7% (845±160.62). There was no difference in DFS between those who had >15% /<15 % blasts after course 1 (31.6% vs. 35.5%; p=0.916). Age, gender, FAB subtype & CNS positivity had no association with outcome.
Conclusion: High TRM precludes satisfactory outcomes in AML. Infections are responsible for the majority of TRM. One fourth of the cohort died during the first induction. Improving supportive care and combating infection is the need of the hour for decreasing TRM to improve survival in a developing country set up.

PD-054

CHILDHOOD ACUTE MYELOID LEUKEMIA: AIIMS EXPERIENCE

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Background/Objectives: From India, the data of outcome in childhood acute myeloid leukemia (AML) is below par and still not adequate as compare to west. There are modest survival outcomes 23% to 53.8%.To evaluate the outcome of childhood acute myeloid leukaemia (AML) treated during 2011-2014 at our centre.
Design/Methods: Case records of AML patients treated (MRC10 protocol) at our centre were reviewed.
Results: A total of 63 patients were enrolled during 2011-2014. 98% patients presented with fever. Bleeding was present in 18/63, proptosis 10/63 and CNS disease in 4/63 patients. Median duration of the disease related symptoms was one month. Karyotypes of 27 patients were available. 50% had cytogenetics abnormalities with good prognosis (inv 16, t(8;21) or t(15;17)). Fifteen patients presented with cytogenetics abnormalities with intermediate prognosis. Patients in intermediate cytogenetic risk group fared poorly than patients in favourable cytogenetic risk group in terms of both event free survival and overall survival ($p = 0.0059$). Of 63 patients 15 declined therapy, 3 were lost to follow up. Fifteen (31%) patients died before completion of therapy while rest completed treatment. Initial presentation with bleeding came out to be significant for poorer event free survival ($p = 0.0071$). Higher TLC count at diagnosis is also a poor prognostic factor in terms of event free survival ($p = 0.01$). Among survivors the median duration to the first neutopenic episode is 8 weeks. In 86% survivors the time to first neutropenic episode was > 1.5 weeks after induction ($p = 0.02$). Overall survival probability came out to be higher for patients who completed treatment ($p = 0.0001$).
Conclusion: It was noticed that initial presentation without bleeding, absence of high TLC delayed occurrence of first neutropenic episode is associated with significantly better outcome. Those who took treatment and completed it have performed better in terms of overall survival.

PD-055

EPIGENETIC ALTERATIONS COMMON TO ADULT AND PEDIATRIC MYELOID MALIGNANCIES PREDICT SURVIVAL AND RELAPSE IN BOTH AGE GROUPS SIGNIFICANTLY BETTER THAN MUTATIONAL OR CYTOGENETIC PROFILES ALONE

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Background/Objectives: Both adult and pediatric acute myeloid leukemia (AML) are characterized by diverse mutational and cytogenetic profiles, poor outcomes, and high incidence of relapse, as well as relatively few advances in treatment over the past 30 years. Given the high incidence of fusions and mutations affecting components of the epigenetic machinery, we sought to characterize features conferring better or worse outcomes within a risk group among pediatric cases, having previously shown the power of this approach in two large adult cohorts.
Design/Methods: The most comprehensive assay results among adults stem from the Cancer Genome Atlas (TCGA) AML project (Ley et al., NEJM 2013); the assays in the TARGET pediatric AML project are most comparable to those conducted in the TCGA AML cohort, allowing direct transfer of DNA methylation signatures, copy number variation, and gene expression markers from the former to the latter and vice versa. Without any modification or refitting, we applied to the pediatric cases a DNA methylation signature derived from the adults (non-FAB M3 cases) which outperformed all known mutational and cytogenetic markers as well as the standard of care.
Results: The risk scores in pediatric cases (derived from the adult risk panel) significantly and profoundly separated a higher-risk subgroup of children from a standard- or low-risk subgroup, as we had previously observed in the adults. Further, the association with time to relapse was stronger in the pediatric cases than we had observed in the adults, suggesting that further analysis of the pediatric cases may uncover predictors which can also be applied to the treatment of adult cases.
Conclusion: We suggest that our approach uncovers significant, clinically relevant aspects of leukemic progression, which have been overlooked by studies focusing solely or primarily on mutational covariates, and may provide a means to better stratify patients in both age groups for more effective treatment.

Poster Discussion: Neuroblastoma

PD-056

MXI1 AND MXI0 HAVE DIFFERENTIAL IMPACT ON N-MYC FUNCTION IN NEUROBLASTOMA GROWTH AND CHEMOSENSITIVITY

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Background/Objectives: Neuroblastoma is the most common extracranial malignancy of childhood. The Myc family of proteins, implicated in the etiology of many cancers, regulates cell growth and proliferation. *MYCN* amplified neuroblastoma is associated with a poor prognosis. Mxi1 is a member of the MAD family that inhibits N-Myc activity. We identified Mxi0, an alternatively spliced variant of Mxi1 with a different first exon (Exon 0), whose function is unknown. Our hypothesis is that Mxi1 and Mxi0 differentially impact N-Myc-dependent neuroblastoma cell proliferation.
Design/Methods: We expressed Mxi1 and Mxi0 in SHEP neuroblastoma cells and SHEP cells stably transfected to express high levels of *MYCN* (SHEP/*MYCN*). We also utilized native neuroblastoma cell lines with inducible expression of Mxi1 and Mxi0. Cell proliferation and survival were quantified. Apoptosis was measured by propidium iodide staining and caspase-3 immunohistochemistry. Subcellular localization of Mxi1 and Mxi0 proteins was detected by immunofluorescence.
Results: Overexpression of Mxi1 inhibits N-Myc mediated cell proliferation and improves chemosensitivity. In the absence of N-Myc, Mxi1 overexpression independently inhibits cell proliferation and induces cell apoptosis. Conversely, overexpression of Mxi0 leads to enhanced proliferation and chemoresistance, suggesting that Mxi0 is counter-regulatory to Mxi1. Finally, examination of Mxi1 and Mxi0 subcellular location reveals that Mxi1 resides in the nucleus while Mxi0 is found in the cytoplasm; this differential localization appears to be determined by the presence of Exon 0.
Conclusion: Overexpression of Mxi1 in neuroblastoma cell lines leads to inhibition of N-Myc-mediated cell proliferation while Mxi0 appears to promote cell growth. Mxi1 expression enhances chemosensitivity of neuroblastoma cells, while Mxi0 has the opposite effect. Exon 0 may play an important role in the differential function. A better understanding of the interaction between Mxi1 and Mxi0 and how they affect neuroblastoma physiology may aid in developing more effective targeted therapies to improve outcomes in children with neuroblastoma.

PD-057

INTERLEUKIN-2 ADDS TOXICITY BUT NO MEASURABLE ACTIVITY IN RELAPSED/REFRACTORY NEUROBLASTOMA PATIENTS TREATED WITH LONG-TERM INFUSION OF ANTI GD2 ANTIBODY CH14.18/CHO

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Background/Objectives: Long-term infusion (LTI) of ch14.18/CHO emerges as a promising treatment concept for relapsed/refractory neuroblastoma patients. The role of additional stimulation of the immune system by concomitant treatment with scIL2 is unclear in this setting.
Design/Methods: Pts (74) were treated with 5 cycles of LTI with 100 mg/m^2 ch14.18/CHO (d8-17) combined with 6×10^6 IU/m^2 sc IL-2 (d1-5; 8-12) (53 Pts) and without IL2 (21Pts) in a single center program. Surrogate parameters for activity and pain toxicity were determined using the whole blood cytotoxicity test (WBT) (d1, 8, 15) and analysis of the intravenous (iv) morphine usage (d8-17).
Results: GD2 specific killing of neuroblastoma cells analyzed in the WBT assay was found in all patients and cycles. The cytotoxic activity in base line samples preceding subsequent ch14.18 applications increased over cycles, indicating persistent lytic activity over the entire treatment period of 6 months. Interestingly, there was no difference in GD2 specific cytotoxic activity against neuroblastoma target cells at any time point between patients treated with or without IL2.Analysis of iv morphine usage in cycle 1 of patients treated in combination with scIL2 revealed a cumulative dose of 2.5 mg/kg/cycle in contrast to patients treated with ch14.18/CHO only (1 mg/kg/cycle). This corresponds to a >60% increase of the ch14.18/CHO associated pain toxicity by additional scIL2 treatment. Reduction of iv morphine usage in subsequent treatment cycles was observed in both cohorts. However, in patients treated without additional scIL2, 0% of patients required iv morphine in cycles 3 or greater in contrast to 29% in the scIL2 combination group.
Conclusion: Neither the surrogate WBT activity parameter nor the higher pain toxicity profile support the combined treatment in above pilot studies. Ongoing SIOPEN trials (EudraCT 2009-018077-31; EudraCT2006-001489-17) randomizing LTI ch14.18/CHO ± scIL2 in front line and relapsed/refractory patients will clarify the optimal approach.

PD-058

RELAPSED/REFRACTORY NEUROBLASTOMA PATIENTS RESPOND TO ANTI GD2 ANTIBODY CH14.18/CHO DELIVERED BY LONG-TERM INFUSION COMBINED WITH INTERLEUKIN-2 AND SHOW IMPROVED SURVIVAL RATES COMPARED TO HISTORICAL CONTROLS

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Background/Objectives: Patients (pts) with high risk relapsed/refractory neuroblastoma (NB) may benefit from treatment with long-term infusion (LTI) of ch14.18/CHO.
Design/Methods: 97 pts were treated with LTI of 100 mg/m^2 ch14.18/CHO (d8-17), 6×10^6 IU/m^2 sc IL-2 (d1-5; 8-12), and 160 mg/m^2 oral 13-cis-RA (d19-32) (SIOPEN Phase II; APN311-202; EudraCT 2009-018077-31; 44 pts; single center program; APN311-303; 53 pts). Response assessments followed INRG criteria. Fcγ-receptor polymorphisms FCGR2A (H131R), -3A (V158F) and -3B (NA1/NA2) were determined.
Results: Clinical overall responses were 30% (APN311-303) and 31% (APN311-202). The survival update of the APN311-303 cohort revealed a 1-y & 4-y OS of 94.2±3.2% & 60.9±9.0% (median FU 2.9 y [0.7-5.2 y]) and a 1-y & 4-y PFS of 54.4±6.9% & 32.3% ±6.9% (median FU 2.8 y [0.7 - 4.9 y]). Median TTP was 571 d (95% CI: 232.7 d). The comparator is the reported historical gold standard with 1-y & 4-y PFS of 19±2% & 8±3% and OS of 56±3% & 14±4% and a median TTP of 63 d (95% CI: 56.8 d). NB pts with high affinity FCGR alleles and an increase in ADCC (cut off 15%) had better PFS and OS rates ($p<0.03$; $p<0.005$), which supports NK-cell mediated ADCC as the mechanism of action.PK of ch14.18/CHO was analyzed in cycle 1: C_{max}=12.2±0.4 μg/ml, $t_{½}$=8.4±1.1 d, AUC=145.3± 5.8 μg*d/ml, Vd=9.3±0.5 L/m^2. A pro-inflammatory cytokine response (IL-2, IL-6, IL-8, IFNγ) translated into the expansion of effector NK- (3x) and T-cells (2x). We observed HACA in 17/97 pts (17.5%) of which only 9/97 (9.3%) were neutralizing with respect to the inhibition of CDC and WBT activity. In HACA negative patients, levels of ch14.18/CHO and functional parameters (CDC, WBT) analyzed before subsequent treatment cycles indicate persistent anti-NB activity for the entire treatment period.
Conclusion: High-risk relapsed/refractory NB patients respond to LTI of ch14.18/CHO.

PD-059

MOLECULAR PROFILING INCLUDING GENOMIC ABERRATIONS CAN REVEAL ULTRA HIGH-RISK GROUP IN THE JAPAN NEUROBLASTOMA STUDY GROUP'S CLINICAL TRIAL FOR HIGH-RISK NEUROBLASTOMA

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Background/Objectives: The Japan Neuroblastoma Study Group (JNBSG) prospectively enrolled patients with high-risk neuroblastoma according to the Children's Oncology Group risk group for a phase II clinical trial JN-H-07. The trial consisted of five courses of induction chemotherapy (vincristine, cyclophosphamide, cisplatin, pirarubicin and operation), followed by high-dose chemotherapy (melphalan, etoposide and carboplatin with autologous PBSCT) and radiation therapy.
Design/Methods: From March 2007 to February 2009, 50 patients were enrolled. Median age at diagnosis was 36 months (range: 13-174 months). Array comparative genomic hybridization (CGH) was used for genomic grouping in 45 patients.
Results: The five-year overall survival (OS) and progression-free survival (PFS) for 50 patients were 48.4 ±7.2% and 32.2 ±6.8%, respectively. The five-year PFS of patients with *MYCN* amplification (n=20) was 40.0 ±11.0%, while the PFS of *MYCN* non-amplified cases (n=30) was 26.7 ±8.4% (p=0.62). Thirty-nine tumors were in partial chromosomal gain/losses (GG-P), four were in whole chromosomal gain/losses (GG-W), and two were in silent with no obvious losses and gains except *MYCN* amplification (GG-S). The five-year PFS of GG-W (0.0 ±0.0%) was significantly poorer than that of GG-P (37.5 ±7.9%; P=0.018). In GG-P, 13 tumors were P1a (1p-loss, *MYCN* amplification) and 13 were P3s (11q-loss, *MYCN* single). The five-year PFS for P1a and P3s were 33.3 ±27.2% and 34.2 ±13.8%, respectively. Notably, the five-year PFS of P1s (1p-loss, *MYCN* single; n=4) was 0.0 ±0.0%, which was previously reported as having 71% of OS in all stages of neuroblastoma. Of 45 cases analyzed, the *ALK* gene was mutated in five cases whose PFS was 40.0 ±21.9 %, similar to 34.0 ±7.6% of non-mutated cases.
Conclusion: PFS of high-risk neuroblastoma according to the genomic classification has been improved in comparison with the previous report. Molecular profiling including genomic aberrations could reveal ultra high-risk neuroblastoma, which should be required further analysis by genomic sequencing.

PD-060

NATIONAL NEUROBLASTOMA NETWORK (NNN): A WAY FORWARD FOR NEUROBLASTOMA CARE IN INDIA

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Background/Objectives: In India, exact epidemiology and outcome of neuroblastoma (NB), is not known due to the lack of appropriate network and reporting system. National Neuroblastoma Network (NNN) has been formed to bridge this gap. The objectives of NNN are to study epidemiology, establish diagnostics, prepare uniform risk group stratification and to create uniform therapeutic protocols to improve outcomes of NB.
Design/Methods: In July 2014, NNN was formed amongst the members of Indian Pediatric Hematology Oncology group and started the fortnightly online meetings using the St. Jude hospital's website portal www.cure4kids.org. Participating centres are reporting data every month but final data analysis will be done on yearly basis.
Results: Over 7 months (July2014-Jan2015), NNN held 9 online and 2 physical meetings (attended by 64 members). Fourteen case based discussions were held covering histopathology, staging, role of N-myc, risk stratification and treatment. From 37 centres across 13 states, 120 new cases were reported (range 12-23/month). Sixteen centers provided details of 57cases. Male to female ratio was 1.28:1. Sixteen (28%) aged less than 18 months. *N-myc* could be done in 32/57 (56.14%) cases and it was amplified in 8/32. Twenty six (65%) had stage 4 disease with bone marrow involvement seen in 18/57. Risk stratification at presentation could be done in 53 children, 31 (58.49 %) were high risk, 13 intermediate and 9 were low risk. Further data is being collected and will be analysed at 1 year. Treatment protocols for low & intermediate risk NB have been finalized while those for high risk and relapsed NB are being prepared.
Conclusion: NNN has successfully linked 37 centres reporting data to a centralized registry. NB care is being improved across these centres by online tumor board meetings. As majority of cases are high risk so co-operative group like NNN is needed to improve outcomes.

PD-061

PROGNOSTIC SIGNIFICANCE OF COPY NUMBER VARIATIONS IN CHILDREN WITH NEUROBLASTOMA UNDER 18 MONTHS

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Background/Objectives: To investigate the copy number variations (CNVs) and determine their prognostic significance in neuroblastoma patients aged less than 18 months. The retrospective study has been conducted in Pediatric Oncology and Hematology Center, Regional Children's Hospital, Ekaterinburg, Russia.

Design/Methods: Among 103 children under 18 months (median of age 6 months) with primary neuroblastoma admitted to our clinic since April 1993 till November 2014 74(72%) were undergone CNV investigation by MLPA. All the investigated patients were treated according to NB90, NB97 and NB2004 protocols: 2(3%), 15(20%) and 57(77%) correspondingly.
Results: Patients' distribution by stage was as follow: stage I–18(24,3%); stage II–6(8,1%); stage III–22(29,7%); stage IV–15(20,3%); stage IVS–13(17,6%). In univariate analysis in the whole group of investigated children only stage IV of disease and MYCN-amplification had the prognostic significance. 15-years event free survival (EFS) in patients with stage IV was 29%±21% and overall survival (OS) was 65%±12% in comparison with other children: 82%±5% and 89%±4% (p=0,03) respectively. 8(10,8%) patients with MYCN-amplification had significantly worse prognosis: EFS did not exceed 25%±15% vs. 78%±7% and OS 37%±17% vs. 89%±4% (p<0,001). Among 66(89,2%) patients without MYCN amplification prognostic significance had following CNVs: 1p deletion and 2p23-24 gain. EFS in children with 1p deletion was 26%±20% vs. 89%±7% and OS 53%±17% vs. 96%±2% (p<0,01). In patients with 2p gain EFS was 31%±23% vs. 87%±4% and OS 62%±17% vs. 94%±3% (p=0,02). Multivariate analysis demonstrated only MYCN-amplification has prognostic significance in EFS and OS of whole group of patients: 6,74 (95%CI 2,355-19,291; p<0,001) and 9,084 (95%CI 2,618-31,521; p=0,001). Presence of 1p deletion had a significant negative influence on EFS: 4,409 (95%CI 0,993-19,565; p=0,05).
Conclusion: The results of this study demonstrate that MYCN-amplification and 1p deletion are significantly influencing on outcome in children with neuroblastoma under 18 months.

PD-062

MINIMAL BONE MARROW DISEASE IS FREQUENTLY DETECTED IN LOCALIZED NEUROBLASTOMA PATIENTS

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Background/Objectives: The clinical importance of minimal disease detection in bone marrow (BM) of localized neuroblastoma patients at diagnosis remains unclear. In this prospective multicenter study, BM samples at diagnosis of a large cohort, were studied using Real-time quantitative PCR (qPCR).
Design/Methods: In total 160 BM samples from localized patients were prospectively collected at Dutch and German centers between 2009 and 2013. qPCR was performed by using five neuroblastoma specific markers: PHOX2B, TH, DDC, GAP43 and CHRNA3. The association with other biological factors and the prognostic impact of BM positivity and clinical response were assessed.
Results: In 58 out of 160 patients neuroblastoma mRNA was detected in BM. In 47 of the 58 positive samples only one marker was found positive. BM positivity was significantly associated with MYCN amplification (p=0.02) and deletion of chromosome 1p (p=0.04). In total 31 patients had an event, of which only 5 patients had progression to stage 4. BM positivity was not associated with an unfavorable outcome. However, the detection of more than one marker was associated with an unfavorable outcome (systemic or local relapse) (EFS 48% vs 85%; p=0.03) in the whole cohort and in the observation group.
Conclusion: BM positivity was associated with unfavorable biological factors and might represent more aggressive tumors. Patients with qPCR positive BM should not be upstaged, because of very few systemic events in the cohort. However, for patients in the observation group with more than one marker positive a more careful follow-up might be required.

PD-063

CONFIRMATION OF THE INRG SURVIVAL TREE ANALYSIS BY A DIFFERENTLY COMPOSED REPRESENTATIVE NATIONAL COHORT OF PATIENTS

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Background/Objectives: In 2009 a new International Neuroblastoma Risk Group (INRG) classification system was introduced by Cohn et al. This system was based on a large international cohort. Our aim was to apply this classification system on a representative independent national cohort with respect to event free (EFS) and overall survival (OS).
Design/Methods: Data of 1,209 patients from the German trials NB97 and NB04, diagnosed between 01.01.2002 and 31.12.2010, age at diagnosis <21 years were compared with the published INRG data for the risk factors: INSS stage, histology, age at diagnosis (</≥12 and </≥18 months), LDH, ferritin, MYCN, 1p, 11q and 17q status. In addition, survival trees based on EFS and OS including these risk factors were calculated.
Results: Differences between distribution of the German and INRG cohort were not found for ferritin, age </≥ 12 months, 11q and MYCN status but for age </≥ 18 months (p=0.003), INSS stage (p<0.001), LDH (p=0.001), histology (p=0.017), 1p (p<0.001) and 17q status (p=0.026). Both survival trees assigned stage (localized, 4S vs. 4) as first node. As in the INRG tree, the branch of localized and 4S stage was split for EFS into unfavorable and favorable histology followed by MYCN status as third node which was second node for OS. Subgroup of stage 4 was separated into age <12 vs. ≥12 months for EFS and OS, while branching for EFS stopped here. For OS the younger group was divided according to MYCN (normal vs amplified) while the older group was divided according to LDH (</≥ 587 U/L).
Conclusion: Applying survival tree analysis on a differently distributed neuroblastoma cohort with diverse endpoints resulted in similar selection and ranking of risk factor as in the published INRG survival tree. Interestingly in our cohort, cutoff of 12 months instead of 18 months was chosen by the survival tree method.

Poster Discussion: New Drugs/Experimental Therapeutics

PD-064

SEARCHING FOR TARGETED TREATMENT FOR PEDIATRIC TUMORS BY DNA SEQUENCING

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Background/Objectives: Sequencing pediatric tumors in order to identify any druggable alteration in patients with incurable tumors with conventional therapy.
Design/Methods: A prospective study that includes pediatric patients with incurable o relapsed tumors, has been designed to search for druggable gene alterations since 2014. For targeted next generation sequencing analysis we used the PGM™-Ion Torrent Systems platform and a targeted gene panel assay, (Ion AmpliSeq™ Cancer Hotspot Panel v2). DNA was extracted from a formalin-fixed and paraffin-embedded tissue sample from patient's tumor and peripheral blood sample (normal control). When needed, other molecular techniques such as *in situ* hybridization, were used in order to characterize genetic alterations not covered by the targeted gene sequencing panel.
Results: We have studied to date 18 pediatric tumors either at relapse or at diagnosis when prognosis is dismal. Eleven patients had a brain tumor. We have made sequencing analysis with Ion-Torrent System in 12 patients. Also, we have applied other molecular studies. We have found druggable gene alterations in four patients, all of them with CNS tumors: two *V600E BRAF* mutations, one *PDGFRA* gene amplification and one mutation in *CDKN2A*. We have treated three patients with targeted therapy: Dabrafenib to *BRAF* mutation, Dasatinib to amplification of *PDGFRA* and Vorinostat with retinoic acid to *CDKN2A* mutation.
Conclusion: The pediatric tumors highlight the current molecular heterogeneity of cancer and prove the need for further understanding of molecular biology in order to identify any druggable alteration which can improve the clinical management of these patients, especially those affected by the most aggressive types. It is not about sequencing the whole tumor, but only about searching the mutations which have targeted therapy.The massive sequencing panels are initially oriented to adult tumors. Our goal is to redesign these studies to include all relevant alterations in pediatric tumors.

PD-065

TRABECTEDIN FOLLOWED BY IRINOTECAN CAN STABILIZE DISEASE IN ADVANCED TRANSLOCATION-POSITIVE SARCOMAS

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Background/Objectives: Preclinical data indicate that trabectedin followed by irinotecan has strong synergistic effects in Ewing sarcoma. This is presumably due to

hypersensitization of the tumor cells to the camptothecin as an effect of trabectedin. A strong synergistic effect was also reported in a human rhabdomyosarcoma xenograft. Twelve patients with end-stage, refractory translocation-positive sarcomas were treated with trabectedin followed by irinotecan within a compassionate use program.
Design/Methods: Twelve patients with refractory sarcomas, all heavily pretreated with chemotherapy were treated with trabectedin followed by irinotecan. Diagnosis was Ewing sarcoma in eight and soft tissue sarcoma in four patients.
Results: As of February 20, 2015, partial remission according to RECIST criteria was achieved in one patient, stable disease in five patients, progressive disease was seen in six patients. Median survival was 0.7 at three months after start of this therapy. In the majority of patients significant hematological toxicity (grade 3 and 4) was observed. Reversible liver toxicity and diarrhea also occurred. Only one patient suffered from dose limiting diarrhea and severe prolonged neutropenia, so that irinotecan had to be omitted in subsequent courses.
Conclusion: Our experience with the combination of trabectedin followed by irinotecan in patients with advanced sarcomas showed promising results in controlling refractory solid tumors. While the hematological toxicity was significant, it was reversible. Quality of life during therapy was maintained. These observations encourage a larger clinical trial.

PD-066

TROUGH LEVEL MONITORING OF INTRAVENOUS BUSULFAN TO ESTIMATE THE AREA UNDER THE PLASMA DRUG CONCENTRATION-TIME CURVE IN PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANT RECIPIENTS

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Background/Objectives: Optimizing systemic busulfan exposure, the area under the concentration-time curve (AUC), improves the outcomes for hematopoietic stem cell transplantation (HSCT). The AUC is conventionally calculated using six plasma concentrations ($AUC_{0-\infty}$) drawn after the first of 16 intravenous busulfan doses given as a two-hour infusion every six hours. The aim of this study was to develop limited sampling strategies (LSSs) using three or fewer busulfan concentrations with which to reliably calculate $AUC_{0-\infty}$ in children undergoing HSCT.
Design/Methods: Following the administration of a single dose of busulfan as a test dosing and the first dosing of busulfan for the conditioning regimen, blood samples were collected from each patient at six time-points (1, 2, 2.25, 2.5, 3 and 6 hours from the start of the infusion). The busulfan concentrations in the plasma were measured using high performance liquid chromatography. The busulfan $AUC_{0-\infty}$ was calculated according to the trapezoidal method using MOMENT program, employing all six of the available data points. LSSs using one, two, or three plasma busulfan concentrations were developed by multiple linear regression.
Results: Pharmacokinetics samples (total: 46 AUCs) were collected from all 29 patients. LSSs using one (C_6: busulfan plasma concentration six hours after the start of the infusion), two (C_2 and C_6), or three (C_2, C_3, and C_6) plasma busulfan concentrations were developed by multiple linear regression that showed excellent agreement with actual $AUC_{0-\infty}$. The $AUC_{0-\infty}$ predicted based on C_6 was significantly correlated with, and not statistically different from, actual values as follows: $AUC_{0-\infty} = 2556.5\ C_6 + 320.9$ ($r^2 = 0.929$, $P < 0.0001$, mean bias 0.282%, precision 7.91%). In contrast, the predicted AUCs derived from the other sampling single points did not meet the criteria.
Conclusion: In single-point sampling strategies, the $AUC_{0-\infty}$ predicted by the LSS (C_6) and $AUC_{0-\infty}$ using the six data points demonstrated excellent agreement.

PD-067

NOVEL CLINICAL TRIAL DESIGNS IN PAEDIATRIC CANCER: MULTI-ARM MULTI-STAGE (MAMS) DESIGNS

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Background/Objectives: Most children's cancers are rare and, with increased understanding of the underlying genetic features of many tumour types, increasing numbers of targeted therapies may become available and need to be evaluated reliably. There also remains a need to identify the optimal conventional therapies (e.g. chemotherapy, radiotherapy, surgery), given the frequent paucity of reliable evidence.
Design/Methods: Most randomised controlled trials (RCT) consist of two arms, while many single arm studies are also undertaken. Running a trial is a long process from concept to publication, including a substantial set up period. If several treatments are of interest, rather than just selecting one (possibly the wrong one) for evaluation against the standard, a MAMS design permits all of the treatments to be assessed, with insufficiently active treatments in terms of intermediate outcome being dropped after Phase II, with recruitment continuing to the remaining arms for Phase III evaluation. Furthermore, as novel agents or regimens of interest come along, they can be incorporated into the trial. This adaptive design is a much more efficient process than setting up separate trials to test each new agent, and being randomised and comparative avoids the biases on single-arm Phase II trials.
Results: MAMS trials are underway or planned in several tumour types, including: the rEECur trial for relapsed Ewing sarcoma, comparing four widely used chemotherapy regimens; a trial in relapsed rhabdomyosarcoma evaluating several novel agents added to a conventional chemotherapy backbone; a trial in newly diagnosed rhabdomyosarcoma comparing three novel regimens; a trial in neurofibromatosis-1 low grade glioma; the BEACON trial in neuroblastoma, which is being adapted to become a MAMS design by adding two new arms as the initial step.
Conclusion: The more widespread use of MAMS designs will enable the quicker identification of effective therapies, leading to improved outcomes for children with cancer.

Poster Discussion: Rare Tumours

PD-068

GORHAM-STOUT SYNDROME: A RARE DISEASE AND DIFFICULT TO TREAT

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Background/Objectives: Gorham-Stout syndrome is characterized by lymphatic vascular malformation leading to progressive osteolysis. Chylothorax is the most serious component. Because of the rarity there is limited treatment experience.
Design/Methods: Four patients diagnosed with Gorham-Stout syndrome in our department were evaluated regarding clinical findings and treatment experience.
Results: Patients were diagnosed median 9-year-old and were followed-up 17-113 months (median 56). All had extensive bone lesions. Three patients were presented with chylothorax and one with abdominal lymphangioma. Interferon was used as first-line in two patients, second-line in other two patients. Sirolimus was used with minimal response. Calcitonin was used in one, pamidronate and zoledronic acid was used in two patients for osteopenia and bone lesions. There was no response to propranolol. First patient had progression in bone lesions and chylothorax with interferon. Second-line treatment was started with bevacizumab. Chylothorax regressed but due to pathological fracture bevacizumab had to be stopped after 10 months. Sirolimus was 3-line treatment and she has stable disease with restrictive lung disease.Second patient had spleen cysts, abdominal macrocystic lymphangioma and bone lesions. After 3 months with interferon treatment new bone lesions occurred, sirolimus was given and she remained stable with sirolimus.Third patient with chylothorax and bone lesions received sirolimus as first-line treatment. Within 3 months chylothorax increased, treatment changed with interferon. He still has been receiving interferon with stable disease.The last patient had massive chylothorax and bone lesions. Chylothorax didnot respond sirolimus but decreased with interferon. She is off-therapy and has severe restrictive lung disease.
Conclusion: There is no standard treatment recommendation for Gorham-Stout syndrome. Interferon seems to have some benefit but sirolimus and propranolol showed no positive effect. Bevacizumab might help chylothorax but bone lesions might be worsen. Biphophonates might have some effect on bone lesions. Multicenter studies for prospective trials of treatment regimens should be undertaken.

PD-069

ENDEMIC KAPOSI SARCOMA IN HIV-NEGATIVE CHILDREN IN CENTRAL MALAWI: CLINICAL CHARACTERISTICS AND TREATMENT OUTCOMES

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Background/Objectives: Endemic Kaposi sarcoma (eKS) was first described in Africa well before the HIV-epidemic. However, the clinical characteristics and outcomes of children with eKS are not well described. We aimed to describe our experience with pediatric eKS.
Design/Methods: We retrospectively analyzed 10 HIV-negative children with eKS between 8/2010 – 6/2013 in Lilongwe, Malawi. Diagnosis was established clinically except in two patients who underwent confirmatory biopsies. HIV-serostatus was confirmed with rapid antibody test as well as DNA PCR methodology. Local 1st-line chemotherapy included bleomycin and vincristine.
Results: Median age was 11.7 years (2.0-16.3); one female & nine males. Common sites of presentation were: woody edema (70%), skin (60%), subcutaneous nodules (40%),

lymph node (40%), oral (10%). Utilizing our previously described pediatric KS staging classification, 2/10 were stage 2 (lymphadenopathic subtype), 6/10 were stage 3 (woody edema subtype), and 2/10 were stage 4 (based upon widespread involvement of the skin with > 20 skin lesions). None of the patients presented with visceral disease. Overall survival was 60% with a median follow-up of 24.5 months (range 20-34). Four patients died, with median time to death of 4 months (range 0.5-19). The two stage 2 patients achieved long-term CR, however one died in CR of another cause. Of the six stage 3 patients, 1 achieved long-term CR, 1 died of progressive KS at 19 months after multiple relapses, and 4 are alive with stable disease. Amongst the 4 with stable disease, 3 experienced relapse and required further chemotherapy to stabilize. The two stage 4 patients died < 2 months from KS diagnosis with refractory and progressive disease.
Conclusion: This case series demonstrates the high rate of woody edema subtype in HIV-negative children with eKS. Outcomes stratify according to the severity of clinical presentation, however long-term survival is possible with moderately-intense chemotherapy regimens.

PD-070

KAPOSI SARCOMA INFLAMMATORY CYTOKINE SYNDROME IN HIV-INFECTED CHILDREN IN CENTRAL MALAWI, A DISTINCT CLINICAL PRESENTATION CHARACTERIZED BY INTERLEUKIN-6 RELATED VIRAL PATHOPHYSIOLOGY

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Background/Objectives: The NIH first described Kaposi sarcoma (KS) inflammatory cytokine syndrome (KICS) in HIV-infected adults in 2010. Interleukin-6 (IL-6)-related pathophysiology is driven by human herpesvirus-8 (HHV-8). KICS has never been described in children or in Africa. We aimed to describe our pediatric KICS experience.
Design/Methods: We retrospectively analyzed 6 HIV-infected children diagnosed with KS between 8/2010 – 6/2013 in Lilongwe, Malawi that fit the clinical presentation characterized by KICS. Local 1st-line chemotherapy included bleomycin and vincristine (BV). HAART was prescribed according to national guidelines.
Results: Median age was 3.5 years (range 2.2–6.2); 3 females & 3 males. All 6 patients presented with the following constellation of clinical findings: (1) bulging lymphadenopathy, (2) persistent fevers, (3) massive hepatosplenomegaly, and (4) severe cytopenias. At diagnosis, median hemoglobin was 5.1 (range 4–6.2) and median platelet count was 13 (6–24). Additionally, 2 patients had KS skin lesions, 3 had subcutaneous nodules, and one had facial edema. Lymph node biopsy was obtained in one patient revealing KS histology without evidence of multicentric Castleman disease (spindle cell infiltrate with immunohistochemical stains positive for HHV-8 LANA and CD31, CD20-negative). Virologic testing was available for one patient and was characteristic of KICS, revealing HHV-8 viral load of 1.9×10^4 copies/10^6 cells, IL-6 level 450 pg/mL, and interleukin-10 level 320 pg/mL. Failure to BV was apparent, so prednisone was added to treat the systemic inflammatory syndrome. Cytopenias dramatically improved 2 weeks after starting prednisone with median platelets reaching 587 (range 148–789) without transfusion. Four patients achieved long-term complete remission with median follow-up of 35.5 months (range 24-50 months). Two patients died early due to complications of other opportunistic infections.
Conclusion: This case series demonstrates the distinct and severe clinical presentation of IL-6 related KICS in HIV+ children. Long-term cures can be achieved by adding prednisone to BV plus HAART.

PD-071

CHEST WALL EWING SARCOMA; A POPULATION BASED ANALYSIS

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Background/Objectives: The globally low incidence of pediatric chest wall Ewing sarcoma (CWES) has limited prior studies of this disease to mostly small, single institution reviews. Our objective was to assess incidence, demographics, treatment patterns, and long-term survival of this disease through a population based analysis.
Design/Methods: The Surveillance, Epidemiology, and End Results (SEER) database was used to identify patients aged 0-21 diagnosed with CWES from 1973-2011. Patients were grouped by decade to assess changes in treatment patterns and outcomes. The effects of clinical, demographic, and treatment variables on overall survival were assessed by the computation of Kaplan-Meier curves and the log-rank test, with Cox proportional hazard regression used for multivariate analysis.
Results: A total of 193 pediatric patients with histologically-confirmed CWES were identified. The disease was more common in males (60.6%), whites (92.2%), and 11-17 year-olds (48.7%). It was metastatic at presentation in 36.8% of patients. When grouped approximately by decade, 10-year overall survival improved progressively from 38.2% in 1973-1979 to 65.4% in 2000-2011 (p=0.033). The use of radiation decreased from 84.2% in the earliest time period to 40.0% in the most recent, while the proportion of patients receiving surgery increased from 75.0% to 84.9%. When controlling for covariates on multivariate analysis, male patients were found to have a higher mortality than female patients (HR: 2.4; CI: 1.4, 4.4; p=0.0028).
Conclusion: This population-based analysis of CWES demonstrated an impressive trend of improving overall survival, with increasing use of surgery and decreasing use of radiation therapy. As has been previously noted for Ewing sarcoma in general, our study demonstrated a gender difference in survival of CWES, with girls having a better prognosis.

PD-072

PAPILLIARY UROTHELIAL NEOPLASMS OF LOW MALIGNANT POTENTIAL IN CHILDREN AND YOUNG ADULTS.TREATMENT AND FOLLOW UP GUIDELINES

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Background/Objectives: To describe the Scottish experience of Papilliary Neoplasia of Low Malignant Potential (PUNLMPS) in Children and Young Adults and to produce treatment and follow up guidelines.
Design/Methods: A search of the Scottish Cancer Registry of the Information Services Division and a Systematic Review of the Literature.
Results: The Scottish data combined with a search of PUBMED, CINAHL and EMBASE using the terms Papilliary Neoplasia of Low Malignant Potential (PUNLMPS), child and young adult revealed 9 publications and 32 cases under the age of 20. All tumours were superficial and did not invade muscle. 2 studies confirmed the rarity of genetic aberrations in these tumours in children and young adults under the age of 20.
Conclusion: PUNLMP was introduced to describe the histology of urothelial neoplasms of low biological risk of progression in 2004. PUNLMPS are increasingly recognised in children and young adults. The diagnosis of PUNLMP is subject to significant controversy and registry data may under estimate true incidence. Although locally aggressive they do not metastasise. A malignant cancer diagnosis with attendant psychological burdens can be avoided. Staging for spread is unnecessary making painful procedures such as bone marrow trephines redundant. Exposure to ionising radiation is similarly not needed. PUNLMPS should be completely excised. Overall survival is excellent (100%) but close follow up with ultrasound is necessary to guard against recurrence. Routine, frequent cystoscopy should be avoided to prevent trauma to the growing urethra.

PD-073

LIPOBLASTOMA: AN HETEROGENOUS ENTITY

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Background/Objectives: Background: Lipoblastomas (LB) are rare benign tumors of embryonic fat, mostly found in extremities of children before age three. They represent less than 1% of neoplasms, but 30% of adipocitic tumors in children. *Objective*: To present our experience treating pediatric patients with LB at a single center. We describe clinical and epidemiological factors, as well as follow up.
Design/Methods: Pediatric patients with histologic confirmation of LB were evaluated between 2004 and 2014. Age, sex, history, clinical findings, primary site, surgical procedure, pathology reports and outcomes were evaluated.
Results: There were nine boys and three girls, with ages ranging from 4 to 38 months (median age of 13 months). Time to diagnosis ranged from three days to 21 months. Most common primary sites were head and neck (5 patients) and trunk (5 patients), followed by extremities and scrotal (1 patient each). Preoperative evaluation included USG in six, CT scan in seven, and MRI in four patients. All presented with increased volume. Fourteen resections were performed. Tumor size ranged from 3.5 to 18 cm. All lesions were completely resected, with histologic confirmation. There was one local

recurrence.Surgical time ranged from one to four hours. Blood loss was minimal. Average hospital length of stay was 1.5 days.There were no surgical complications and no perioperative mortality. Follow up from one month to 7 years.
Conclusion: LB are rare, benign tumors of embryonic fat, affecting children under three years of age. There is a marked male preponderance. Initial diagnosis is seldomly suspected by the primary care physician. MRI is the study of choice for extremity and paraspinal tumors. CT scan is optimal for head and neck, and retroperitoneal lesions. Our study differs from previous reports, since we found larger lesions, with most tumors in the head and neck. Interestingly, recurrence occurred only in one girl.

PD-074

EBSTEIN-BARR VIRUS ASSOCIATED SMOOTH MUSCLE TUMOURS IN CHILDREN WITH AIDS AT CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL

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Background/Objectives: Despite the AIDS epidemic that has ravaged the South African population EBV-associated smooth muscle tumours have remained rare. These tumours are associated with severe immune suppression and were previously diagnosed as myofibroma. The objective was to review patients with biopsy proven disease.
Design/Methods: The study was initiated from pathology and the children were traced from their biopsy records. Our paediatric oncology unit's patient files were also reviewed from 2003 to 2014 for any additional cases. Six cases were found in total and the data extracted. Ethical consent for retrospective data collection was obtained.
Results: A strong female predominance (6/0) was noted, the age range at presentation was 10 to 15 years, with a mean of 12 years 9 months. Symptoms featured pain predominantly - abdominal or back, 3 patients had spinal compression, 1 a paraspinal mass, 1 gallbladder involvement, 1 an eye mass (iris). Prior treatment for suspected TB contributed to delay with diagnosis. The CD 4 count varied from 3 to 1331, 5 patients were virally suppressed, 1 was in virological failure. Tumour site was single (2) patients -spinal (1), eye(1); multiple (4) patients, spinal(3), adrenal(2), ribs(1) and 1 had an unproven basal ganglia lesion.Therapy included surgery (3), radiation(3), chemotherapy (1), and palliation(4). Survival ranged from 5 months to 109 months. One patient died of AIDS related sepsis, one is lost to follow up, 4 are alive, but 1 is deteriorating, weight 13kg at 13years.
Conclusion: EBV-associated tumours may have a prolonged survival but AIDS related comorbidities contribute to mortality. A spinal lesion presentation was most frequently found.

PD-075

A PERSONALIZED, MOLECULAR-BASED APPROACH TO THE TREATMENT OF RARE, RECURRENT, OR REFRACTORY PEDIATRIC AND ADOLESCENT CANCERS

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Background/Objectives: Many pediatric patients with cancer are cured of their disease, yet there is a subset of patients for whom therapy is unsuccessful. The primary goals of our research program are to collect tumor and germline specimens from patients with rare, recurrent, or refractory cancer and to perform whole genome sequencing (WGS) on both tumor and germline samples and mRNA sequencing on the tumor sample. Sequencing data is used to characterize the molecular signature of the cancers, to assess how the disease may have circumvented therapy, and to identify ways in which the cancer may be treated.
Design/Methods: Sequencing data is analyzed in independent bioinformatics pipelines to maximize validity of results. Genomic variation, identified by WGS, is integrated with gene expression information from mRNA sequencing, to develop a molecular profile of each tumor. The process culminates with a multidisciplinary team meeting where results are interpreted and a clinical action plan is developed.
Results: Through the end of 2014, 314 potential participants have been identified. Of those, 224 participants and/or families provided consent; 83 had suspect recurrent or refractory disease and 141 had a suspect new diagnosis. WGS of the tumor and normal genomes has been undertaken for 70 patients; of the patients for whom sequencing has been performed, 11 cases are from patients newly diagnosed with cancer. Whole genome data has been obtained from the following: brain tumors (n=11), acute leukemias (n=16), sarcomas (n=14), lymphomas (n=4), ganglio/neuroblastomas (n=4), mixed germ cell tumors (n=3), and carcinomas (n=3). The remaining data include that obtained from one each of hemophagocytic lymphohistiocytosis (HLH), hepatoblastoma, melanoma, myelodysplastic syndrome (MDS), and Wilms tumor.
Conclusion: Our experience has demonstrated the feasibility and effectiveness of clinical sequencing in pediatric and adolescent oncology and has yielded results that have informed treatment choices as well as refined diagnoses.

Poster Discussion: Renal Tumours

PD-076

LATE EFFECTS IN CHILDREN TREATED FOR WILMS TUMOR AT A SINGLE CENTER IN BRAZIL

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Background/Objectives: Over 80% of patients with Wilms tumor (WT) can be cured from their disease, most of them with minimal late effects; nonetheless, patients with advance stage tumor, unfavorable histology or disease relapse are at increased risk of long-term complications. *Objectives*: to assess renal dysfunction, cardiomyopathy, musculoskeletal deformities, puberal problems, infertility and second neoplasm in WT survivors.
Design/Methods: From 1991 to 2001, 204 patients with WT were registered and 126 were eligible for the study: 70 from group 1 (patients treated from 1991 to 2001, on the Brazilian Cooperative Group protocol - GCBTTW) and 56 from group 2 (treated from 2002 to 2011, on SIOP protocol). We reviewed the medical charts, performed a full physical exam (vital signs, anthropometric measurements, body composition, puberal development and musculoskeletal deformities), and assessed renal and cardiac function.
Results: Initial treatment was different between the two groups: GCBTTW indicated initial surgery and SIOP preoperative chemotherapy. Intraoperative tumor rupture, abdominal radiation and use of doxorubicin were more common in group 1. Seventy-nine patients underwent a complete evaluation: 32 from group 1 and 47 from group 2. No differences between the groups were noted regarding weight and BMI z-scores, abdominal fat, musculoskeletal deformities, pubertal development, cardiomyopathy or renal dysfunction. Group 1 patients had shorter standing height and sitting height than group 2. Radiation affected the growth in both groups; however, this effect was statistically worse in group 1 patients, who had already reached their final height. Hypertension (29.1%) was the most common late effect, followed by reduction of the glomerular filtration rate (26.6%), musculoskeletal deformities (24.1%), cardiac (21.9%) and pubertal abnormalities (2.5%).
Conclusion: At least one late effect was found in 63.3% patients; 39.2% presented only one complication; 20.3% two and 3.8% three. Despite high cure rates, long-term follow-up is required in survivors of WT.

PD-077

REDUCED USE OF RADIOTHERAPY IN THE MANAGEMENT OF METASTATIC WILMS TUMOR

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Background/Objectives: It is recognized that lung radiation can be avoided successfully in the management of metastatic Wilms tumor(WT). We report our experience in treating stage IV WT at our institution.
Design/Methods: We conducted a retrospective analysis of children (<18years) with stage IV WT who presented from July 2006 until December 2014. Patients' characteristics, treatment modalities and outcome were analyzed. All cases were discussed in multidisciplinary clinic that included pediatric oncologists, radiologists, pediatric surgeons and radiation oncologists. According to our local protocol, radiotherapy (RT) was decided based on radiologic response after 5-6weeks of initiating chemotherapy.
Results: We identified 21 patients (9males) who presented with stage IV WT. The median age at diagnosis was 4.3years (range1.7to11.3). Fifteen patients (71%) had locally stage III disease, 2 stage I, one stage II, and three had bilateral disease. Lung only metastasis was present in 19 patients (90%); the other three had metastasis to: ovary in one patient, lung and skin in the second, and lung and liver in the third. Four patients were treated according to SIOP protocol while the rest were treated according to NWTS5. Upfront

nephrectomy done only in three patients. Preoperative tumor rupture detected in four patients; all of them received whole abdomen RT. Ten patients had complete response in lung metastasis after 5-6weeks of chemotherapy and didn't receive lung RT; the other ten had partial response and were given whole lung RT. The estimated 5-yearEFS and OS were 83%±8.9% and 89%+/-11%, respectively. Although not statistically significant, there were less percentage of patients irradiated among those diagnosed after 2010(42%vs.56%) and those treated with SIOP protocol (25%vs.53%).
Conclusion: Patients with metastatic WT had excellent outcome despite omitting radiotherapy in half of our patients. Use of radiotherapy decreased over time, possibly related to our team experience with response assessment. It might be decreased further with judicious use of metastectomy to accurately assess response.

PD-078

CENTRAL RADIOLOGY REVIEW FOR WILMS TUMOUR (WT) PATIENTS REGISTERED IN THE UK IMPORT STUDY: A CHALLENGING BUT USEFUL PROCESS

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Background/Objectives: Central Pathology Review introduced in the SIOP WT 2001 trial proved successful with rapid review allowing clinicians to modify treatment when discrepancies were found. In the UK, Improving Outcome for Renal Tumours of Childhood (IMPORT) study, started in 2012, Central Radiology Review (CRR) was initiated with the ultimate goal to improve the definition of metastatic and bilateral disease through standardisation of radiological techniques, and promote use of MRI.
Design/Methods: Images (CT and/or MRI scans) from diagnosis and preoperative assessment are requested on all patients registered and a proforma'd report compiled for each case reviewed. We report herein the first experience of CRR in WT in the UK.
Results: From September 2012 to March 2015, 192 patients were registered in the IMPORT study from 21 centres. A hundred and twenty-two patients (63%) have had imaging submitted for radiology review. Eighty-Nine patients (46%) had both diagnostic and pre-operative images submitted, 32 patients (17%) only at diagnosis and a single neonatal case had ultrasound alone. Diagnosis of lung nodules was done on 113 chest CT and 5 X-Ray. Abdominal assessment was performed on 41 CT and 83 MRI at diagnosis, four patients having had both. Discrepancies in the reporting of possible lung metastases and bilateral lesions have been found in 12% of the patients considered as metastatic or having CT only nodules and 3.5% of the patients considered to have bilateral disease by either local or review radiologist. Only 4 patients had insufficient imaging for formal assessment.
Conclusion: CRR has been shown feasible and useful when complete imaging sets were received to influence clinical decision-making process. The next step will be to implement 'real-time' feedback review as an integrated report combining radiology and oncology contextual review.

PD-079

EFFECTS OF PROVIDING FINANCIAL SUPPORT TO PATIENTS WITH WILMS TUMOR IN KENYA ON ABANDONMENT AND SURVIVAL RATES

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Background/Objectives: Survival from Wilms tumor (WT) in Kenya is a dismal 36% due to on-therapy mortality and a 25% treatment abandonment rate. Parents who answered multi-center surveys and tracing calls confirmed financial constraints as a barrier to treatment completion. We therefore aimed to study the impact of financial support on treatment abandonment and survival rates.
Design/Methods: In this prospective cohort study, we planned for all patients newly diagnosed with WT at 4 collaborating Kenyan hospitals between 2012-2013 to be offered $500 U.S. dollars toward their treatment in exchange for paraffin blocks of their tumors at the time of resection. Patient visits and treatments were recorded in the Kenyan WT registry and patients were called by our research nurse if they abandoned therapy.
Results: Twenty-four patients were enrolled on this study, but due to poor documentation, 1 was excluded from analysis. Ten patients abandoned treatment with curative intent (43.5%). Nine patients died while on-therapy (39.1%) and 4 patients remained alive and adherent to treatment (17.4%). Of the patients who abandoned treatment, 10% abandoned prior to post-operative chemotherapy, 60% abandoned during post-operative chemotherapy and 30% abandoned prior to radiation therapy. Fifty percent of patients who abandoned care were confirmed alive, giving a known survival rate of 39.1% at 18 months after the last patient was consented. While abandonment occurred slightly later than in our previous study, it actually occurred at a higher frequency. This intervention therefore failed to reduce treatment abandonment or increase survival.
Conclusion: Survival remains dismal despite provision of funding. Hospital administrative issues with releasing funds were problematic at one site. Tracing calls made to patients from all sites revealed continued financial barriers and parental beliefs that the children were healthy and no longer needed therapy as the reasons for abandonment. Financial provision without improved infrastructure and education is insufficient to reduce treatment abandonment.

PD-080

LONG TERM FOLLOW-UP IN CHILDREN UNDERGOING NEPHRON SPARING SURGERY FOR NON-SYNDROMIC UNILATERAL WILMS TUMOR

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Background/Objectives: Wilms tumor (WT) represents approximately six to seven percent of all pediatric cancers and accounts for more than 95 percent of all tumors of the kidney in the pediatric age group. Recently some centers have explored the role of nephron sparing procedures in children with unilateral Wilms tumors because of the concern about late occurrence of renal dysfunction after unilateral nephrectomy. We assessed the long term renal functional outcome after parenchymal-sparing procedure for non-syndromic unilateral Wilms tumor at our center.
Design/Methods: We retrospectively reviewed the records of all children with unilateral Wilms tumor who had undergone nephron sparing surgery at our center. Patient's long-term renal function, tumor recurrence, and survival, were determined from a review of each patient's medical record.
Results: A total of eight patients underwent partial nephrectomy (PN) and the remaining three with polar tumors underwent hemi-nephrectomy (HN) following chemotherapy. Smaller tumor volumes were associated with not only preservation of renal function but also increase in eGFR during the follow-up period. The median preoperative eGFR was 106 and median eGFR at the last follow-up was 131.0.
Conclusion: In properly selected children with non-syndromic unilateral Wilms tumor, nephron sparing surgery provides excellent renal function preservation.

PD-081

ABANDONMENT OF TREATMENT AT BASELINE IN THE COLLABORATIVE WILMS TUMOUR AFRICA PROJECT

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Background/Objectives: Incomplete treatment (often called abandonment of treatment) is a major cause of treatment failure in low-income countries. Poverty, direct cost of treatment and associated costs for the family play a major role. A consensus adapted Wilms tumour treatment guideline is implemented in 8 centres in sub-Saharan Africa. The treatment guideline includes strategies to prevent incomplete treatment. We performed a baseline evaluation of the situation before the start of the project to help decide on priorities to improve outcome and to assess improvements over time.
Design/Methods: A retrospective chart review was performed of patients admitted with Wilms tumour in the three years (2011-2013) preceding the collaborative project. The percentage of patients who did not start or complete their treatment was documented. We interviewed representatives from the participating institutions about costs of medical treatment, health insurance, government and external support and remaining treatment costs for the parents. Availability of money for travel to the hospital and accommodation and food during the stay in the hospital was documented as was the availability of adequate counseling.
Results: Average rate of incomplete treatment was 31% (54/176) ranging from 14% (8/59) to 48% (26/54). All centres have strategies in place to prevent incomplete treatment but lack the funds to completely cover the costs for parents. The remaining

costs of treatment for the parents range from around US$ 100 in Malawi to US$ 1100 in Ghana. Some centres pay for travel and provide food during the hospital stay.
Conclusion: Incomplete treatment is the most common cause of treatment failure and this is preventable. We aim to reduce incomplete treatment to less than 10%. Our strategy includes funding of medical treatment and associated costs, adequate counseling and careful documentation of contact details to enable active follow up.

Poster Discussion: Retinoblastoma

PD-082

IMPROVEMENT IN THE MANAGEMENT AND OUTCOME OF RETINOBLASTOMA AT CHILDREN CANCER HOSPITAL, KARACHI, PAKISTAN AFTER INITIATION OF A MULTIDISCIPLINARY TEAM

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Background/Objectives: To analyze data of children with Retinoblastoma treated after initiation of a multidisciplinary team of ophthalmologist, oncologist, radiotherapist, psychologist, social worker ocularist and compare it with the historical control.
Design/Methods: Before initiation of a multidisciplinary team the outcome of Retinoblastoma at our institution had been dismal with abandonment rate up to 50%, poor eye salvage, lack of rehabilitation and a dismal overall survival (including abandonment) of 25%. In July 2012 collaboration began between pediatric oncology and ophthalmology departments of two hospitals in Karachi to develop a multidisciplinary Retinoblastoma team. Retinoblastoma treatment guidelines were finalized. All new cases were discussed in monthly tumor board. Data were prospectively collected. Implants were put at the time of enucleation and prosthesis were put after the completion of treatment. The documentation of staging, protocol compliance, enucleation, adverse histopathology factors, eye salvage, abandonment, placement of implant and prosthesis, screening of siblings and follow up visits were analyzed and compared with the historical control.
Results: Abandonment rate has reduced from 53% to 33%. More parents agreed for upfront enucleation. The documentation of staging in diseased eye has improved from 75% to 94%. More children are treated according to the protocol guideline. Histopathology is now reported as per guideline. Overall survival (including abandonment) has increased from 23% in historical data to 48% in this study. Previously less than 10% children were getting implant and prosthesis and there was no screening of younger siblings. Now almost all children have implant at the time of enucleation and more than 80% have eye prosthesis. Screening of siblings is offered to all families.
Conclusion: After initiation of multidisciplinary team there has been significant improvement in treatment, outcome and rehabilitation of children with Retinoblastoma.

PD-083

SUPERSELECTIVE OPTHALMIC ARTERY CHEMOINFUSION (SOAC) FOR INTRAOCULAR RETINOBLASTOMA: AN EFFECTIVE STRATEGY FOR GLOBE SALVAGE AND PREVENTION OF TREATMENT ABANDONMENT IN LOW AND MIDDLE INCOME COUNTRIES (LMIC)?

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Background/Objectives: Retinoblastoma(RB) continues to pose challenges in LMIC. Unlike the developed world where cure rates are over 95%, outcomes in LMIC are suboptimal due to delayed diagnosis and advanced disease. Additionally, a significant factor for poor outcomes is therapy abandonment, reported to be upto 20% in Indian subcontinent-primarily due to sociocultural non-acceptability of enucleation. Hence it is only imperative that strategies for globe salvage without compromising survival would have a beneficial impact in the overall outcomes of this highly curable disease. We evaluated the role of SOAC for intraocular retinoblastoma in this context.
Design/Methods: This is a retrospective analysis of children with Group B-E retinoblastoma who underwent SOAC between Jan'2013 to Dec'2014. All children underwent standard baseline diagnostic and staging evaluation. Children with extraocular disease, optic nerve involvement or metastatic disease were excluded. Melphalan and Carboplatin were the drugs administered in age dependent doses.
Results: A total of 63 sessions of SOAC were performed on 21 eyes of 19 children. The procedure was successful 92.06%. Favourable response (CR/PR) with resultant globe salvage was seen in 17 eyes giving a globe salvage rate of 80.95% at median follow up of 11.7 months (1-22). 3/21 eyes ultimately needed enucleation and one eye underwent EBRT due to inadequate response. 92% of treatment naïve eyes were salvaged and in 62.5% of previously treated eyes enucleation was avoided. Eye salvage rates were 100% in sporadic retinoblastoma and 42% in familial retinoblastomas. Treatment abandonment rate reduced from 26% (2010) to 2.6% (2014). Complications were minimal (<10%) and included lid edema, opthalmic artery spasm and conjunctival chemosis. Grade III neutropenia was seen in 5% of the procedures performed. The results were comparable with Western published literature.
Conclusion: SOAC is a feasible and successful strategy for globe salvage in LMICs. It is a powerful tool in the strategy to prevent treatment refusal and abandonment.

PD-084

INTRA-ARTERIAL CHEMOTHERAPY (IAC) AND/OR INTRA-VITREAL CHEMOTHERAPY (IVC) AS AN ALTERNATIVE TO AVOID ENUCLEATION IN INTRA-OCULAR RETINOBLASTOMA (RB) PATIENTS

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Background/Objectives: To evaluate efficacy and safety of IAC and IVC as first-line or salvage therapy to patients with locally advanced RB.
Design/Methods: Retrospective observational cohort study with review of charts of RB patients from 01/2012 to 12/2014. One to five cycles every three weeks of IAC with melphalan for newly diagnosed patients or melphalan and topotecan for salvage treatment ; with carboplatin to all patients with no response or progression after 2 drugs. Addition of local therapy was indicated between IAC procedures. IVC was performed for all patients with vitreous seeds after IAC. Primary outcome was defined as rate of enucleating after IAC and IVC. Secondary outcome was defined as objective response of therapy by Retcam every one cycle of IAC/IVC. The safety was defined as number of moderate to adverse events (grades 2 to 4).
Results: There were enrolled 33 patients (37 eyes), median age at diagnosis was 8,8 months (1 month to 3,5 years), 43% as salvage therapy and 57% as first-line therapy. According to international classification was : 3% group B, 19% C, 67% D, 11% E. 18 were bilateral, four patients received IAC to both eyes. Median of cycles was 2 (1-5) and drugs were 2 (1-3). 30 eyes were preserved and 7 eyes were enucleated, 3 received as first-line and 4 as salvage. 24% had no response to IAC. Seven patients with vitreous seeds received IVC, with no response in 1 eye. Six (18%) patients had ocular adverse events, (grade 3 and 4) Neither haematologic event nor metastasis occurred.
Conclusion: IAC and IVC as first-line and salvage treatment were feasible and well tolerated with high rate of response and preservation of eye (30/37). IAC and IVC can be included in multimodal treatment strategy for RB patients.

PD-085

SMALL BLUE ROUND CELLS TUMORS AFTER HEREDITARY RETINOBLASTOMA : LATE METASTATIC RELAPSE OR SECONDARY TUMOR?

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Background/Objectives: Long-term survivors of hereditary retinoblastoma (Rb) are at an increased risk of developing and dying from a subsequent non-ocular cancer. Among these late occurring secondary tumors, we observed rare cases of small blue round cells tumors (SBRCTs), raising the issue of late metastatic relapse versus secondary tumors.
Design/Methods: From 1981 to 2014, we identified 8 children carrying a *RB1* constitutional mutation and/or bilateral and/or familial Rb who developed a secondary extra-CNS (Central Nervous System) tumor, labeled as SBRCT. 7/8 SBRCTs were localized; 7 developed in bones and one in the ovary. Clinical, pathological, radiological and genetic features of these 8 SBRCTs were centrally reviewed.
Results: The median age at SBRCT diagnosis was 12.8 years (y) [5.8-25.6] ; the median time between last Rb treatment and SBRCT diagnosis was 11.5y [3.1-20.3]. The analysis of pathological and radiological features could not discriminate between true secondary SRBCT and late Rb metastatic relapse. The comparison between *RB1* mutations in Rb and matched SBRCT in 3/8 patients showed that i) the normal *RB1* allele was constantly lost, confirming that SBRCT development was due to the predisposition context, and ii) the second *RB1* hit in SBRCT and matched Rb were different, thus proving that the former tumor was not derivative from the latter. Similarly, when available (in 2/8 cases), the comparison of aCGH profiles from Rb and matched SBRCT were strikingly different.
Conclusion: Our results argue in favor of SBRCT not being late Rb metastases, but rather secondary undescribed tumors, linked to the RB predisposition syndrome. Further analyses, such as transcriptome profilings and exome sequencings are ongoing to better characterize this emerging type of SBRCTs.

PD-086

SECOND PRIMARY MALIGNANCIES IN CHILDREN AND ADOLESCENTS AFTER RETINOBLASTOMA TREATMENT

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Background/Objectives: Children with retinoblastoma carry a high risk to develop second primary malignancies already in childhood and adolescence. This study characterizes the type of pediatric second primary malignancies after retinoblastoma treatment and investigates the impact of different treatment strategies and genetic predisposition.
Design/Methods: All national patients treated for retinoblastoma at the German reference center with a current age of 6-27 years were invited to participate in a study to characterize late effects.
Results: Data on pediatric second primary malignancies were recorded from 488 patients. Ten developed a malignancy before the age of 18 years. For children heterozygous for oncogenic variants of *RB1* in germline, the cumulative incidence to develop a second malignancy at the age of 10 years was 5.2 +/-1.8%. This results in an elevated risk for sarcoma (SIR 147.98; 95% confidence interval: 39.81-378.87) and leukemia (SIR 41.38, 11.13-105.95). The type of *RB1* mutation or its origin showed no significant impact. Previous radiotherapy increased the risk. Three of 91 children with chemotherapy or combined radio- and chemotherapy developed acute leukemia. Treatment modality influenced incidence, latency and type of malignancy, but 2 children with heterozygous *RB1* germline mutation developed a second primary malignancy without previous chemotherapy or external beam radiotherapy.
Conclusion: Screening for second primary malignancy is a critical part of pediatric oncological follow-up in patients with *RB1* germline mutation. Especially for patients with sporadic unilateral retinoblastoma, genetic information is important for treatment decisions and allows tailoring of follow-up schedules.The *Deutsche Kinderkrebsstiftung* financed this study.

Poster Discussion: Soft Tissue Sarcomas

PD-087

TUMOR EXPRESSION OF SURVIVIN, P53, CYCLIN D1 AND OSTEOPONTIN PREDICTS RESPONSE TO CHEMOTHERAPY IN CHILDREN WITH MPNST

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Background/Objectives: A number of altered cell cycle regulators and extracellular matrix glycoproteins have been recently found involved in the development, proliferation and progression of adult sarcomas. Their roles in pediatric malignant peripheral nerve sheath tumours (MPNST) have not been investigated. The aim of the study was to determine whether the tumor expression of survivin, p53, cyclin D1, fibronectin (FN) and osteopontin (OPN) at diagnosis, correlate with the response to neoadjuvant CHT in children with MPNST.
Design/Methods: Twenty six children (14M/12F; median age: 130 months), diagnosed with MPNST and treated with CWS protocols between 1992 and 2013 in Poland were included. Response to CHT was assessed after 3 cycles and defined as good (tumor reduction ≥33% <100%) and poor (tumor reduction <33% or progression). Immunohistochemical expression of analyzed markers was assessed on tissue microarrays and determined as negative or positive based on semiquantitative criteria.
Results: Response to neoadjuvant CHT was assessable in 21 patients, of whom ten (48%) achieved good response and 11 - poor response. It was significantly worse in NF1 patients.Survivin was expressed in 16/21 (76%) patients, OPN in 14 (67%), cyclin D1 in 11 (52%) and p53 in 11. Expression of p53, survivin and OPN was significantly more frequent in poor responders than in good responders (p=0.00892, p=0.0124, p=0.0183 respectively). The correlation for cyclin D1 was borderline and FN not significant. Most of good responders (8/10) expressed maximum of two markers and only one patient expressed all 4 markers. The majority of poor responders (9/11) expressed at least 3 markers and none of them had all markers negative.
Conclusion: It is suggested that survivin, p53, cyclin D and OPN are important in the biology of MPNST and their tissue expression may help to identify patients prone to benefit from neoadjuvant CHT.

PD-088

KAPOSI'S SARCOMA IN CHILDREN IN CAMEROON BEFORE AND DURING THE HIV EPIDEMIC

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Background: Kaposi's sarcoma was endemic in Cameroon before the AIDS epidemic, involving lymph node, with poor prognosis. With the onset of AIDS increased frequency of Kaposi sarcoma (KS) has been reported. However, studies in sub Saharan Africa are scarce.
Patients and methods: This retrospective study included 78 cases of children with Kaposi sarcoma observed in Cameroon within a period of 25 years. The study analyzed the demographics, clinical presentation, laboratory investigations, treatment and prognosis.
Results: The demographic results showed 50 males and 28 females. The mean age is 5,9 years. Lymph node is the most common site of involvement and the diagnosis of early cases is not easy. Skin lesions are found amongst 20% of the children.4 children in this seies had eyes involvement. HIV serology was performed only in 50 % of the cases as the parents usually refuse testing. Out of 50% of performed tests, 20% of the children are HIV positive. The treatment for KS included chemotherapy and was based on Cyclophosphamide, anthracycline and prednisone. The chemotherapy was associated with HAART when the child is HIV positive. The prognosis of HIV negative children after treatment is better than in HIV positive children.
Conclusion: Children with Kaposi sarcoma in Cameroon is a common finding before and during AIDS epidemic.

PD-089

PEDIATRIC RHABDOMYOSARCOMA; CLINICOPATHOLOGICAL FEATURES AND OUTCOME; A SINGLE INSTITUTION EXPERIENCE IN PAKISTAN

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Background/Objectives: To study clinico-pathological characteristics, and outcome of Rhabdomyosarcoma in a tertiary care hospital in Pakistan.
Design/Methods: A retrospective chart review of children less than 18 years with initial diagnosis of Rhabdomyosarcoma from 1998 till 2014. Most were treated with IRS protocol, some received alternating courses of CVD (Cyclophosphamide, Vincristine, Doxorubicin,) and IE (Ifosphamide, Etoposide). Local control (surgery and radiotherapy) was based on protocol guideline. Demography, clinical presentation, primary site, histopathology, stage, treatment received and outcome were analyzed.
Results: Total 155 children included with male to female ration of 1.5: 1. Median age was 5 years (range 0.3 -18 years). Swelling and pain in the local site were the most common clinical presentation. Head and neck (41%) was the most common primary site followed by extremities (20%) genitourinary (13%), orbital (9%) and abdomen and pelvis 7% each. Majority children presented with advanced stage disease (61% stage III and 11% stage IV). Embryonal histology was the most common type. 43% children received radiation to local site. 53/155 (35%) abandoned treatment,15/155(10%) were given palliative treatment, 83/155 (55%) complied with protocol treatment. 18/155 (12%) died due to toxicity 20/155 (13%) due to disease progression and relapses. Overall survival with and without abandonment is 30% and 54%. Because second treatment were not offered there was no difference between event free (EFS) and overall survival (OS).
Conclusion: The outcome of rhabdomyosarcoma in our study is suboptimal. High rate of abandonment, toxicity death and advanced disease at presentation are major adverse factors.

PD-090

NEOADJUVANT ALTERNATING INTRAARTERIAL AND SYSTEMIC CHEMOTHERAPY FOR TREATMENT OF ADVANCED MALIGNANT ABDOMINAL AND PELVIC TUMORS IN CHILDREN

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Background/Objectives: We present our experience of neoadjuvant alternating intra-arterial and intravenous chemotherapy for the treatment of advanced malignant abdominal and pelvic tumors in children.
Design/Methods: From 1999 to 2012, twenty-two patients aged 5 months to 14 years with advanced malignant abdominal or pelvic tumors (not including hepatic and renal tumors) received neoadjuvant alternating intra-arterial infusion chemotherapy and systemic chemotherapy. There were rhabdomyosarcoma of urinary bladder in 5 cases, ovarian yolk sac tumor in 5 cases, sacrococcygeal malignant germ cell tumor in 4 cases, vaginal rhabdomyosarcoma in 3 cases, vaginal endodermal sinus tumor in 1 case, endodermal sinus tumor of omentum in 1 case, pelvic rhabdomyosarcoma in 1 case, pancreatoblastoma originating from mesentery in 1 case, and abdominal promoting proliferation connective tissue tumor in 1 case.The selected artery for intra-arterial infusion chemotherapy were bilateral iliac arteries for pelvic tumors and superior mesenteric artery for abdominal tumors. The drugs were cisplatin 80 mg/m^2, pirarubicin 40 mg/m^2, and vindesine 3 mg/m^2. Intravenous chemotherapy using vindesine, ifosfamide and etoposide administered 3 weeks after arterial chemotherapy. Alternating arterial and intravenous chemotherapy with a 3-week interval repeated each 1 to 3 courses before operation. After operation the patients underwent intravenous chemotherapy or radiotherapy.
Results: The most common side effects after alternating arterial and intravenous chemotherapy were grade II-III bone marrow suppression. No drug-induced cardiotoxicity, nephrotoxicity or hepatic dysfunction were observed. All patients were followed-up 2 to 13 years (median 5 years). Disease-free survival rate was 86.4% (19/22), and overall survival rate 90.9% (20/22).
Conclusion: Neoadjuvant alternating arterial and intravenous chemotherapy is safe and effective for the treatment of advanced malignant abdominal and pelvic tumors in children.

PD-091

DECLINE IN SURVIVAL IN PEDIATRIC RHABDOMYOSARCOMA IN SWEDEN? CHARACTERISTICS AND OUTCOMES IN CHILDREN WITH RHABDOMYOSARCOMA DIAGNOSED IN SWEDEN DURING THE YEARS 1984 -2010

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Background/Objectives: The outcome for paediatric rhabdomyosarcoma (RMS) in Sweden was high during the nineties. During the last decade we have seen decreasing trends in Overall Survival (OS). The aim was to investigate incidence, patient and disease characteristics, treatment and outcome, and whether any reason for the possible decline in OS could be found.
Design/Methods: Two hundred and ten children aged 0-14 years diagnosed with RMS in the population-based Swedish Childhood Cancer Registry during the years 1984-2010 were included in the study. Complementary information was collected from medical charts.
Results: The overall annual incidence was 4.9 per million. The 5-year OS for the periods 1984-1989, 1990-1999 and 2000-2010 was 59±7%, 78±5 % and 71±5% respectively. When patients with localised disease were analysed separately, there was no difference in outcome between the periods 1990-1999 and 2000-2010 (5-year OS 82±5% and 81±5%), but outcome in 1984-1989 (5-year OS 53±8%) was significantly worse. The prevalence of metastatic disease was unexpectedly high during the last period with a metastasis rate of 28% (p=.010), in contrast to 18% for the material in total.
Conclusion: The results suggest that a higher rate of metastatic disease may explain the declining trend in OS in paediatric RMS in Sweden over the last decade. The reason for this higher rate remains unclear but could be due to coincidence.

Poster Discussion: Supportive Care/Palliative Care

PD-092

THE IMPACT OF COMMUNICATION WHEN A BROTHER OR SISTER IS DYING OF CANCER AND THEREAFTER - A NATIONWIDE LONG-TERM FOLLOW-UP IN SWEDEN

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Background/Objectives: The purpose of this study was to examine siblings' long-term psychological health in relation to their perception of communication with their family, friends and health-care professionals during their brother or sister's last month of life.
Design/Methods: A questionnaire study was conducted nationwide in Sweden in 2009, of individuals who had lost a brother or sister to cancer two to nine years earlier. Of the 240 siblings contacted, 174 (73%), participated. The Hospital Anxiety and Depression scale (HADS) was used to assess psychological health. Data are presented as proportions (%) and relative risks (RR) with 95% confidence interval (95% CI).
Results: Siblings who were *not* satisfied with the amount they talked about their feelings with others during their brother or sister's last month of life were more likely to report anxiety, 15/58 (26%) than those who were satisfied, 13/115 (11%), RR=2.3 (1.2-4.5). The same was true for those who had been unable to talk to their family after bereavement, RR=2.5 (1.3-4.8). Avoiding health-care professionals for fear of being in their way increased siblings' risk of reporting anxiety at follow-up, RR=2.2 (1.1-4.6), especially avoidance in the hospital setting, RR=6.7 (2.5-18.2). No such differences were seen when the ill brother or sister was cared for at home.
Conclusion: Lack of communication was associated with a higher risk of anxiety in bereaved siblings long-term, and so was avoiding health-care professionals, especially when the brother or sister was cared for at the hospital.

PD-093

QUALITY OF CLINICAL PRACTICE GUIDELINES FOR FERTILITY PRESERVATION IN CHILDREN WITH CANCER

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Background/Objectives: There is little uniformity in fertility preservation care for children diagnosed with cancer. To ensure high-quality care, evidence-based clinical practice guidelines are essential. As a step towards guideline development, we aimed to identify existing guidelines for fertility preservation in children and young adults diagnosed with cancer, evaluate their quality, and explore differences in recommendations.
Design/Methods: We performed a systematic search in PubMed (2000-October 2014), guideline databases and websites of cancer, paediatric and fertility organisations. Two reviewers evaluated the quality of the identified guidelines using the Appraisal of Guidelines Research and Evaluation Instrument (AGREE II). From the high quality guidelines, we evaluated areas of concordance and discordance among the recommendations.
Results: We identified 26 guidelines, 20 guidelines focused on adults and children and 6 on adults only. Five guidelines were not appraised, as these were older versions from other identified guidelines. Of the 21 guidelines that underwent a full critical appraisal, the average AGREE-II domain scores varied from 0% on applicability and editorial independence to 100% on clarity of presentation. We found areas of discordance regarding the clinical questions "Who should receive fertility preservation?", "What fertility preservation method should be used?", "When should fertility preservation be discussed and initiated?", "Who should be involved in the discussion and decision for fertility preservation? and "What are the ethical aspects?".
Conclusion: Our findings show that variations in fertility preservation recommendations exist, which can affect the quality of care. Clinical practice guidelines including a transparent decision process for fertility preservation at the start of cancer treatment can help health care providers deliver optimum care and improve the quality of life of children with cancer.

PD-094

INFECTIOUS COMPLICATIONS IN CHILDREN WITH ACUTE MYELOGENOUS LEUKEMIA: INCREASED MORBIDITY, BUT DECREASED MORTALITY IN MULTICENTER TRIAL AML-BFM 2004

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Background/Objectives: Infectious complications are an important cause of morbidity and mortality in children undergoing therapy for acute myelogenous leukemia (AML). Therefore, specific recommendations for the prevention and treatment of infectious complications had been implemented in the protocol of the multicenter trial AML-BFM 2004. In addition, since 1999, training courses on anti-infective strategies are regularly offered to pediatric hematologists.

Design/Methods: The medical records of children treated according to AML-BFM 2004 were reviewed and data on infectious complications were gathered by two of the authors (CP and JG) in the hospital where the patient was treated. Patients with Down syndrome were excluded from the analysis.
Results: Overall, 1,361 infections occurred in 405 patients [203 girls, 202 boys; median age (range) at diagnosis 8 years (0-18)]. The median number of infections (range) per patient was 3.3 (0-11). Specifically, fever of unknown origin (FUO) was observed in 55.5% of the infectious episodes (n=756), clinically documented infections in 10.6% (n=144), and microbiologically documented infections in 33.9% (n=461). Neutropenia was present in 1,251 (90%) of all infectious episodes. Bacteremia was diagnosed in 325 episodes, of which were 18 (5.5%) polymicrobial. Overall, 245 Gram-positive and 101 Gram-negative pathogens were isolated in the blood. A total of 9 children died due to infectious complications (median time after diagnosis of AML: 23 days). As compared to the multi-institutional trial AML-BFM 93, which had a lower dose-intensity than BFM-AML 2004, the incidence of infectious complications was significantly higher (2.8 versus 3.3 infectious episodes per patient; P=0.046), whereas the infection-related mortality had significantly decreased (6.6% versus 2.2%; P=0.004).
Conclusion: Specific anti-infective recommendations in the treatment protocol and the implementation of training courses in the education of pediatric hematologists may be the reason of reduced infection-related mortality in children with AML. However, further studies are needed in order to decrease infection-related morbidity.

PD-095

NON-PHARMACOLOGICAL ANTI-INFECTIVE MEASURES MAY INFLUENCE INFECTIOUS COMPLICATIONS IN CHILDREN WITH ACUTE MYELOGENOUS LEUKEMIA

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Background/Objectives: Infections are an important cause of morbidity and mortality in children treated for acute myelogenous leukemia (AML). Although most centers apply non-pharmacological anti-infective measures, little is known on their impact on infectious outcomes.
Design/Methods: We surveyed sites to determine institutional standards regarding recommended restrictions of social contacts (6 items), pets (5 items), and food (8 items) in children treated for AML according to AML-BFM 2004. A scoring system was developed with a restriction score for each item (2 for always restricted, 1 for sometimes restricted, and 0 for no restriction), resulting in a total restriction score ranging from 0 to 38. Univariate and multiple Poisson regression were used to estimate the impact of the restrictions on the incidence ratios of fever, bacteremia, pneumonia and diarrhea during intensive treatment.
Results: Data on non-pharmacological anti-infective measures were available from 37 institutions treating 429 children with AML. Median (range) of the overall restriction score was 29 (13-37). When combining all items (social contacts, pets, and food), there was a small, but significant influence of the restriction score on the incidence of fever [IRR (incidence rates ratio) 0.98 (95%CI 0.978-0.998); P=0.022] and bacteremia [IRR 1.02 (1-1.046); P=0.045]. Further analysis demonstrated that a higher restriction score of social contacts increased the incidence of bacteremia [IRR 1.21 (1.074-1.377); P=0.002], whereas a higher restriction score of pets decreased the incidence of pneumonia [IRR 0.877 (0.755-0.993); P=0.038]. No other non-pharmacological anti-infective measures had an impact on the incidence of any of the infectious complications analyzed.
Conclusion: Our data suggest that non-pharmacological anti-infective measures may have some impact on the incidence of fever and bacteremia. However, since we did not include potential confounders such as antibiotic prophylaxis, results may be confounded by other supportive care practices. More research is required to identify the independent effect of non-pharmacological interventions.

PD-096

EXPERIENCES OF EARLY DISCHARGE, WITH A FOCUS ON PAEDIATRIC FEBRILE NEUTROPENIA: A META-ETHNOGRAPHY

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Background/Objectives: Many children have no significant sequelae of febrile neutropenia. A systematic review of clinical studies demonstrated patients at low risk of septic complications can be safely treated as outpatients using oral antibiotics, with low rates of treatment failure. However, this review raised concerns that reductions in therapy, particularly outpatient treatment, may not be acceptable to patients, parents and healthcare professionals.
Design/Methods: This meta-ethnography explored qualitative studies to inform theories of experiences of early discharge in paediatric febrile neutropenia, including reports a) from studies of adult febrile neutropenia, for its disease specific data, and b) from other paediatric conditions, to provide a broader social context. Systematic literature searching preceded our analysis which used an adapted version of Noblit and Hare's phases of meta-ethnography.
Results: Nine papers were included. The overarching experience of patients, parents and healthcare professionals is that decision making in early discharge is complex and difficult. This experience is influenced by various common factors, including fear, timing and resources. Within this decision making, we identified two distinct themes. First, families struggled with some practical aspects associated with maintaining successful treatment regimens, namely childcare, finances and attendance at follow-up. Second, parents struggled with various social and emotional issues raised by early discharge. These included social isolation, relational and environmental issues. In linking these two themes, participants noted the importance of continuity of care and the need for information if they accepted early discharge. Participants described strategies that might circumvent some of the practical challenges faced and alleviate some of the feelings of isolation experienced.
Conclusion: Decision making about accepting early discharge is complex, featuring practical, social and emotional considerations along with a desire for more information and continuity of care. This work should inform the design of supportive care services and the development of future research strategies.

PD-097

GASTROSTOMY COMPLICATIONS IN ONCOLOGY PATIENTS – A NATIONAL STUDY

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Background/Objectives: Survival from childhood cancers has substantially increased over the decades. Up to 50% experience some degree of malnutrition. This is related to the both the disease and it's treatment. Gastrostomy feeding provides a means of supplemental nutritional support. Neutropenia can increase the risk of gastrostomy complications. We sought to assess the incidence of such complications nationally across paediatric surgical oncology centres.
Design/Methods: All national paediatric surgical oncology centres were contacted for participation through a national committee. An audit pro-forma was designed for data collection. This included patient demographics, patient diagnosis, treatment protocol, dates of gastrostomy insertions/changes, need for granulocyte colony stimulating factor (GCSF) treatment and any complications. All patients with a gastrostomy sited between January 2012 and December 2013 were included in the study.
Results: Four centres responded for participation in the study with a total of 49 patients in the study period. 71% of patients had a diagnosis of either central nervous system (primarily medulloblastoma) or other solid extra-cranial malignancies. The median age at insertion of gastrostomy was 8 years (10months-17yrs). Median duration between last chemotherapy and gastrostomy insertion was two weeks (1-30 weeks). 25% of patients were given GCSF prior to gastrostomy insertion in line with reducing counts. 47% of patients had their gastrostomies removed within two years of insertion with a median duration of use of 9 months (2-31 months). Only one patient had their gastrostomy removed for recurrent infections when neutropenic. Overall there was a 16% infection rate, mainly with Staphylococcus aureus causing superficial skin infections. One other patient developed a local myositis and one patient suffered from a blocked gastrostomy.
Conclusion: Gastrostomy feeding appears to be safe in oncology patients with minimal complications. The duration of use is often short providing an effective means of supporting nutrition in a catabolic state.

PD-098

RESTING ENERGY EXPENDITURE AND BODY COMPOSITION IN CHILDREN WITH CANCER: RESULTS OF A CROSS-SECTIONAL COMPARATIVE STUDY

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Background/Objectives: The assessment of body composition and energy requirements in children with cancer is necessary for the development of individualized nutritional support regimens and recommendations. Our aim was to estimate body composition of

children with cancer, to compare measured versus predicted energy requirements, and to develop new predictive equations for use in pediatric oncology.
Design/Methods: Resting energy expenditure (REE) by indirect calorimetry and body composition by bioimpedance analysis (BIA) were accessed in three groups of children aged 5–18 years. Group 1 (n=181) – patients in remission of cancer, group 2 (n=55) – children with cancer receiving chemotherapy or in the early period after hematopoietic stem cell transplantation, group 3 (n=63) – hospitalized children with non-malignant diseases of the gastrointestinal tract. To eliminate the influence of age and gender on the intergroup comparison, body composition parameters were expressed as standardized values (z-scores) relative to a reference group of healthy Russian children (n = 138,191).
Results: Group 1 was characterized by excess fat content and intact fat-free mass (FFM). Groups 2 and 3 showed significant FFM depletion more pronounced in group 2 and masked by the increase in percentage fat. In groups 1 and 3, all used conventional formulae (WHO, Harris–Benedict and others) underestimated REE as compared to indirect calorimetry. A new formula for REE providing unbiased estimate in the group 1 was proposed: REE (kcal/day) = 28.7 × BCM (kg) +10.5 × Height (cm) – 38.6 × Age (years) – 134, where BCM is the body cell mass according to BIA ($R^2 = 0.67$, SD = 196 kcal/day).
Conclusion: Significant differences in malnutrition prevalence and body composition were observed between the study groups. The suggested formula for REE can be used in children with cancer in remission for the assessment of the effectiveness of dietotherapy and nutritional support.

Poster Discussion: Surgery (IPSO)

PD-099

ESTABLISHMENT AND PRELIMINARY CHARACTERIZATION OF NOVEL CELL LINES IN RARE PEDIATRIC TUMORS WITH PERITONEAL DISSEMINATION

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Background/Objectives: Introduction: There is a lack of information about primary and metastatic pediatric peritoneal tumors, which impair the diagnosis and treatment of these children diseases. The inexistence or the low number of established and well-characterized cell lines representative of these tumors contributes greatly to this scenario. Tumor cell lineages can be studied *in vitro*, and novel targets for inhibition of proliferation, metastasis and/or survival can be determined. Moreover, the sensitivity for chemotherapeutic agents can also be analyzed *in vitro*, improving the preclinical evaluation of novel treatment protocols. *Objective*: to establish cell lines of pediatric tumors with peritoneal dissemination.
Design/Methods: Primary and metastatic pediatric peritoneal tumors were collected immediately after surgeries, and samples were subjected to mechanical separation of the cells and/or preparation of explants. *In vitro* cultures in enriched medium allowed the isolation of 2 cell lines, out of 5 samples.
Results: Cell lines from a peritoneal desmoplasic tumor and from a peritoneal ovary tumor metastasis were established and expanded. Preliminary characterization of these cell lineages showed a high tumorigenic potential in immunosuppressed animals, growing after subcutaneous and intraperitoneal inoculation. Markers of these xenografted tumors were evaluated by immunohistochemistry, which highly expressed human vimentin, and will be compared to the original human tumors. Sensitivity to chemotherapeutic agents was also evaluated, and both cell lines showed resistance to commonly used chemotherapeutic drugs.
Conclusion: We will continue our efforts on the complete characterization of these cells lines, and will also pursue the isolation of other representative cell lines of peritoneal dissemination of pediatric tumors.

PD-100

PREVALENCE OF *C-KIT* COPY NUMBER VARIATIONS (CNVS) IN NEUROBLASTOMA

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Background/Objectives: Immunopositivity for c-kit has been observed by us in a number of tissues of neuroblastoma patients. This study aimed at evaluating the prevalence of *c-kit* copy number variations (CNVs) and its prognostic significance in neuroblastoma.
Design/Methods: Thirty-seven histologically confirmed neuroblastoma (NB) specimens were evaluated. Genomic DNA was amplified through real-time PCR. Relative copy number of c-kit gene was calculated with respect to three housekeeping genes, Succinate dehydrogenase (*SDH-C*), N-acetylglucosamine kinase (*NAGK*), and Rnase *P*. Patient's samples having values ≥10, at least with respect to two reference genes, were considered as amplified.
Results: Age ranged from 1-132 months (mean 38.48; SD±33.26). Seven (18.9 %) of 37 patients were below 12 months. There were 10 (27%) females and 27 (70.3%) males. The location of tumors was adrenal in 26 (70.3%) and non-adrenal in 11 (29.7%). There were 19 (51.3%) stage 4 and 18 (48.6%) non-stage 4 patients. Out of 37 cases 33 (89.2%) received neo-adjuvant chemotherapy (NACT), of which 2 (5.7%) achieved CR, 27 (77.1%) PR, 2 (5.7%) NR and 2 (5.7%) had PD. Final response was assessed in 36 (97.3%) patients, of which CR was achieved in 21 (58.3%), PR in 3 (8.3%), NR in 3 (8.3%) and PD in 9 (25%). Out of 37 patients, 10 (27%) died while the rest 27 (73%) survived till the end of the study.Real-time PCR, showed that *c-kit* CNVs was present in only one case. Patient was 8 months old male with adrenal neuroblastoma, stage 4; undifferentiated histology and high mitosis-karyorrhexis index (MKI). Making it unfavorable histology. The patient died soon after presentation during workup without receiving any treatment.
Conclusion: *c-kit* gene amplification was observed in only one case (2.7%). This suggests that *c-kit* amplifications are rare events in neuroblastoma and may not be responsible for the observed immunopositivity of c-kit. It may not be helpful in prognostication.

PD-101

GLYPICAN-3 AS A NOVEL MARKER OF PROGNOSIS IN WILMS TUMOR

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Background/Objectives: Glypican-3 (GP3), is a heparan sulfate proteoglycan, found in fetal tissues and in some cancers, playing role in cell growth and differentiation and tumorigenesis. Increased levels of GPC3 correlate with poor outcome in hepatocellular carcinoma and hepatoblastoma. This study aimed to evaluate the expression of GPC3 in Wilms tumor and to correlate it with histopathology and outcome, and thereby establish its prognostic role.
Design/Methods: A prospective study on 75 cases of Wilms tumor from 2009 to 2012. Real time Polymerase chain reaction (RT-PCR) for Glypican mRNA was performed on tumor and normal samples collected from fresh nephrectomy specimens. GPC-3 gene expression in fold change was determined and was compared with adjacent normal kidney and GAPDH. GPC-3 fold change of >1.5 was considered elevated. GPC3 expression was correlated with each of the prognostic variable independently.
Results: GPC3 was overexpressed in 37/75 (49.3%) cases. Stage was not significantly related to GPC3 overexpression (p=0.2). GPC3 was overexpressed in 25/45 (56%) cases that received neo-adjuvant chemotherapy while it was overexpressed in only 12/30 (40%) of those who were operated upfront (p=0.03). GPC 3 was found overexpressed in 82% cases with blastema predominant histology while it was overexpressed in around 50% of the other histologies. All the 5 deaths among blastema predominant tumors and 4/5 deaths among triphasic tumor had overexpressed GPC3. The only death among the stroma and epithelial predominant tumors did not have GPC3 overexpression. The overall survival (OS) was 73% among those with GPC3 overexpression and 93% among those without overexpression (p= 0.016;HR 5.3; 95CI 1.1-24.8). However, the event free survival (EFS) was not significantly different among those with GPC3 overexpression (p=0.11;HR 2.09; 95CI 0.82-5.3).
Conclusion: Overexpression of GPC3 levels correlated with poor OS (p=0.016) but not with EFS (p=0.11) among Wilms tumor. It might serve as a molecule for targeted therapy in future.

PD-102

OUTCOME OF PULMONARY METSTASECTOMY IN PEDIATRIC SOLID TUMORS

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Background/Objectives: To evaluate surgical management and outcome of patients undergoing pulmonary metastasectomy.
Design/Methods: Retrospective review of patients operated for pulmonary metastases from September 2001 till January 2015 for their presentation, surgery and outcome.
Results: A total of 46 patients underwent 69 thoracotomies for removal of 196 lung metastases (range 1-20 metastases). Primary diagnosis was Osteosarcoma (OSa) 23; Wilms tumor (WT)11, hepatoblastoma (HB)5, malignant germ cell tumor (MGCT)3

and 1 each had Ewing sarcoma (EW), malignant mesenchymal tumor (MMT), rhabdomyosarcoma (RMS) and synovial sarcoma (SS). Thirty-eight thoracotomies were done for lung metastases that were already present at the time of diagnosis while 31 thoracotomies were done when lung metastases that presented as recurrence. Sixteen patients (12 OSa, 3 HB and 1 WT) had bilateral metastases and 12 of them underwent staged metastasectomy. One patient with bilateral re-recurrence followed by surgery on one side and other whose metastases resolved with alternate chemotherapy did not undergo second metastasectomy. Three patients with bilateral disease are waiting for contralateral surgery following unilateral metastasectomy. Nine repeat thoracotomies were required in 7 patients (5 OSa, 1 WT and 1 HB). Fifteen patients underwent lobectomy (>1 lobe was removed in 4 patients), 31 patients had wedge resections, 9 had subpleural resections and 11 had both wedge and subpleural resections. Only biopsy was performed in 1 patient for an unresectable tumor. Two had negative thoracotomy. Ten patents died and 20 patients (9 OSa, 5 WT, 4 HB, 1 MMT and 1 MGCT) had re-recurrence in the lungs giving a 3-year overall survival of 77%(95 CI 58-88) and 3-year event-free survival of 43%(95CI 26-59).
Conclusion: Pulmonary metastasectomy, even when done for bilateral and metachronous disease, is a viable option for achieving survival in patients. It leads to acceptable event-free (43%) and overall survival (77%) rates in patients who otherwise would have progressed and died.

PD-103

COMPARATIVE EFFICACY OF ULTRASOUND INVESTIGATION IS IN THE DIAGNOSIS OF MALIGNANT ABDOMINAL TUMOR IN CHILDREN IN OUTPATIENT CONDITIONS AND IN A SPECIALIZED ONCOLOGY HOSPITAL

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Background/Objectives: Ultrasonography is method of choice for primary diagnosis of abdominal solid tumors in pediatric patients. However, there are significant proportion of advanced forms of cancer among children admitted for inpatient treatment. The purpose of this study was to compare the effectiveness of ultrasonic method for primary diagnosis of pediatric abdominal malignancies on for outpatient phase and in specialized clinic.
Design/Methods: Analyzed the medical records of 216 patients of both sexes aged 1 day - 13 years (median 2.1 years), successively admitted for further examination and/or treatment to pediatric oncology hospital. The spectrum of disease consisted from: retroperitoneal neoplasms - 49 patients; tumor and tumor-like processes of the liver - 35, kidneys - 101, adrenal - 31. Was evaluated the diagnostic accuracy of the ultrasonic method.
Results: The results of a comprehensive analysis of the data for the presence of solid malignancies in a child using the estimates of the aggregate of the classical signs of ultrasound are detailed documented in outpatient conditions in only one-fifth of cases, and in the hospital - in three-quarters of cases. Accuracy of the method in evaluation of the diagnostic data levels (differentiation of the tumors and tumors-like processes; differentiation benign and malignant tumors; assumptions about the nosological form) in these cases was in the range of 82% -31% and 95% -53% in outpatient conditions and in the hospital respectively. With regard to nosological forms - the most lowest effectiveness of ultrasound diagnosis according with these criteria was set for retroperitoneal tumors.
Conclusion: The effectiveness of ultrasound diagnosis to outpatient phase was lower than that in a specialized medical facility. It is necessary to make more use of the possibility of comprehensive assessments of ultrasound data according to diagnostic criteria of malignancy successively from ascertaining the existence of the tumor till to assess the symptoms of malignant growth.

PD-104

OUTCOMES OF PRETREATMENT RE-EXCISION AFTER UNPLANNED EXCISIONS FOR NONRHABDOMYOSARCOMA SOFT TISSUE SARCOMAS IN CHILDREN

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Background/Objectives: It is not uncommon to come by children with initial unplanned surgical intervention for nonrhabdomyosarcoma soft tissue sarcomas (NRSTS). The aim of this study was to evaluate the presence of residual disease, the treatment outcomes in terms of local and distant recurrence and survival in patients with unplanned excision of NRSTS treated with pretreatment re-excision (PRE).
Design/Methods: The records of 35 patients presenting with unplanned excision of NRSTS between January 2006 and October 2014 were reviewed. The records were compared with 25 patients with planned excision of NRSTS in the similar period.
Results: Total 33 patients underwent PRE and two were considered unsuitable for PRE. Tumor was present in the PRE specimen of 16 (48.5%) patients. Brachytherapy was offered to 12 of the 21 patients who received radiotherapy following PRE. On comparison with planned excision, patients with extremity (p=0.01) and invasive tumors (p=0.03) more often had a PRE. There were four relapses (distant: 3, local: 1) in the PRE group and seven relapse in the planned excision (distant: 5, local: 1 and progression: 1) group (p=0.17). The 5-year overall and event free survival were, respectively 95.5% and 83.6% for the PRE group and 86.6% (p=0.3) and 65.7% (p=0.08) in the planned excision group.
Conclusion: The probability of residual disease following unplanned excision of NRSTS is high therefore PRE should be considered whenever feasible. The outcomes following PRE are similar to that with planned excision. An associated advantage is the feasibility of brachytherapy during PRE which could minimize the morbidity associated with external radiotherapy.

PD-105

NEOADJUVANT THERAPY FOR LOCALISED, INITIALLY UNRESECTABLE NON-RHABDOMYOSARCOMA SOFT TISSUE SARCOMAS

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Background/Objectives: Treatment of localised initially unresectable non-rhabdomyosarcoma soft tissue sarcoma (NRSTS) is challenging considering the unavailability of robust neoadjuvant therapy. The aim of this study was to describe the neoadjuvant therapy and the outcomes in children with initially unresectable NRSTS.
Design/Methods: The records of patients with initially non-metastatic and unresectable NRSTS treated between January 2006 and March 2014 were analysed.
Results: Non-extremity tumours (n=15) were the commonest amongst the 22 patients analyzed. More than 80% of the patients had tumours with high-risk features (tumour size > 5 cm, high grade, invasiveness). Neoadjuvant therapy included chemotherapy alone in 20 patients while one patient each received radiotherapy alone or along with chemotherapy. None of the patients had a complete response while major responses (>50 regression) were recorded in 23.8% and minor (<50% regression) in 47.6% of cases. Stable or progressive disease was seen in 28.6%. The 3-year event-free and overall survival was 42.6% and 49.4% respectively. Of the nine relapses, three each were at the local site, abdominal cavity and lung respectively. The response to neoadjuvant therapy did not predict outcome.
Conclusion: Initially unresected NRSTS commonly present with high-risk features and respond poorly to neoadjuvant therapy. The outcomes remain dismal, which compels the need for more effective therapy for these patients.

PD-106

IS BLEOMYCIN EFFECTIVE ANTI- ANGIOGENIC AGENT FOR VASCULAR ANOMALIES?

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Background/Objectives: Vascular anomalies many a times pose a tremendous therapeutic challenge due to type, site, rapid growth, disfigurement and complications. *Objectives*: 1) To emphasize the need for early intervention in patients with vascular anomalies especially of the head and neck. 2) To establish the efficacy of Injection Bleomycin as sclerosant for vascular anomalies.
Design/Methods: Children with vascular anomalies (malformations) of varying sizes, sites and behaviour, were selected for Injection Bleomycin therapy and subjected to sclerotherapy regime three weeks apart in the dose 0.66units to 1unit/kg/dose diluted in 1:1 normal saline and not exceeding more than 1 unit/kg per session, between January 2004 till December 2014. The lesions were measured and photographed serially. The clinical response and complications were recorded. Regression of lesions were termed excellent (>75%), significant (50-75%) or poor (<50%).
Results: Total 117 children were included in the study, mean age being 16.3 months (range, 2 months to 9 years).The mean number of injections given was 5.6(range, 3-8). The mean total dose administered was 30 mg (range, 15-42). 73 patients (62.4%) achieved a response of greater than 75% reduction in size (51 had complete resolution). 28 (24%) showed 50-75% reduction in the size of the lesion while 16 (13.7%) showed <

50% reduction in size. Ulceration occurred in 5 children and 78% developed patchy hyperpigmentation. None developed pulmonary fibrosis.
Conclusion: Vascular lesions traditionally were left alone for spontaneous regression to occur for which was neither certain nor complete and occurred if at all over many years, or were treated surgically or with steroids giving partial responses and recurrences. Moreover the lesions over head, face, neck cause disfigurement and are often rapidly progressive. The anticancer, antiangiogenic agent Bleomycin cause permanent cure in a large number of children providing excellent cosmetic results and with resolving minor side effects of the drug.

PD-107

MANDATORY COCCYGECTOMY IN SURGICAL MANAGEMENT OF SACROCOCCYGEAL TUMOURS

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Background/Objectives: Sacrococcygeal tumours are germ cell tumours within a diverse group of masses that may occur within the region of the pericoccygeal area. At the time of surgical resection the exact diagnosis is not always known. The UKCCLG guidelines on resection of sacrococcgeal teratomas mandates coccygectomy, either primary or delayed, due to risk of malignant recurrence.
Design/Methods: In a tertiary paediatric surgical centre, a retrospective review was undertaken of all lesions resected from the pericoccygeal region to determine compliance with mandatory coccygectomy for suspected or potential saccrococcygeal teratoma. Cases were identified from pathology reports and SNOMED codes for relevant topography and morphology within a 15 year period to 2014. Each case was assessed to tabulate the precise diagnosis and presence or otherwise of coccygectomy specimen.
Results: There were 19 tumours excised. Coccygectomy was performed in 10 cases. In 8 cases there was no evidence of coccygectomy and in one the presence or absence of a coccyx was not apparent from the wording of the report. There were 14 germ cell tumours resected; 11 mature teratomas and 3 immature teratomas. The remaining cases were retrorectal cystic hamartomas (3), fibrolipoma (1), and lipoblastoma (1) In 43% of germ cell tumours, mandatory coccygectomy was not performed. To date there has been no tumour recurrence.
Conclusion: This review shows poor compliance with UKCCLG guidelines for mandatory coccygectomy in suspected or potential germ cell tumours. The evidence base for this guideline is controversial and practice worldwide varies. The implications and a literature review will be presented.

PD-108

NEPHRON-SPARING SURGERY FOR UNILATERAL RENAL TUMOR IN CHILDHOOD: TWENTY-TWO YEARS EXPERIENCE AT A SINGLE CENTER

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Background/Objectives: Whether the adverse effects of nephrectomy for unilateral renal tumor (URT) in childhood outweigh the adverse effect of nephron-sparing surgery (NSS) remains controversial. The aim of present study was to evaluate the adverse effects of nephrectomy and NSS in our cohort of children with URT.
Design/Methods: We conducted a retrospective review of the records of all children with URT who underwent surgery at our institution between 1992 and 2014. All patients older than six months of age had neo-adjuvant chemotherapy and delayed surgery. Nephrectomy was performed in 31 children, partial nephrectomy in 8 children, and tumor enucleation in 6 children. Renal dysfunction (RD) was defined as eGFR < 90 ml/min/1.73m^2.
Results: One child treated with multiple Wilms tumor enucleations underwent unnecessary completion nephrectomy elsewhere. Another child, with stage II disease after partial nephrectomy, developed local recurrence and underwent completion nephrectomy and pericaval lymphadenectomy associated with radiotherapy and chemotherapy (stage III disease). In both instances, kidney remnants were tumor-free. Three children who underwent partial nephrectomy presented positive margins and were successfully treated with chemotherapy alone (stage II disease). At mean $\pm$ SD age of 14.6 ± 6.4 years after NSS the overall and the event-free survival rates were both 100% (one patient is still under treatment). None of the patients treated with NSS presented with renal dysfunction, whereas 9 of 23 patients with stage I-III who underwent nephrectomy presented with RD ($p=0.01$).
Conclusion: In our experience partial nephrectomy or tumor enucleation for treatment of children with URT appear to be oncologically safe at a reasonable therapy price. At short-term follow-up, more than 1/3 of the patients who underwent nephrectomy may be at the increased risk for cardiovascular disease and overall mortality.

PD-109

ASSESSMENT OF DURATION OF THE MAIN STEPS OF NEPHRECTOMY FOR WILMS TUMOUR

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Background/Objectives: Since 1950-ties, the nephrectomy for Wilms tumour (WT) has been composed of well specified steps performed the similar way. Aim of the study was to assess the importance and the duration of the particular steps.
Design/Methods: 55 WT patients submitted to post-chemotherapy nephrectomy by the same operating team within last 4 years. Nephron sparing resections and patients with the IVC thrombus were excluded (21 cases). Further analysis was conducted on 34 pts with unilateral WT. The surgical steps analysed were: approach, abdominal inspection, access to the renal pedicle, identification and ligation of renal vessels, resection of the tumour, lymph nodes sampling and closure of the abdomen.
Results: The approach used was transvers trans-abdominal and lasted 10-15 minutes (M=12). As all the patients had CT or MRI prior to surgery, the abdominal inspection focused on searching for peritoneal implants and lasted 3-7 minutes (M=4). The Kocher manoeuvre (right side) or laterocolonal (left sided) access to the renal pedicule lasted 5-15 minutes (M=12), the identification and ligation of renal vessels - 5-22 minutes (M=12), resection of the tumour in together with the adipose capsule - 12-25 minutes (M=14), the lymph nodes sampling (>6) - 8-20 minutes (M=14), closure of the abdomen - 12-30 minutes (M=20). The duration of the whole procedure lasted from 60 minutes to 2 hrs (M=80 minutes). There were no major intra operative complications (tumour ruptures or major vascular injuries).
Conclusion: *Summary*: Post-chemotherapy nephrectomy for WT is well organised procedure usually lasting less than 2 hrs. Time consuming appeared the closure of the abdomen (M=20, 25% of the whole operating time), whereas so called crucial steps as ligations of the renal vessel and dissection of the mass were shorter (M=12 and 14 respectively). This seems to confirm the need of comfortable exposure and adequate order of steps.

PD-110

INNOVATIVE PROTON AND CARBON ION-BASED RADIOTHERAPEUTICAL PROGRAM. PERSPECTIVES AND BUSINESS PLAN OF A FUTURE FRENCH PROGRAM, INCLUDING A PÆDIATRIC POPULATION

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Background/Objectives: Initiating a new program of hadrontherapy in France, providing both protons and carbon ions, including a mixed adult (Ad) and pædiatric (Ped) patients (pts) population. Assess the financial viability of the proton project, based on current clinical indications, and expected availability of 3 French Centers within 5 years (Y).
Design/Methods: ARCHADE is a project that aims to develop hadrontherapy from bench to bedside. It is estimated to 120 M€. It should become partially operational in 2018, for protontherapy (PT), in Ad and Ped pts, and fully operational 3 to 4 years later for both particles. This ramping-up has been considered necessary to account for the learning curve of this innovative technology. Financially, it will be supported by the Sécurité Sociale national agency, based on an estimated 1,009 € reimbursement cost per fraction in French pts and approx. 2,000€ in foreigners, and conventional fractionation. This program will concern both currently validated indications, with emphasis on Ped, and new indications. 345 pts /Y are expected in full capacity. Main Ped indications, have been anticipated, as follows: sarcomas of bones (15), and soft tissue (20), brain (30), neuroblastomas (15), others (10).
Results: Various simulations were realized. The expected optimal solution, is presented for a mixed French (85%), and foreign (15%) population. Total "beam cost" (including staff salaries) is estimated 2,300 to 2,500€/hr. Y1: 150pts (Ad: 125, Ped: 25); Total/Y: #fractions: 4,500; beam time: 1,500; income: 4,900M€; expenditures (exp): 4,660 M€Y2: 250pts (Ad: 200, Ped: 50); Total/Y: #fractions: 7,500; beam time: 2,500; income: 8,100M€; exp: 7,450 M€Y1: 345 pts (Ad: 255, Ped: 90); Total/Y: #fractions: 10,750; beam time: 3,790; income: 11,750M€; exp: 11,000 M€.
Conclusion: This ambitious project combining protons and carbon ions, looks financially viable. A large proportion of foreign patients is recommended, since it allows substantial financial flexibility. It seems not compatible with a clinical program devoted entirely to paediatric patients.

PD-111

THE PERIPHERAL PORTACATH PROVIDES SAFE AND CONVENIENT VENOUS ACCESS IN PAEDIATRIC AND ADOLESCENT PATIENTS

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Background/Objectives: Adolescent patients with chronic conditions rely on permanent venous access for safe treatment and supportive care. Traditionally venous access is provided by a Hickmann or portacath (PaC) inserted in a central vein under general anaesthetic. Lymphomas represent the most frequent malignancy in adolescents often presenting with mediastinal masses, which complicates general anaesthetic (GA). We explored the safety and feasibility of insertion of peripheral PaC which could be performed under local anaesthetic. We present our case series of 18 patients.
Design/Methods: Eighteen patients underwent insertion of peripheral PaC into the antecubital fossa of the non-dominant arm under ultrasound guidance at our institution since Jan 2012. The medical records were reviewed to ascertain diagnosis, age at insertion, mode of anaesthetic, time to removal and complications. Patients and nursing staff were given a questionnaire to assess their experience and satisfaction with peripheral PaC.
Results: Since 2012, 18 peripheral PaC were inserted by two consultants at our institution. There were 11 female and 7 male patients aged between 13.58 years and 18.4 years. 4 PaC were inserted under local anaesthetic in patients who were not fit for GA due to mediastinal mass or lung disease. At the time of analysis 7 ports remained in situ, with a mean duration of 7.35 months (range 3 - 14.5 months). Removal of x PaC was under LA in 7 cases and under GA in 2. Complications were observed in 7 cases but only necessitated early removal or replacement in 2 cases (blockage and disconnection). Thrombosis was not observed.
Conclusion: This study shows that the use of peripheral PaC is safe with acceptable complications. The experiences and feedback from patients and nursing staff fully supports the use of the peripheral PaC. We are exploring additional patient groups that might benefit from this device.

PD-112

PROFILE OF SURGICAL TUMOURS PRESENTING TO A TERTIARY CENTRE IN GHANA

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Background/Objectives: Paediatric Surgical tumours span quite a diverse presentation. The frequency of occurrence of such tumours differs from developed to developing countries.
Design/Methods: We have reviewed the cases presenting to the Paediatric Surgery Unit at the Korle-Bu Teaching Hospital in Accra, Ghana from 1st January 2013 to 31st December 2014.
Results: There were 49 cases with a female to male preponderance of 1.7:1. Forty-two percent of patients were under the age of 2 years. Seventy-one percent of cases had Wilms tumour with only 29% being from other causes. Fifty-nine percent of surgeries were for some form of nephrectomy. Of the final outcomes recorded, 60% were discharged from the wards whilst 40% were transferred to the Paediatric Oncology service or other specialised units.
Conclusion: In Ghana, the majority of paediatric surgical tumours seen are Wilms tumours. A large number of the tumours seen are in patients presenting below the age of 2 years. Late presentation is still a feature and more public education needs to be undertaken at all levels.

PD-113

STEP BY STEP RESULTS OF 15 YEARS SURVEILLANCE OF PERMANENT CENTRAL VENOUS CATHETERS IN PATIENTS WITH MALIGNANT TUMOR

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Background/Objectives: There are some problems of insertion and using Permanent Central Venous Catheters (CVC). The aim of the study is to find the best personalized method for the CVC insertion and line management based on the long term surveillance of the CVC insertion technique.
Design/Methods: This is a longitudinal single center study from 2000 to 2014. We collected the data of indication for CVC insertion, technique and complications of insertions and problems developed during the treatment including infections, thrombosis and mechanical failure.
Results: All together 1065 CVCs have been inserted in 912 patients. The indication of CVC insertion in ratio of the patients: 27% in 2001, 91% in 2014. The technique of insertion, ratio of per cutaneous insertion: 20% in 2001, 98,9% in 2014. The type of CVC: 25% port-a-cath, 75% Hickmann line in 2001, 78% port-a-cath, 8% Hickmann line, 7% peripheric miniport, 6% PICC line in 2014.Complications of insertion, haemothorax, pneumothorax: 10% 2003, 1,2% in 2014.Malposition, kinking: 20% in 2001, 6% in 2014. Removal due to infection: 40% in 2001, 3,7% in 2014. Thrombus, septic thrombosis: 20% in 2001, 3% in 2014.Occlusion: 15% in 2001, 2% in 2014. Mechanical failure, disconnected port-a-cath: 5% in 2001, 5% in 2014.
Conclusion: The longitudinal surveillance led us to improve the result of insertion and outcome of CVC, such as decreased complication rate of insertion, increased rate of using port-a-cath, longer event free period of CVCs and more usage of peripheric permanent lines. All the steps behind the improvement were well concerned based on the previous results. The main steps of improvement were: standardized procedures, per cutaneous insertion, widened indication, application peripheric lines. Currently we are on to decrease the mechanical failure using the preconnect port and to decrease the complications of insertion using US guidance.

PD-114

WHETHER LAPAROSCOPY ASSISTED POSTERIOR SAGITTAL EXCISION OF PRESACRAL MASS IS BETTER OVER CONVENTIONAL APPROACH?

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Background/Objectives: Pelvic neuroblastoma (NB) includes 2-6% of all NB and most of these arise from organ from Zuckekandl. Presacral neuroblastoma is a rare tumor with very few case reports. We report our experience in managing two cases of presacral NB. Complete resections by one of the open abdominal or sacral/posterior sagittal were traditionally advocated as the best treatment for these presacral /retrorectal tumor but resection of these tumors often entails combined abdomino-sacral or abdomino-posterior sagittal approach with morbidity in terms of neurovascular damage. We share our innovative idea of laparoscopy assisted posterior sagittal removal of a presacral neuroblastoma.
Design/Methods: Retrospective study of all the presacral neuroblatoma treated in the department of Paediatric Surgery, JIPMER from February 2009 to February 2015, and were analyzed in terms of their clinico-pathological profile and postoperative outcome in terms of hospital stay, wound infection and neurogenic bladder if any.
Results: A total of 3 cases presacral mass was operated over this period. Of these, one was presacral teratoma (Altman type III) and the other two were presacral neuroblastoma. One of the case with presacral NB was operated via combined abdomino-posterior sagittal approach and one was operated by laparoscopy assisted posterior sagittal approach. It was observed that the case that had laparoscopy assisted posterior sagittal excision of presacral mass had less postoperative pain, shorter hospital stay and no neurogenic bladder involvement in the postoperative period.
Conclusion: We feel that laparoscopic mobilization of the pelvic part of presacral mass followed by mobilization of the lower part via posterior sagittal approach and excision of the presacral mass has the definitive advantage over conventional abdomino-sacral and abdomino-posterior sagittal approach in terms of pain relief, morbidity and risk of neurovascular damage as it provides better and magnified view of pelvis in the presacral area.

PD-115

URINARY RETENTION IN CHILDREN: AN UNUSUAL PRESENTATION WHICH MAY HERALD A BLADDER TUMOUR - A 20-YEAR REVIEW

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Background/Objectives: Recent institutional experience highlighted the frequency of urinary retention as a presenting symptom of children with bladder tumours. Unlike in the adult population, urinary retention is rare in children and should always precipitate detailed investigation to identify any underlying cause. Earlier tumour diagnosis generally improves clinical outcome. Modes of presentation of patients with bladder tumours were reviewed.
Design/Methods: A retrospective case-note review was undertaken of all children diagnosed with bladder/prostate rhabdomyosarcoma (RMS) in the West of Scotland between 1994 and 2014 inclusive. Initial presenting symptoms and clinical signs were noted.

Results: Twelve children (two girls) with a mean age of 6 years (range 1 to 15 years) were diagnosed in the study period with bladder/prostate RMS. Five children initially presented in urinary retention. Two of these were also in obstructive renal failure. Other presenting symptoms included dysuria/urinary tract infections (4), abdominal swelling/distension (4), frank haematuria (3), abdominal pain (3), change of bowel habit (constipation/diarrhoea) (3), and urinary frequency/urgency (2). Ten children had embryonal RMS, one child had alveolar RMS, and one child had undifferentiated RMS. Neither IRS staging nor tumour size were associated with presentation in urinary retention. Patients who had a delay in diagnosis of the underlying bladder/prostate tumour following treatment for symptomatic relief of urinary retention or presumed urinary tract infection are presented.
Conclusion: Urinary retention in children is rare and may have a varied aetiology including bladder/prostate tumours. Other causes include bladder outlet obstruction secondary to external compression from constipation or a pelvic mass, intra-vesical calculi or debris, prolapsed ureterocele, posterior urethral valves or neurogenic causes. Therefore all children presenting with urinary retention should undergo a course of urgent investigation following a structured protocol. Our protocol includes initial imaging with renal tract ultrasound scan.

PD-116

EWINGS SARCOMA OF THE CHEST WALL IN CHILDREN – A SURGEON'S PERSPECTIVE

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Background/Objectives: Pediatric Ewings Sarcoma of chest-wall(ESCW) is rare. Wide local excision (WLE) and reconstruction can be challenging. We describe our experience over 17 years.
Design/Methods: Retrospective chart-review of 21 patients with ESCW from June-1997 to August-2014 revealed 15 boys and 6 girls with a mean-age of 9.9-years (range 3-20 years). Presenting symptoms were respiratory-distress(n=9), pain(n=9), mass(n=7), fever(n=6), cough(n=4), Horner's syndrome(n=2) and cord compression(n=1). Three patients needed initial respiratory intensive supportive care. The site of origin was ribs(n=20) and sternal-body(n=1). Sixteen tumors measured >8cms (8 occupying the entire hemithorax) and 5 were metastatic at presentation. Fifteen underwent neoadjuvant-chemotherapy(NACT) followed by local therapy(POG#9354/CCG#7942 protocol). Four had upfront resection and adjuvant chemotherapy. Seven received radiotherapy for: inoperable tumor(n=1), positive resection margins(n=1), palliative(n=1) and large tumors with Huvos grade I/II necrosis(n=4). Surgery entailed resection of average 2.35 ribs in 17 patients (range 1-4 ribs). Reconstruction involved synthetic materials (prolene mesh, biopore) and musculucutaneous flaps (latissimus dorsi, pectoralis major/minor). One patient was inoperable despite second line chemotherapy, hence given radiotherapy.
Results: Two metastatic patients progressed before local therapy. Another 3 had progression during therapy. One patient succumbed to Adriamycin-induced cardiotoxicity. Three patients are currently on, and 12 have completed therapy. Two of 12 had fatal local relapse at 24 and 32 months; 1 of which was metastatic at presentation. No metastatic ESCW survived beyond 24-months. Mean Follow-up in 13 surviving patients was 29.1 months (range 7-87 months). Event free survival was 91.6% (24 months) and 88.8% (36 months). Cosmetic appearance was acceptable in all and 2/13 had minimal chest-wall deformity. None had respiratory compromise at the time of last follow-up.
Conclusion: Newer prosthetic materials enable the surgeon to achieve free resection margins without physiological compromise even in large ESCW. Tumor stage is the key prognostic factor for survival. Aggressive multimodality approach can facilitate better survival in localized ESCW.

PD-117

RELAPSED SYNOVIAL SARCOMA IN CHILDREN AND ADOLESCENTS: PROGNOSTIC FACTORS, TREATMENT AND OUTCOME

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Background/Objectives: The outcomes following relapse in synovial sarcoma are dismal. The treatment, outcomes and prognostic factors in this setting are not clearly defined.
Design/Methods: The records of patients with initially non-metastatic synovial sarcoma treated between June 2006 and May 2013 who experienced relapse were analysed.
Results: Of the total 18 patients with relapse, local recurrence occurred in 10 patients, distant metastases in seven and regional metastases in one patient. The time to relapse ranged from seven to 39 months (median 17 months). Treatment of relapse consisted of surgery in 15 patients, second-line chemotherapy in 14 and radiotherapy in 9 patients. The projected 5-year overall and event free survival was 47.2% and 41.3% respectively. The factors significantly influencing survival were local relapse only, complete surgical excision and use of chemotherapy at relapse and chances of a secondary remission.
Conclusion: The overall outcome of patients with relapsed synovial sarcoma is poor especially with distant relapse. Complete surgical excision and chemotherapy at relapse is associated with a better outcome.

PD-118

HOW DEEP SHOULD THE PUNCTURE BE TO OBTAIN CENTRAL VENOUS ACCESS IN PEDIATRIC ONCOLOGY?

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Background/Objectives: Central venous puncture with Seldinger technique is often used to obtain short and long-term catheters. Although safe, this technique can have some complications and the depth that the needle is inserted is not standardized. In order to avoid such problems, we developed a study to determine the maximum depth that should insert the needle in an internal jugular vein catheter insertion.
Design/Methods: Anthropometric data of pediatric patients submitted to long-term catheter implantation were collected. A portable ultrasound evaluated the morphometric parameters of the internal jugular during surgery and the needle insertion depth was calculated. Relationship between depth, weight and age were analyzed by scatter plots and linear correlation coefficients of Pearson. Age and weight were categorized and constructed graphs of average depth (with respective 95% confidence intervals). For the comparison between age groups and depth was used analysis of variance technique (ANOVA). The results were analyzed by the software "STATISTICA".
Results: The study included 275 patients. The depth of needle insertion was positively correlated with age ($r = 0.433670$, $p < 0.05$) and weight ($r = 0.595541$, $p < 0.05$). Mean graphs show that the depth increases with age and weight rise. This result was confirmed by ANOVA that showed statistically significant differences ($p < 0.001$) between the subgroups of age categories. By multiple regression analysis, unsatisfactory quality adjustment was observed ($R^2 = 0.382$) to develop a mathematical model. However, linear regression could be a guide to know which depth we can insert the needle securely. The formula to calculate how insert the needle is $1,7 + 0,017X$ weigh (Kg).
Conclusion: This study showed a positive relationship between depth of needle insertion, age and weight. Moreover it is possible to know which depth insert the needle in a jugular vein puncture. An approximate formula is $1,7 + 0,017X$ weight (Kg).

PD-119

REMNANT LEFT LOBE TORSION CAUSING INFERIOR VENA CAVA OBSTRUCTION AFTER HEPATIC RIGHT LOBECTOMY FOR FIBOLAMELLAR HEPATOCELLULAR CARCINOMA

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Background/Objectives: Hepatic venous outflow obstruction is a recognized lethal complication after living donor transplantation. A torsion of liver can cause obstruction in hepatic vein. This condition is very rare after hepatectomy. The previous related cases had obstruction in hepatic vein (Budd-Chiari syndrome). Obstruction just in vena cava is extremely rare, justifying this description.
Design/Methods: We report the case of a 14-year-old boy with left lobe torsion causing acute inferior vena cava obstruction after right hepatectomy, which was successfully treated with surgery.
Results: A 14-year-old boy underwent a right hepatectomy for PRETEXT II fibrolamellar hepatocellular carcinoma. After mobilization of right lobe, bilateral section of triangular ligament, and section of falciform ligament, the operation was in a standard fashion with both inflow (right hepatic artery and portal vein) and outflow (right hepatic vein) ligation prior to hepatic section. After right hepatectomy, he developed edema of lower limb and inferior abdominal wall. He increased the weight by 10 kg. The patient had diuresis just with furosemide. Doppler ultrasonography did not find any vein obstruction. Abdominal computed tomography (CT) revealed that remnant liver was dislocated in the right subphrenic space and a narrow retrohepatic vena cava. After surgical repositioning of the left lobe into its anatomical position, the venous congestion disappeared progressively. The falciform and round ligaments were fixed to the anterior abdominal wall to keep the remnant liver in the anatomical position. His postoperative course was uneventful. The posoperative CT showed improvement in inferior vena cava flow.

Conclusion: Fixation of remnant liver may be effective for preventing hepatic venous outflow obstruction after right hepatectomy.

PD-120

VIDEO-ASSISTED PERICARDIOSCOPY AND INTRAPERICARDIAL AMPHOTERICIN FOR INVASIVE ASPERGILLOSIS IN BONE MARROW TRANSPLANTAION PATIENT

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Background/Objectives: Invasive fungal infections have become an important problem in patients undergoing bone marrow transplantation. Pericardial aspergillosis is an uncommon and lethal condition.
Design/Methods: We describe a patient with invasive aspergillosis that had an evaluation with video-assisted pericardioscopy and intrapericardial amphotericin.
Results: A 13-year-old boy, diagnosed with myelodysplastic syndrome (RAEB type 2) associated with left leg lymphedema (agenesis of lymphatic vessels). He started treatment with azacitidine (5 cycles) while waiting for an unrelated donor for bone marrow transplantation. He underwent allogeneic unrelated bone marrow transplant. The myeloablative conditioning regimen was done with busulfan, cyclophosphamide, melphalan and thymoglobulin. The graft versus host disease prophylaxis was performed with cyclosporine and methotrexate. He presented grafting of leukocytes on D+17, but evolved with graft dysfunction from D+41, holding periods of neutropenia since that time. The patient developed pulmonary aspergillosis treated with oral voriconazole, with stabilization of the clinical signs, but without falling levels of galactomannan, requiring several changes in the antifungal scheme (liposomal amphotericin, intravenous voriconazole, voriconazole associated with micafungin). He presented significant pericardial effusion on echocardiography with indirect signs of cardiac tamponade. He underwent pericardiocentesis, with exudate with galactomannan levels quite high. Video-assisted pericardioscopy was performed. This procedure allowed visibility of the pericardial sac and a good site to be biopsied. An intrapericardial catheter was inserted. He received intra-pericardial infusion of amphotericin B for 5 days, while keeping systemic treatment with voriconazole. Aspergillus fumigatus was isolated in the pericardial fluid culture. Currently, the patient is receiving systemic treatment with voriconazole, even with positive galactomannan, but clinically stable.
Conclusion: Video-assisted pericardioscopy is a minimally invasive technique that allows prognosis evaluation of pericarditis, do a pericardial biopsy and insert pericardial catheter. Intrapericardial amphotericin is an option for pericardial invasive aspergillosis.

PD-121

RISK FACTORS ASSOCIATED WITH IRS CLINICAL GROUPS AND CHARACTERISTICS OF SOFT TISSUE SARCOMAS OVER A PERIOD OF 13 YEARS IN A NATIONAL REFERENCE CENTER

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Background/Objectives: This study aims to characterize pediatric soft tissue sarcomas in a national referral hospital in Spain and to analyze the risk factors associated with the degree of surgical resection and their evolution.
Design/Methods: Pediatric patients belonging to the group of soft tissue sarcomas newly diagnosed from 2002 to 2014 were included. Clinical charts were reviewed to assess their characteristics and risk factors associated with the possibility of degree of surgical resection based on their clinical grouping system developed by the Intergroup Rhabdomyosarcoma Group (IRS). Comparisons were made using SPSS 12.0 with a threshold of significance of 0.05.
Results: Sixty seven patients (35 males and 32 females) aged 6.36 (range 0-17 years) at diagnosis were included. Fifty three (79.1%,) remain alive today, albeit 17 of all the cases (25.4%) presented metastases and 10 relapsed during their evolution . There were 18 different histological types, being the most frequent embryonal rhabdomyosarcoma (29.9%) and alveolar rhabdomyosarcoma (14.9%). Non-survivors patients died after a mean follow-up of 21.14 (range 7-55 months). Mean follow-up was 69.04 months (range: 6-149 months). Tumor location was in the lower limbs (22.4%), head (20.9%), abdomen (17.9%), liver (8.95%), chest (8.95%), upper limbs (7.5%) and others (13.4%). The IRS surgico-pathologic grouping system was strongly associated with survival (P=0.002): I 40 cases (92.5% alive), II 3 cases (100% alive), III 13 cases (61.5% alive) and IV 11 cases (45.5% alive). Twenty out of the 57 known-risk factors were presented among the patients but none of them were associated with IRS group.
Conclusion: Only IRS group was associated with survival, probably due to the wide histological variety of these tumors. Multicenter and supranational studies are necessary to draw conclusions about other risk factors probably associated to prognosis.

PD-122

RARE NEONATAL AND EARLY INFANTILE TUMOURS: CHALLENGES IN MANAGEMENT

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Background/Objectives: Neonatal tumours and infantile tumours have varied presentations and diagnosis. The management is challenging and should be tailored case-based. We describe our experience with challenging tumours.
Design/Methods: To retrospectively review cases of challenging malignancies encountered in neonates and infants.
Results: Four cases of malignancies presented in the infantile age group over a period of nine months. The age at presentation varied from 34 weeks gestation to 3 months age. There were three females and one male. The presenting complaints included respiratory distress, poor urinary stream, haematuria with abdominal lump, neck mass and a sacral mass. The patient with abdominal lump had a large heterogenous enhancing mass occupying pelvic cavity in presacral region displacing Urinary bladder with rectal luminal compromise. Biopsy was suggestive of Embryonal Rhabdomycosarcoma. He was given half dose Vincristin, Adriamycin, Cyclophosphamide (VAC) chemotherapy. He did not tolerate chemotherapy and succumbed. Three patients were operated. The baby with respiratory distress had a thoracic mass occupying the whole hemithorax. He was started on VAC chemotherapy with a probable diagnosis of Neuroblastoma. However, the distress worsened and the baby was subjected to emergency thoracotomy. The final diagnosis was Congenital peribronchial myofibroblastic tumour. The 3 month old child with a neck mass was initially given bleomycin with a diagnosis of cystic hygroma outside before being referred to us. He was operated with a suspicion of cervical teratoma. The final diagnosis was infantile fibrosarcoma. The preterm girl with sacral mass was operated at 1 week age and diagnosed as a mature sacrococcygeal teratoma.
Conclusion: Neonatal tumours may present as thoracic, abdominal, sacrococcygeal or neck masses. Surgical excision should be the main crux of management in neonatal and infantile tumours. The histopathological report is more confirmatory after surgery. Neonates do not tolerate chemotherapy well and it should be reserved only for selected non-operable cases.

PD-123

TREATMENT AND PROGNOSIS OF SOLID MALIGNANT TUMOR WITH PULMONARY METASTASES IN CHILDREN

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Background/Objectives: To discuss the treatment and prognosis of malignant solid tumors with lung metastasis in children.
Design/Methods: Cases of malignant solid tumor with pulmonary metastasis in children enrolled from 2009 to 2014 were collected from department of pediatric surgery of Shanghai Xinhua Hospital. The Results were discussed including classifications, treatment, prognosis.
Results: A total of 10 cases (7 male and 3 female) age ranged from 21 months to 6 years with a median of 5 years, including 2 cases of hepatoblastoma, 5 cases of nephroblastoma, 2 cases of rhabdomyosarcoma, 1 case of medulloblastoma. In 9 cases, patients underwent biopsy or primary resection before chemotherapy. After 6-8 course of treatment, pulmonary metastasis was localized and stable which usually become 1 - 2 of peripheral pulmonary nodules. After thoracoscopic lung metastases resection, malignant tumor cells were detected with the same primary pathology in 9 cases while no active tumor cell was discovered in 1 case. After the surgery, chemotherapy was continued according to the plan. Patients were followed up for 2 months to 5 years.
Conclusion: Children with stage IV malignant solid tumors still should be treated actively. Resection and pathological examination is helpful in the evaluation of prognosis and making further treatment options in patients whose lung metastases is stable after chemotherapy and removal of primary tumor. Thoracoscopy- a minimally invasive technique, provides an acceptable option for parents.

Posters: Acute Lymphoblastic Leukaemia

P-001

MTHFR C677T, PT G20120A AND FV LEIDEN AS RISK FACTORS FOR THROMBOSIS IN EGYPTIAN PEDIATRIC ALL PATIENTS

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Background/Objectives: Thrombosis is a well-known side effect associated with Acute Lymphoblastic Leukemia (ALL) treatment leading to significant morbidity rates. Thrombosis occurrence in ALL patients seems to be due to the interaction between the disease, therapy and inherited thrombophilia. We aimed to assess the prevalence of FV Leiden, MTHFR (Methylene Tetra HydrofolateReductase enzyme) C677T &prothrombin (PT) G20210A mutations in Egyptian pediatric patients with ALL and its impact on the risk of thrombosis onset as well as to evaluate the impact of single versus multiple prothrombotic mutations on thrombosis.
Design/Methods: Sixty three pediatric ALL patients with thrombotic event treated with Total XV protocol at the Children's Cancer Hospital in Egypt and 63 matched ALL control patients were enrolled in the study. Restriction fragment length polymorphism technique was used to assess the prevalence of the FV Leiden and MTHFR C677T while Allele specific PCR was used for Prothrombin G20210A.
Results: MTHFR C677T prevalence between the ALL patients with and without thrombosis was 65% and 38.1% respectively (p value = 0.002), while FV Leiden prevalence was 17.5% and 15.9 % respectively, (p value= 0.81). Prothrombin G20210A prevalence was 3.2% in both groups.Patients who were older than 10 years or on SR/HR treatment protocol or in induction treatment phase showed higher risk of thrombosis. The risk of thrombosis was 3 folds more in patients with MTHFR C677T (OR =3.02), while FV Leiden and PT G20210A didn't affect the thrombosis risk. Having more than one mutation didn't show a significant effect on increasing the risk of thrombosis (p= 0.087).
Conclusion: MTHFR C677T is an important risk factor for thrombosis in Egyptian pediatric ALL patients. These results may help in the prediction of the thrombosis susceptibility for ALL patients and a prophylaxis therapy may be considered before having the thrombosis.

P-002

MATURE B CELL ACUTE LYMPHOBLASTIC LEUKEMIA PRESENTING WITH HYPERCALCEMIA

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Background/Objectives: Hypercalcemia is rarely observed in acute lymphoblastic leukemia. So far, all cases presenting with hypercalcemia are pre-B cell ALL. In this case, a mature B-cell ALL patient presenting with hypercalcemia is discussed.
Design/Methods: A three-year-old boy had a history of fever, weakness, swelling and pain in both kness. In the patient's blood smear, 93% L3 type blasts were seen and 90% L3 type large blasts with vacuoles were seen in the bone marrow aspiration smear.
Results: The flow cytometry results were as follows: CD10: 87%; CD19: 85%; KAPPA: 66%; and Lambda: 35% was compliant with mature B cell ALL. His calcium level: 15 mg/dl. Although previous cases imply that hypercalcemia is usually treated with pamidronate, calcium levels gradually decreased to normal levels within five days with intravenous fluid therapy, furosemide, and steroids in our case.
Conclusion: Consequently, hypercalcemia is rare in leukemia. So far, all cases presenting with hypercalcemia are pre-B cell ALL. It is important to know that hypercalcemia could be seen in the mature B-cell ALL.

P-003

NUTRITIONAL ASSESMENT AND SERUM ZINC CONCENTRATION IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKAEMIA

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Background/Objectives: Acute lymphoblastic leukaemia(ALL) is a common malignancy in children which may cause significant nutritional deficiency and affect the outcome of the patient.The study was done to identify the relationship of height, weight and serum zinc in children with acute lymphocytic leukemia (ALL).
Design/Methods: This observational study was carried out in the Department of Pediatric Haematology and Oncology, Dhaka Medical College Hospital, Dhaka over a period of one year from July 2013 to June 2014. All children ranging from 1 – 10 years with newly diagnosed ALL were enrolled as case. The diagnosis was made by means of bone marrow smears and immunophenotyping. An equal number of healthy children of similar age and sex were also included as control. The outcome measures werewasting and stunting in children< 5 years and BMI in children > 5 years of age. The serum zinc level was also studied as a measure of micronutrient status.
Results: The mean ages of the children of cases and controls were almost similar (p = 0.265). The groups were significantly different in terms of male/ female(p = 0.028). Majority (83.3%) of the children in the case group was wastedas opposed 22.2% in the control group (p < 0.001). About 38% the children in the case group were stunted as opposed to 16.7% in the control group (p = 0.031). The mean BMI was significantly lower in the case group than that in the control group (p < 0.001). Serum zinc level was also much lower in the ALL group than that in control (0.7 ± 0.1 vs. 1.5 ± 0.5 mg/dl, p = 0.003).
Conclusion: Children with Acute Lymphoblastic leukaemia may present with wasting and stunting and low BMI. Serum zinc level may also be reduced which may hamper various enzymatic functions in the body thereby reducing growth.

P-004

SERUM LEAD LEVEL IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Background/Objectives: There are some reports where serum lead levels were measured and change in concentration of serum lead level was found among acute Lymphoblastic leukemia (ALL) patients. The aim of this prospective study was to determine serum lead levels in patients with ALL.
Design/Methods: In this cross sectional study all children suffering from acute lymphoblastic leukemia ranging 2 to 12 years (30 patients) were evaluated for serum lead levels who were admitted at the Department of Pediatrics in DMCH, from February 2013 to January 2014. Serum level of age and sex matched healthy children were taken as control. Serum measurements for lead were performed by Atomic absorption spectrophotometer in Analytical Chemistry Laboratory of Atomic Energy Centre Ramna, Dhaka.
Results: Among the 63 children there was no significant difference in age and sex between the patients and control. The mean serum lead level of Acute lymphoblastic Leukemia patient group (234.8±162.9 g/L) was significantly higher than that of the control group (23.6±12.6 μg/L). There was significant difference of serum lead level in children with ALL and control group (p<0.05).
Conclusion: From the findings of the study it can be concluded that there is significant difference between Acute lymphoblastic Leukemia patient and normal control in terms of serum Lead (pb) level.

P-005

RESPONSE TO RE-VACCINATION IN CHILDREN AFTER TREATMENT FOR ACUTE LEUKEMIAS

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Background/Objectives: The aim of this study was to examine effectiveness of vaccination in pediatric patients with leukemia at least one year after the cessation of the treatment.
Design/Methods: The study was performed prospectively in 32 patients (28 ALL, 4 AML). Diphtheria, tetanus, acellular pertussis, hepatitis B, hepatitis A, measles-mumps-rubella (MMR) and varicella vaccines were applied to patients.
Results: Among leukemia patients, 71.8% of patients had complete protection against diphtheria, 84,3% against tetanus and 37,5% against hepatitis A before vaccination. All of seronegative patients achieved protective antibody levels after one dose against diphtheria, tetanus and hepatitis A. Forty-nine percent of patients were protected against pertussis and 37% against hepatitis B before vaccination. For pertussis, 66,7% achieved protective antibody levels after one dose, but only 55,5% for Hepatitis B. Thirty-four point four percent of patients were seropositive against measles before vaccination. 73,3 % of seronegative patients achieved protection after one dose. Seventy-eight point five percent and 71,9 % of patients were seropositive against rubella and mumps respectively before vaccination, all seronegative patients achieved full protection against rubella and mumps after one dose. Fifty-nine point four percent of patients were seropositive against varicella before vaccination. 87,5 % became seropositive after one extra dose.
Conclusion: In our study, patients had very good antibody response against to diphtheria, tetanus, hepatitis A, rubella and mumps vaccines at least 12 months after the cessation of therapy. Performing one booster dose appeared to be sufficient for all

groups. Protection after pertussis, hepatitis B, measles and varicella zoster vaccines were in moderate levels. The patients showed different antibody responses to vaccines, depending on age, the time passed after the cessation of treatment and their primary vaccination status. Antibody levels should be followed to evaluate the response obtained. A booster should be considered when there is a decrease or loss in these levels.

P-006

CNS EVENTS IN CHILDHOOD HAEMATOLOGICAL MALIGNANCIES DURING EARLY PHASE OF TREATMENT IN TERTIARY LEVEL HOSPITAL

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Background/Objectives: The purpose of this observational study is to evaluate the pattern of CNS complications along with risk factors during early phase of treatment in children with hematological malignancies.
Design/Methods: This observational study was conducted in 50 children with hematological malignancies (ALL, AML, NHL) who were admitting in paediatric haematology and oncology department of BSMMU Dhaka, from july ,2013 to june , 2014. After clinical examination and positive lab investigation findings, the diagnosed patients were treated according to specified protocol based chemotherapy and was evaluated during induction phase of treatment.
Results: During one year period, total 12 patients out of 50 (24%) showed CNS events. CNS complications included convulsion were 9 (75%), peripheral neuropathy 8(66.6%), change in mental status 8(66.6%), altered consciousness 8(66.6%), L-asperginase related suspected complication 5(41%), IT therapy related toxicity 4(33.2%), cerebral infection 2(16.6%), cranial nerve involvement with unilateral hemiplegia 2(16.6%). Based on history, clinical lab finding different possible risk factor or co-morbid conditions for this events were expected like thrombocytopemia (75%) with coagulation disorder , severe febrile neutroperia (66.6%) , history of traumatic IT therapy 3-4 days before CNS event (33.2%) , dyselectrolytaemia with hypocalcemia (16.6%), history of ear infection(16.6%), L-asperginase related complication (41%) and metabolic abnormalities (8.3%). Only 7 (58.3%) of out of 12 patients were recovered from complications.
Conclusion: Central nervous system (CNS) complications during treatment of childhood haematological malignancies remain a challenging clinical problem. This may be related to various factors like disease itself, chemotherapy induced neurotoxicity and to some co- morbid conditions along with the treatment method. As many of these neurological complications are treatable, early diagnosis and prompt treatment is essential to limit permanent damage.

P-007

OBESITY IMPACT ON SURVIVAL PROGNOSTIC AND RELAPSE IN MÉXICO'S STATE LINFOBLASTIC LEUKEMIA ACUTE CHILDREN'S

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Background/Objectives: In Mexico childhood cancer and obesity are public health problems. Malnutrition but not obesity, had been associated with a lower chance of survival and relapse. *Objective*: Assess the impact of obesity on the prognosis of survival and relapse in children with Lymphoblastic Acute Leukemia (LAL).
Design/Methods: We included in a cohort study, children with LAL. There were evaluated nutritional status at diagnosis, according to BMI in children, in search of Association of obesity and other factors with the presence of relapse of disease and survival using Kaplan-Meier and Cox regression.
Results: We evaluate 161 patients, 70% of patients with obesity of male gender of these 43% with all of very high risk. Obesity increased the risk of relapse (OR 3.6, IC95%1.7-7.6,p 0.001) of death (OR 3.4 95% 1.51-7.48 p0.002) and limited 52% to 77 months survival an Exp β of 3.35 in the Cox regression was obtained for patients with obesity and high risk leukemia.
Conclusion: In our patients, obesity increases the risk of relapse and decreases the survival time. Perhaps due to considerable increase in toxicity and some growth factors that determines poor response to the chemotherapy in neoplastic cells. Biological factors influencing the prognosis of the disease may not be modifiable however is essential to establish health policies aimed at early diagnosis and prevention of obesity and overweight.

P-008

DETERMINING FREQUENCY OF MORTALITY AND THE CAUSES OF DEATH IN PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Background/Objectives: During three decades with recent progress in chemotherapy regimens, the survival rate of children with ALL has improved significantly. But developing countries still have high mortality rate of patients with ALL. The present study examined the prevalence and causes of death in children with ALL.
Design/Methods: In this retrospective cross-sectional study, medical records of patients with ALL who referred to Ali-Asghar hospital during 2004-2012 and died during treatment, were studied. Information about demographic characteristics, cause of death, age, sex, WBC count, response to treatment, type of ALL, underlying disease, and recurrence were recorded. Data analyzing was performed using SPSS 18 software.
Results: In this study, 442 patients that have been referred to Ali Asghar hospital were included, which 80 of them (18%) were dead. Mean age of dead patients was 6.5±3.7 years and 63.8% of them were male.2.5% also had other underlying disease (down syndrome). WBC count in 76.2% was less than 50000 cell/mm3 and only 23.8% have more than 50000 cell/mm3. 61.25% of the patients had a relapsed during treatment. 35% had recurrence after treatment. The most common site of relapse was bone marrow (71.8%). Infectious causes included 72% of the causes of death. Among the infections, sepsis and pneumonia were the most common causes of death in patients with ALL. Also bleeding was the cause of death in 13.8% of the patients.
Conclusion: According to this point that the most common causes of death in ALL patients was infectious causes such as sepsis and septic shock and pneumonia, providing appropriate treatment and infection control measures, is essential to improve patients outcome and reduce mortality of patients.

P-009

OSTEOPOROSIS IN PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA TREATED ON MODIFIED ST JUDE TOTAL XV THERAPY

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Background/Objectives: Today,one of the challenges faced in treating children with acute lymphoblastic leukemia is steroid induced osteonecrosis which can be detected during and/or after therapy.
Design/Methods: To determine the incidence, risk factors and morbidity, we retrospectively collect the data in our single center on which Modified St Jude Total XV therapy was given since 2008. The St Jude Total XV protocol was adapted with minor modification which include high dose methylprednisolone (HDMP) treatment during remission induction, all other therapy was the same with the original one.
Results: There were 130 newly diagnosed ALL patients aged 1-17 years between 1 Jan 2008 and 1Jan 2014 at Hacettepe University Pediatric Hematology Department. Of these 130 patient, 4 were deceased during induction because of severe infection(n=2), tumor lysis syndrome(n=1) and traffic accident(n=1) and from those remaining 126 patients, there were 15(11.9%) patients diagnosed with osteonecrosis during the treatment period. The incidence was significantly higher among adolescent females($p<0.05$).The hip was the most frequently involved site however 5 patient had multiple skeletal sites involvement.
Conclusion: When we compare our results with the original protocol, the incidence of osteonecrosis seems to be much more higher (11.9% vs 6.4%)in our group. As we don't know the osteonecrosis associated genotype of these patients, we can not argue the genetic susceptibility. However, not only steroid but also L-Asparaginase and other known risk factors such as age, gender may facilitate this devastating complication.

P-010

IDENTIFICATION OF CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA AT LOW RISK FOR TUMOR LYSIS SYNDROME

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Background/Objectives: Tumor lysis syndrome (TLS) could occur before, during or after the initiation of chemotherapy in patients with hematologic malignancies. This study was designed to determine the prevalence and predictors of TLS in children with acute lymphoblastic leukemia (ALL) and to develop a sensitive prediction rule to identify patients at low risk of TLS.

Design/Methods: In this cross-sectional retrospective analytic study, one hundred and sixty children diagnosed as ALL in Ali-Asghar Children Hospital, Tehran were recruited from 1996-2010. Predictors of TLS were determined using univariate and multiple logistic regression analyses.
Results: TLS was diagnosed in 41 (25.6%) cases. The most common laboratory abnormality was hypocalcaemia observed in 30% of cases. Univariate analysis showed that splenomegaly [odd ratio(OR)= 2.38; P=.005], mediastinal mass (OR= 4.45; P=.003), T-cell phenotype (OR= 4.66; P=.001), central nervous system involvement (OR= 10.93; P=.001), lactate dehydrogenase ≥2000 U/L (OR= 3.88; P=.003), and white blood count (WBC) ≥20×109/L (OR= 4.18; P <.001) were predictors of TLS in these cases. Multiple regression analysis of variables that were available at presentation identified CNS and renal involvement, mediastinal mass, and initial WBC ≥ 20 × 109/L as independent predictors of TLS. When all 4 of those predictors were absent at presentation (n = 83 patients), the negative predictive value of developing TLS was 92.22%, with a sensitivity of 82.93%.
Conclusion: The above predictors could be used to evaluate the risk of TLS in patients with hematologic malignancies before initiative chemotherapy. Finding a model of independent factors to define a group of ALL children at low risk of TLS could be used to prevent excessive the monitoring and high cost of prophylactic treatment modalities.

P-011

CHROMOSOME 7 ABNORMALITIES IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKAEMIA

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Background/Objectives: Losses involving chromosome 7 are a rare cytogenetic abnormality in paediatric patients with acute lymphoblastic leukaemia (ALL) with unclear prognostic significance when treated on UK protocols.
Design/Methods: Cytogenetic results were obtained for all patients under 20 years of age with a confirmed diagnosis of ALL who were treated at the Royal Marsden, England from January 1995 to January 2015. Bone marrow and/or blood samples for cytogenetic study were processed for G-banded chromosome analysis following short-term culture using standard procedures.
Results: There were 279 patients with ALL for whom a chromosome study was successful. There were 15 patients (5.4%) with complete or partial loss of chromosome 7 involving 7q with median age at diagnosis of 10.6 years (range 3.1-19.9 years). Three patients had isolated monosomy 7 and one patient had 53 chromosomes. The other eleven patients had a complex karyotype including two patients with Philadelphia chromosome (Ph) in addition to monosomy 7 and two patients with abnormalities resulting in 7q-. Of 14 patients with available data, 3 had a diagnostic WBC > 50x 10^9/L and 9 patients (including both patients with Ph) had a rapid response to induction characterised by <25% blasts at Day 8/15. Both patients with Ph proceeded to transplant in first remission. 7 patients experienced a relapse (6) or had initial refractory disease (1). 3 of these patients subsequently died – one with refractory disease, one with secondary myelodysplastic syndrome post transplant and one with transplant-related hepatic failure. 12 patients remain alive to date (5 on maintenance treatment, 4 completed treatment in remission, 2 patients with relapsed disease currently undergoing allogeneic transplant, 1 Ph relapsed patient on nilotinib).
Conclusion: Chromosome 7 abnormalities in ALL patients in this series are observed more frequently in patients > 10 years and almost half of these patients experienced a relapse or had refractory disease.

P-012

POSSIBILITIES OF OVERCOMING DRUG RESISTANCE OF BLAST CELLS IN CHILDREN WITH RELAPSE OF ACUTE LYMPHOBLASTIC LEUKEMIA

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Background/Objectives: Relapses of childhood ALL are the main causes of treatment failures. Bortezomib (Velcade ®) can modify the sensitivity of tumor cells to chemotherapy.
Design/Methods: From June 2011 to January 2015 21 patients with relapsed ALL aged 2–21 years (8.6 years) were enrolled in this study. Boys were 15 (71,4%), girls – 6 (28,6 %). Very early revealed in 4 (26,7%), early in 4 (26,7%) children, late -in 7 (46,7%) pts. Chemotherapy consisted on induction (VCR 1.5 mg/m^2 N4, DNR 60 mg/m^2 N1, PEG-ASP 2,500 IU/ m^2 N4, PRED 40 mg/m^2 1–28 days, and bortezomib 1.3 mg / m^2 N4); two courses of post induction: 1) VP-16 100 mg/m^2 N5, CPM 440 mg/m^2 N5, MTX 5000 mg/m^2 N1, bortezomib 1.3 mg/m^2 N3 and 2) ARA-C 6000 mg/m^2 N4, ASP 6000 IU/m^2 N2.
Results: After induction CR achieved 12 (57,1%) children. After the second course – 2 (9,5%) pts. Three (14,4%) pts didn't achieve CR, one (4.8%) died from sepsis on day 23. Evaluation of MRD after the first course of chemotherapy performed in 10 patients (47,6%), and the level of MRD was less than 0.001% in 8 pts (38,1%).Now 6 pts (28.6%) are alive in CR, 1 of them relapsed after BMT. 4 (19.0%) had late isolated BM relapse B-ALL, two pts with late relapse of T-lymphoblastic lymphoma. Three (14.3%) pts with BM relapse underwent a SCT. Relapse developed in 2 (13.4%) children, both died, 6 (40%) died from sepsis (1 – induction death, 5 – in CR).
Conclusion: Thus, bortezomib in combination with standard chemotherapy allowed achieve CR in 66,6% pts, PR in 14,3%, and possibly long remission in pts with late relapse. This therapy is more effective for late relapses ALL and lymphomas.

P-013

NORMALIZATION OF LENGTH SPLEEN ON THE GROWTH OF PATIENT INCREASES IT STATISTICAL SIGNIFICANCE FOR FORECAST OUTCOME OF THE DISEASE IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Background/Objectives: Prognostic factors are used in oncology for selecting appropriate treatment regimens and for the comparative evaluation of it.
Results: The objective of the present study was to identify ways to elaborate independent prognostic indicators for patients with acute lymphoblastic leukemia (ALL) on the basis of the linear spleen size.
Design/Methods: In a retrospective study including 102 children of both sexes with acute lymphoblastic leukemia at the age of 1 to 18 years (median 5.42 years) who underwent the abdominal ultrasound before receipt of protocol treatment MB-2002, was evaluated the significance of ultrasonographic determination of the length of the spleen as of predictor of outcome of diseases. In order to mitigate influence of growth parameters in children of different ages the data were evaluated on based normalized value of the length of the spleen - NLS ((Normalized the Length of the Spleen)=spleen length/patients height). Calculation of the cumulative incidence of relapse was performed by the method of competing risks. Data were censored on 01.01.2014.The statistical differences between measures of frequency of relapse were determined using the Gray test. The differences between the compared parameters were considered statistically significant at $p < 0.05$.
Results: In the level of surveillance for 8 years cumulative incidence of relapse in ALL patients depending on the absolute size of the original length of the spleen in Groups less than or equal and more 12 cm (65 and 37 patients) was 13,2±4,5% and 25,9±7,5%; p=0.0308. In another groups formation (55 and 47 children) with normalized of the spleen length less than or equal 0.093 and more 0.093 they statistically more significantly were different for a cumulative incidence of relapse (8,7±4,4% and 29,1±6,9%; p=0.009).
Conclusion: The findings show prospects elaboration of morphometric normalized indicators associated with survival rates of children with hematologic malignancies.

P-014

VINCRISTINE HURTS!

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Background/Objectives: Vincristine is an important chemotherapeutic agent in the treatment of children with acute lymphoblastic leukemia (ALL). One of the side effects of vincristine is severe painful neuropathy, which is difficult to treat. In our unit this neuropathic pain is often treated with amitriptyline. So far, there is hardly anything described about the treatment of neuropathic pain in children with cancer. *Purpose*: The aim of this cohort study is to show how many children with ALL develop a neuropathy during the treatment with vincristine, how many children are treated with amitriptyline for this neuropathic pain and what is the effect of this treatment.
Design/Methods: We performed a retrospective cohort study, using questionnaires. The study population was a random sample; children (0-18 years) with ALL diagnosed and treated in the period from January 1, 2009 to November 1, 2011 at the Academic Medical Centre, Amsterdam.
Results: Thirty-four patients were enrolled, 71% completed the questionnaire (N = 24). 95.8% developed a symptomatic neuropathy, in 41.7% neuropathic pain was found. 33.3% were using pain medication for this neuropathic pain. Only one respondent used amitriptyline in combination with acetaminophen and tramadol. The mean pain score measured by VAS scale (scale range 0-10) without medication, was 5.6, (N=24). With medication they gave a score of 4.0 (N = 8).
Conclusion: Almost all children with ALL develop symptomatic neuropathy during the treatment with vincristine and give high scores in pain. Vincristine does hurt and there is yet a big profit to win in the fight against this neuropathic pain.

P-015

COMPARISON OF DIFFERENT METHODS FOR MINIMAL RESIDUAL DISEASE CALCULATION IN B LINEAGE ACUTE LYMPHOBLASTIC LEUKEMIA CASES AND DETERMINATION OF THE EASIEST METHOD FOR INDIAN LABORATORIES

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Background/Objectives: Flow cytometric minimal residual disease (MRD) evaluation is being widely used for evaluating treatment response and risk stratification in B-acute lymphoblastic leukemia (B-ALL). Level of ≥0.01% is considered prognostically significant. Different methods of MRD calculation are being used worldwide but no study has been published comparing these methods. In this study, we compared different methods of MRD calculation and its implication for Indian laboratories.
Design/Methods: Post-induction bone marrow specimens from 56 MRD positive B-ALL cases were studied for calculation of MRD using different methods. These methods include calculation of MRD out of M1] total nucleated cells (TNC) using 3-tubes assay, M2] TNC using 2-tubes assay, M3] TNC by Children Oncology Group (COG) method, M4] all viable cells using single-tube assay M5] all CD45+ cells using single-tube assay. M1 was considered as a method of reference. For statistical analysis (SPSS-16.0v), level of ≥0.01% and ≥0.1% were used for comparison of these methods.
Results: MRD value ranged from 0.002% to 19.386%. Mean, median and standard deviation values for M1 were 1.16%, 0.104% and 2.93% respectively. No statistically significant difference was found between methods M1, M2 & M3. For level 0.1%, M4 calculated 5.4% cases as negative and M5 calculated 2% cases as positive against M1. For level 0.01%, M4 calculated 2% cases and M5 calculated 5.4% cases as positive against M1. Technically M1 was time consuming and complex compared to M2 and M3. Although, M4 & M5 were quick and simple but showed minor discrepancies and were prone for subjective errors.
Conclusion: TNC based MRD calculation methods using Syto-dye are objective, of them M2 and M3 are easy and simple methods. M4 and M5 are cost effective, quick & simple however, prone for subjective variation and needs to be used cautiously.

P-016

PREVALENCE AND RISK FACTORS OF IRON OVERLOAD AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR CHILDHOOD ACUTE LEUKEMIA: AN LEA STUDY

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Background/Objectives: Iron overload (IO) is a common transplant-related complication in adulthood and is associated with an increased long-term morbidity and mortality. However there is no consensus on definition, incidence, risk factors, treatments and complications of IO after hematopoietic stem cell transplantation (HSCT) for childhood acute leukemia (AL). We conducted a prospective multi-centric long-term study to determine the prevalence and risk factors of IO in this population.
Design/Methods: All children under 18 years of age at diagnosis of AL undergoing HSCT (allogeneic or autologous) between 1980 and 2011 and included in the Leucémie de l'Enfant et de l'Adolescent program were eligible. IO was assessed by a serum ferritin level (SFL) ≥350μg/L without any inflammatory process. Among the 420 eligible patients, 379 (90.24%) had at least one recorded measure of serum ferritin and could be included.
Results: Prevalence of IO was 43.80% (166 patients) with a mean SFL at diagnosis of 1336.44μg/L (352-9052μg/L) at a mean of 3.56 years (1-22.8 years) post-HSCT. In univariate and multivariate analysis, independent risk factors of IO were age at HSCT (Odds Ratio (OR)=7.63 and 6.33 respectively for patients older than 12.68 years and aged between 8.23 years and 12.68 years; $p<0.001$), an allogeneic transplantation (OR=5.47 and 3.01 respectively for donors other than matched sibling donors and for matched related donors; $p<0.001$), and a significant graft versus host disease in allografted patients (OR=2.06; $p<0.005$). Recent transplantation period ($p<0.001$) and total body irradiation in preparative regimen ($p=0.043$) were significantly associated with a higher risk of IO only in univariate analysis.
Conclusion: IO is a frequent complication in pediatric long-term survivors post-HSCT for AL and its prevalence seems to increase over time. Further studies and prolonged follow-up of our cohort are warranted to confirm this and to determine the impact of IO on long-term morbidity and mortality in this population.

P-017

ROLE OF EZH2 IN LEUKEMOGENESIS AND DZNEP AS A THERAPEUTIC OPPORTUNITY IN HIGH RISK AND/OR RELAPSED PEDIATRIC B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA

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Background/Objectives: Epigenetic alterations carried out an important role in leukemogenesis and Polycomb group proteins (PRC2) represent a major class of epigenetic regulators in development and transcriptional repression. Deregulation of this histone modification can lead to epigenetic silencing of genes that promote differentiation and leads to leukemogenis. Evidences suggest that over-expression of the histone metil transferasi Enhancer of Zeste Homologue 2 (EZH2) is strongly associated with haematologic cancer progression and poor outcome. 3-Deazaneplanocin (DZNep) is the first molecular inhibitor of EZH2. We have studied EZH2 expression and pharmacological effect of DZNep with conventional chemotherapic agents as Daunoblastine (DBN) and Vincristine (VCR) in pediatric B-cell Acute Lymphoblastic Leukemia (B-ALL).
Design/Methods: We analyzed EZH2 expression levels by Real time PCR and Western Blot analysis in SUP-B15 cell line and in 33 B-ALL patients treated to Paediatric Oncology Service of Second University of Naples. SUP-B15 cell line were treated with DNB, DZNep and VCR, single and in combination. Cell viability assay was analyzed by MUSE 1.4 analyzer (Millipore). Apoptotic cell death and cell cycle were analyzed by Annexin-V- FITC staining and PI fluorescence.
Results: Our preliminary data show that EZH2 RNA was markedly expressed in our high risk samples (>1.2 fold) compared to normal bone marrow. SUP-B15 cell line expressed the highest value. EZH2 protein was detected in 9/33 samples B-ALL and in SUP-B15 cell line. IC_{50} value at 48 h was 12.5 μM, 1.5 μg and 12 ng for DZNep, VCR and DNB, respectively.
Conclusion: Pharmacological targeting of EZH2 might represent a potential feasible approach to be used as adjuvant treatment for making conventional therapy more effective on pediatric high risk B-ALL or in relapsed B-ALL.

P-018

OSTEONECROSIS : A COMPLICATION OF TREATING CHILDHOOD CANCER: A REPORT OF ZOLEDRONIC ACID THERAPY

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Background/Objectives: *Purpose*: To determine the incidence, risk factors, and morbidity for osteonecrosis (ON) in children with acute lymphoblastic leukemia (ALL) and Hodgkin lymphoma(HL) treated with intensive chemotherapy including multiple, prolonged and high dosis courses of corticosteroid. Patients and Methods: The occurrence of symptomatic ON was investigated retrospectively in 278 ALL and 152 HL children ages 1 to 18 years old receiving therapy for their cancer during 1995-2015 in İstanbul university Cerrapasa Medical Faculty pediatric Hematolgy-Oncology.
Results: ON was diagnosed in 4 patients 3 ALL and 1 HL (0.9%). All of the children were >12 years. Two of them were male. The symptoms were diagnosed within 6 months chemotherapy ended. ON was multifocal in all of patients. Girls' ON were found in hip junction while boys had in ankle and knee. Symptoms of pain and immobility were chronic in all, with only one having undergone an orthopedic procedure but three of them considered candidates for surgery in the future. Zoledronic acid was used in all except one for 6 times monthly and for 3 times for the other. Radiological and clinical relevant was achieved in all, only one had undergone operation.
Conclusion: Children ages >10 years who receive multiple courses of corticosteroid, are at significant risk for developing ON. These children must be given information for ON and be careful for extremity pain especially after their chemotherapy finished. Although fur ther evidence-based studies will be needed to precisely define the benefit of zoledronic acid in ON, our clinical experience on 4 children suggest that zoledronic acid may be safely used.

P-019

THE CLASSIFICATION AND COMMON GENETIC ABNORMALITIES IN CHILDREN WITH NEWLY DIAGNOSED ACUTE LEUKEMIAS AT HUE CENTRAL HOSPITAL, VIETNAM

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Background/Objectives: Traditionally acute leukemias (AL) was classified on the basis of morphology and cytochemistry. Accurate subclassification of leukemia is essential to guide therapy and to improve patients' outcome. The aim of this study was to implement immunophenotyping and detect the common genetic abnormalities to classify different subtypes of acute leukemia at Hue Central Hospital.
Design/Methods: This is a single institutional prospective study of 50 children newly diagnosed with AL from May 2012 to May 2014 at HueCentral Hospital. The diagnosis was confirmed by morphological FAB criteria, cytochemistry, immunophenotype.The molecular genetic screening test using Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR) was performed to detect fusion gene transcripts.
Results: Of 50 patients analyzed, there were 38 children with ALL and 12 children with AML, median age was 3.7 year(range 2 months to 15 years).Regarding ALL : L1 was common with 60.5%, L2 was less with 39.5% and L3 was rare.B cell ALL was common with 84.2%, T cell ALL was 15.8%. The frequencies of the genetic abnormalities were as follow: 9(23.7%) with t(12;21)/TEL-AML1, 2(5.3%) with t(9;22)/BCR-ABL , 3(7.9%) with t(4;11)/MLL-AF4, 4 (10.5%) with t(1,19)/E2A-PBX1.Regarding AML : M2 was common with 41.6%. M1 was 25.0%, M4 was 16.7%. M6 was 16.7%., The frequencies were :1(8.3%) with t(8;21)/AML1-ETO, 2(16.6%) with t(15;17)/PML-RARA, 1(8.3%) with t(16,16)/CBFB-MYH11, 2 (16.6%) with t(9;11)/MLL-AF931.6% of ALL and 41.7 % of AML had been chromosomal abnormalities. Hyperdiploidy were 21.1% of ALL and 25.0% of AML.
Conclusion: Diagnosis and classification of acute leukemia in Hue Central Hospital have improved by implementing immunophenotyping and detecting genetic abnormalities which can determine the subtypes of acute leukemia and to decrease errors of morphologic classification.The frequencies of the genetic abnormalities of our patients are higher than in the reported literatures.Our sample size is small; therefore, further study with larger sample size will be necessary to have the true frequencies.

P-020

DEATH ASSOCIATED WITH ACUTE LYMPHOCYTIC LEUKEMIA IN CHILDREN IN HEMATOLOGY AND PEADIATRIC ONCOLOGY UNIT

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Background/Objectives: Acute lymphoblastic leukemia (ALL) is the most common malignant disease in children. It represents 80% of acute childhood leukemia, with a frequency peak of 2 to 10 years. It is more common in boys (sex ratio 1.3 / 1). The purpose of this study is to describe the clinical and epidemiological profile and then deduct mortality's causes of ALL in children.
Design/Methods: It's a retrospective study over nine years (2006-2014), collecting patients aged from 3 months to 20 years. Diagnosis was confirmed by cytology and immunophenotyping. All of the patients were initially included in the MARALL protocol 2006.
Results: Three hundred and thirty-eight patients were treated for ALL from January 2006 to September 2014, with a male predominance (sex ratio: 1.70).The median age was 11.25 years. Hyperleukocytosis was found in 66.3% of cases. Sixty percent were of phenotype B and 34% of phenotypeT. Death occurs in 31.9%, relapse in 6.8%, Complete remission was obteined in 53.5% and 7.7% were lost of sight. In dead patients, 60% were aged over 10 years and 9.2% under 3 years. Two patients had a neurological localization and 5 tumor lysis syndrome. ALL T represents 20.3% and ALL B 33.3%. Hyperleukocytosis was in 19.4% with nine percent of non response to corticosteroid in prephase. A complex karyotype was found in 22 patients with the Philadelphia chromosome in 3 patients. . Eleven percent died in prephase, 25% in induction phase and 63% after remission. Death occurs after relapse (56.4%), after septic shock (13.8%), following drug toxicity (10.18%), before treatment (5.55%), hemorrhage (3.7%), lysis syndrome (0,92%) and non specific causes (14.8%).
Conclusion: Mortality associated with ALL remains a serious complication. Its rate still increased in our unit; so it is important to individualise prognostic groups and to adapt treatment protocol.

P-021

OPTIMIZATION OF FOUR COLOR MULTIPARAMETRIC FLOW CYTOMETRY PANEL TO DIAGNOSE PEDIATRIC LEUKEMIAS

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Background/Objectives: Acute leukemia remains an alarming problem and the second leading cause of death in children even with improvement in current chemotherapy regimens. Flow cytometry plays a vital role in the diagnosis and detection of this disease. At Texas Children's Cancer and Hematology Centers, a multiparametric flow cytometry approach using six color panel and 33 antibodies is used for the diagnosis and follow-up of pediatric leukemias. We investigated the diagnositc potential of a four color panel using 18 antibodies. Potentially, the six-color 33 antibody panel may be reduced to a four color 18 antibody panel without compromising diagnostic potential. A reduced panel would be better for diagnosis in developing countries.
Design/Methods: Retrospective analysis of thirty cases was independently performed by three clinicans. The immunophenotypic expression of 18 antibodies was employed for diagnosis. The cases used for this study consisted of 11 patients previously diagnosed with pediatric B-acute lymphocytic leukemia (B-ALL), nine with T-ALL, and ten with acute myeloid leukemias (AML) using the 33 antibody panel.
Results: The diagnosis of both B- and T-ALL cases by using the 18 antibody panel matched with the previous diagnosis. While 50% of the myeloid cases were diagnosed as AML using the 18 antibody panel by all three clinicians, the remaining 50% cases were grouped mostly as T-ALL.
Conclusion: This study shows that pediatric B- and T-ALL can be diagnosed with the limited 18 antibody panel. However, immumophenotypic abberencies of pediatric AML pose a challenge with the limited panel. Inclusion of intracytoplasmic staining should improve AML diagnosis.

P-022

IDENTIFICATION OF HOST GENETIC VARIANTS ASSOCIATED WITH MINIMAL RESIDUAL DISEASE IN PATIENTS WITH PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA

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Background/Objectives: Minimal residual disease (MRD) is the most significant prognostic factor in acute lymphoblastic leukemia (ALL). We aimed at identification of host genetic variants associated with MRD in patients with pediatric ALL.
Design/Methods: The study group included 174 patients treated according to ALL-IC BFM 2002 protocol, with informed consent and approval of local review board. The study combined a candidate gene approach and a replication of Genome-Wide Association Study (GWAS). It included 24 genetic variants; potentially involved in metabolism of drugs used in ALL: *MDR1* (rs3789243,rs2235046,rs1045642), *VDR* (rs2228570,rs1544410), *NR3C1* (rs6198,rs41423247), *GSTP1* (rs1695), *GSTM1* and *GSTT1* gene deletion, *TPMT* (rs1800460,rs1142345), *MTHFR* (rs1801133), *TYMS* (rs3474033–TSER*2, TSER*3, TSER*3G>C), *RFC* (rs1051266); in anti-tumor immunity: *CCR5* (rs333) and MRD-associated variants as revealed by GWAS: *IL15* (rs10519613), *NALCN* (rs7992226), *CCDC85C* (rs11160533), 3 intragenic variants (rs9871556,rs3862227,rs4888024). For genotyping High Resolution Melting (HRM), TaqMan Genotyping Assays, PCR/PCR-RFLP were used. Flow cytometry was used for MRD assessment at day 15, 33 and week 12.
Results: Significant differences were found in genotypes distribution of CCR5 (rs333;32 bp deletion) between patients with high vs. low/negative MRD levels (cut off 10^{-3}) at day 15 ($p=0.014$; Freeman-Halton extension of Fisher exact test for 2×3 contingency tables). Homozygous wild-type genotype was associated with low/negative MRD ($p=0.029$; Z-test). Significant differences were also found in MRD levels (as a continuous variable) at day 33 and week 12 between patients presenting different genotypes of *IL15* rs10519613 ($p=0,037$) and *RFC* rs1051266 ($p=0.015$) variants, respectively (Kruskal-Wallis ANOVA on ranks). For both *IL15* and *RFC* variants the highest MRD levels were observed in patients with AA genotypes, although *post hoc*

tests for verification of genotypes associated with highest/lowest MRD levels were inconclusive (p>0.05).
Conclusion: Host germline variation is a potential source of prognostic markers, available at the time of diagnosis, which might aid the improvement of risk assessment in ALL through their association with MRD.

P-023

CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA: REFUSAL AND ABANDONMENT OF TREATMENT IN SOUTHEAST OF IRAN

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Background/Objectives: Acute Lymphoblastic leukemia (ALL) accounts for one –fourth of all malignancies in children. ALL treatment is based on standard protocols and treatment abandonment is the main cause of treatment failure. Different factors such as treatment regimen, Socioeconomic Status (SES) and family cultural and educational background are the main cause of treatment abandonment in children with ALL. Therefore, this study aimed to assess effect of SES on the rate of treatment abandonment in children with ALL in southeast of Iran.
Design/Methods: This cross-sectional study was carried out in ALL patients in Zahedan city within April 2011 to May 2013. Study population including 22 children with different subtypes of ALL whom abandoned treatment. A structural questionnaire was filled up by patients or their parents, and the association of these factors with treatment abandonment were assessed with descriptive and analytical tests.
Results: Ninety patients that were diagnosed with ALL within April 2011 to May 2013 in Zahedan Ali Asghar hospital. The rate of treatment abandoned was 22(24.4%) in this area. majority of the patients were boys 60.9 % and with regard to ethnicity, 20 persons (90.9%) were Baluch and the other two, one was Fars and the other Afghan origin .Based on French–American–British (FAB) classification system, we had 18 patients (78.3%) ALL_L1 and 4(17.4%) had ALL_L2.The reasons of treatment abandonment in our study population was low family income, transportation difficulties, father´s education status, belief about cancer as a whole an incurable and life terminating disease and most of them relied on religious and spiritual beliefs for cure.
Conclusion: It seems that low income of patients' parents was the main reason for treatment abandonment in southeast of Iran. Financial problems in this area cause a high rate of treatment abandonment that can impose higher costs to the health care system of this country.

P-024

ACUTE LYMPHOBLASTIC LEUKEMIA IN PATIENTS WITH β-THALASSEMIA MAJOR

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Background/Objectives: β-Thalassemia major is a severe form of anemia that can causes new complications including malignancy. The immune imbalance is responsible for occurrence of different malignancies such as leukemia and lymphomas. In the condition like thalassemia multiple transfusions cause excess iron accumulation and result in generating toxic oxygen free radicals and therefore immune system modification and stimulate growth of infectious organisms. Thus, we assessed rate of malignancy in patients with β-Thalassemia major.
Design/Methods: This long-term (5 years) study was carried out on 30 patients with β-Thalassemia major as well as 30 healthy individuals as control groups. Both groups were regularly checked up for any malignancy with standard protocols in 6 months intervals. In any suspected case to malignancy, further confirmatory tests were performed.
Results: The mean age were 5.2 and 4.9 years in case and control groups respectively (0.08). Seventeen patients were male and all of patients were received defroxamine (DFO) for iron chelating therapy. The mean number of transfused packed cell during the study time was 108 and mean serum ferritin level was 570 (ng/dl). During the time of the study, we found two (a 3.5 years old male and 11years old female) out of thirty cases of patients with β-Thalassemia major who developed Acute Lymphoblastic Leukemia (ALL) while in control group we did not find any evidence of malignancy. Microscopic examination of both patients revealed ALL-L1 (FAB classification). Immunophenotypic analysis revealed the lymphoblast with following phenotypes: CD10-positive, CD19-positive, CD20-positive and CD22-positive in both cases. Molecular analysis demonstrated homozygous mutations that in female patient was IVSI-6 and in male one it was IVSI-5.
Conclusion: Co existence of thalassemia with leukemia emphasize that the possibility of occurrence of malignancy in thalassemia major patients that one possibility for this phenomena is the carcinogenic and toxic effects of excess iron resulted from multiple transfusions.

P-025

DISEASE OUTCOME FOLLOWING THERAPY MODIFICATIONS FOR METHOTREXATE NEUROTOXICITY IN ACUTE LYMPHOID LEUKEMIA

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Background/Objectives: Central nervous system (CNS) therapy is a significant management problem for patients with acute lymphoid leukemia (ALL) who develop methotrexate neurotoxicity (MTX-N). Symptoms include transient events, seizures, hemiparesis or severe necrotizing encephalopathy. Few have reported clinical outcomes following therapy modifications for MTX-N. We report the clinical outcomes of 22 patients with ALL and MTX-N diagnosed between 2011-2014.
Design/Methods: Twenty five events were reported in 22 patients with ALL risk status defined as: high risk or very high risk -16; standard risk – 6; CNS 1 -19; CNS 2 – 2; CNS 3 – 1. Treatment was on or according to COG AALL0232, AALL0932 or AALL1131. Our institutional guidelines include: MRI at time of event and 4-6 weeks later; withholding intrathecal (IT) therapy for 4-6 weeks. If physical findings and MRI changes (diffusion restriction / acute changes) resolve, retreatment with IT MTX plus leucovorin (ITM/LCV) is considered. If physical findings resolve but minor MRI changes remain, IT hydrocortisone / araC (ITH-A) are recommended until MRI normalizes. IT therapy is withheld in patients with persistent physical findings or acute / worsening MRI changes.
Results: MTX-N events by phase of therapy: Consolidation (4), Interim maintenance I (IM-I) - high dose MTX (8), IM-I - Capizzi MTX (2), Delayed intensification (5), IM-II (3), Maintenance (3). Management for patients included: ITM/LCV (4); ITH-A (8); ITH-A and ITM/LCV (10). Events included: Mild TIA/weakness (11), severe TIA (10) and seizure (4). Three patients had second events post ITM/LCV. Eleven patients have been off therapy a median of 9 months. Eleven remain on therapy and 8/11 will complete therapy within one year. One patient had a CNS relapse following ITM/LCV.
Conclusion: Modifications as described for MTX-N are adequate to maintain disease control while posing minimal risk. ITM/LCV may offer a greater risk of a second event occuring.

P-026

PROFILE OF CHILDHOOD CANCER IN CENTRAL SUDAN

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Background/Objectives: In Sudan it is still difficult to know the extent of cancer and its profile among children. This study was conducted to find out the pattern of childhood cancer in a tertiary referral center in a sub Saharan African country.
Design/Methods: It was a retrospective descriptive study. Data was retrieved from medical records of all paediatric patients who were registered at the National Cancer Institute, Sudan over the period from January 1999 to December 2013.
Results: During the study period a total of 766 children below 15 years of age were registered. The predominant age affected was observed in 0 to 5 years age group. The frequency of cancer was found to be higher among boys with a male to female ratio of 1.3:1. Majority of the children were from rural areas. Leukemia (36.9%), lymphoma (26.3%), retinoblastoma (9.8%) and nephroblastoma (9.5%) were the commonly found childhood cancers among the study population. Other less commonly found cancers were neuoroblastoma (7%), central nervous system tumours (6.4%), soft tissue sarcoma (3.7%), bone tumours (3.4%) and nasopharyngeal carcinoma (3.4%). Lymphoma and central nervous system tumours occurred in higher frequency in boys (27 % and 7% respectively) compared to girls (17% and 4 % respectively), whereas retinoblastoma and nephroblastoma occurred less frequently in boys (7% and 6.5% respectively) than girls (11% and 10% respectively).
Conclusion: This study provided some knowledge about the situation of childhood cancer in Sudan and showed that leukaemia and lymphoma represent about 60% of all cases. A dedicated paediatric cancer registry is essential to find out the real incidence, types and survival of childhood malignancies Sudan.

P-027

HAPLOIDENTICAL HEMATOPOIETIC STEM CELL TRANSPLANTATION USING A REDUCED-INTENSITY CONDITIONING REGIMEN WHICH CONSIST OF RITUXIMAB AND MESENCYMAL STEM CELL CO-INFUSION IN CHILDREN: PRELIMINARY RESULTS

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Background/Objectives: Haploidentical stem cell transplantation (haplo-HSCT) has been developed as an alternative transplant strategy for children with hematological disorders without a HLA matched donor. Reduced-intensity conditioning (RIC) regimens allow haplo-HSCT with less toxicity, but graft versus host disease (GVHD) remains still an actual problem. T cell receptor (TCR) α and β/CD3 depletion for the prophylaxis of GVHD achieved a significant success in haplo-HSCT. The aim of our study is to investigate the efficacy of rituximab (RTX) and mesencymal stem cell (MSC) administration for GVHD prevention in haplo-HSCT.
Design/Methods: We analyzed the outcome of fifteen pediatric patients who underwent haplo-HSCT using a RIC regimen and TCR$\alpha\beta$ /CD3 depletion from January 2014 to March 2015. To prevent EBV related posttransplant lymphoproliferative disease and GVHD, RTX was added into conditioning regimen. MSC was co-infused to suppress alloreactive donor anti-host T-cell responses and to use their ability to promote angiogenesis and support micro-environment, which facilitate engraftment.
Results: Reducing α/β of the graft was 99.9%. The grafts contained a median of 28.91×10^6 CD34+ cells. Ten patients engrafted with full donor chimerism. Two patients were mix chimeric. Graft rejection occurred in three patients. Three patients developed grade 3-4 acute GVHD. CMV, Adeno and BK virus reactivation were seen in 3, 3 and 4 patients respectively. None of the patients developed EBV reactivation after HSCT. Severe bacterial infection was seen in three patients after HSCT. Two patients were died and transplant related mortality at day 100 was 13.3%. Our data at +30, +60 and +90 from engraftment showed delayed immune reconstitution.
Conclusion: These data indicate that a selective graft manipulation and MSC results into effective prevention of acute GVHD, rapid recovery of neutrophil and platelet counts without severe complication at acute phase of HSCT and low TRM. Following investigation of advantages and risks of Rituximab and MSC application are required.

P-028

IMPACT OF TRAUMATIC LUMBAR PUNCTURE ON CLASSIFICATION OF CNS LEUKEMIA AND OUTCOME FOR CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA TREATED UNOP PEDIATRIC HOSPITAL IN GUATEMALA

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Background/Objectives: Background: Traumatic lumbar puncture (LP) at diagnosis of acute lymphoblastic leukemia (ALL) can confound the classification of central nervous system (CNS) status and increase the risk of CNS relapse. Traumatic LP rates can be decreased by performing procedures under anesthesia, assuring an adequate platelet count prior to the procedure, and allowing only experienced practitioners to perform the first LP, but implementation of such measures is not universal.
Design/Methods: Procedure: Lumbar puncture practices, the incidence of traumatic LP, CNS risk classification, and outcomes of patients with ALL consecutively diagnosed from May 2007 through December 2012 at the National Pediatric Oncology Unit of Guatemala were analyzed to identify opportunities to improve the quality of care. Traumatic lumbar puncture was defined as at least 10 red blood cells per microliter of cerebrospinal fluid.
Results: Of 587 consecutively diagnosed patients, 3 died prior to their first LP and 114 (19.5%) of the remaining 584 evaluable patients had a traumatic LP. Rates of traumatic LP varied by year ranging from 13.1% (n=130) to 23% (n=103).
Conclusion: A quality improvement project is needed to improve modifiable risk factors for traumatic LP at diagnosis in Guatemala to avoid unnecessary classification to a higher CNS status and extra chemotherapy/radiation secondary to traumatic LP and decrease the rates of CNS relapse that may be secondary to traumatic LP at diagnosis.

P-029

HAS THE TIME COME FOR EFFECTIVE TREATMENT OF CHILDREN WITH PHILADELPHIA CHROMOSOME-POSITIVE ACUTE LYMPHOBLASTIC LEUKEMIA IN CHINA? A RETROSPECTIVE STUDY FROM CHINESE CHILDHOOD CANCER GROUP

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Background/Objectives: This study was designed to provide descripitive review then improve our understanding of barriers to effective treatment of pediatric Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph^+ ALL) in China.
Design/Methods: We collected and centrally reviewed medical records of children with Ph^+ ALL who were treated by 6 large single institutions in China between 2005 and 2012. Follow-up observations extended through September 30, 2014. All patients were assigned to therapy for high-risk ALL or very high-risk ALL. Allogeneic hematopoietic stem-cell transplantation (alloHSCT) was indicated for all patients in first complete remission. Post-induction imatinib was introduced into the chemotherapy regimens recently.
Results: One hundred and seventy-nine patients (118 boys and 61 girls) with Ph^+ ALL were identified from 4439 patients who were newly diagnosed at the 6 participating institutions. Of the 127 patients who achieved remission by the end of initial phase of induction therapy, 87 were treated with chemotherapy alone, 22 underwent alloHSCT with or without imatinib and 18 treated with chemotherapy combined with continuous imatinib. Abandonment (42.1%) was the leading cause of therapeutic failure. However, the abandonment rate decreased by 25% from 2005 to 2010 (50.5%) to 2011 to 2012 (25.7%). The mortality related to transplant was 20.8%. There is no toxic death related to imatinib. The 2-year event free survival (EFS) was 36.8± 6.1% in chemotherapy only cohort, 61.8± 10.7% in alloHSCT cohort and 72.2 ± 10.6% in imatinib cohort ($P = 0.002$). The difference in EFS was not significant between the alloHCST and imatinib cohort ($P = 0.92$).
Conclusion: AlloHSCT is not readily available for children with Ph+ ALL in China. The growing evidence for the benefit of imatinib for pediatric Ph^+ ALL and the economic growth most contribute to the abandonment rate decline between 2005 and 2012. With the generic imatinib getting into market, including imatinib in the therapy would be feasible in China.

P-030

POLYMORPHISMS IN MICRORNAS COULD AFFECT MTX CLEARANCE IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA

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Background/Objectives: Methotrexate (MTX) is a key component in the treatment of childhood Acute Lymphoblastic Leukemia (ALL). Treatment with high-dose MTX often causes toxicity, requiring a dose reduction or cessation of treatment, which has been demonstrated to reduce survival. Therefore, it would be useful to identify a predictor of the adverse effects of MTX. In the last years, several studies have investigated the relationship between genetic variations and MTX toxicity. Nevertheless, most of these studies have focused on coding regions. Nowadays, it is known that genes that do not codify proteins, like microRNAs (miRNAs), can regulate genes involved in drug transport. Recently, it has been described that SNPs in miRNAs could alter miRNA function. In fact, MiRNA related-SNPs have been already associated with MTX toxicity. Therefore, the aim of this study was to determine if SNPs in miRNAs could be useful as new MTX toxicity markers in pediatric B-ALL treatment.
Design/Methods: DNA from blood of 180 children with B-ALL during complete remission and treated with the LAL/SHOP protocol were analyzed. MTX plasma levels were used as an objective and quantifiable marker of toxicity. 235 SNPs in 222 miRNAs were studied. VeraCode GoldenGate platform was used.
Results: Interestingly, we found 2 SNPs in one miRNA targeting the transporter SLC46A1 gene, significantly associated with MTX clearance.
Conclusion: Our results suggest that polymorphisms in miRNA genes may affect the risk of MTX toxicity in childhood ALL. Acknowledgements This project was supported by RETICS (RD/12/0036/0060 and RD/12/0036/0036) and Basque Government (IT661-13, S-PE12UN060).

P-031

POLYMORPHISMS AND VINCRISTINE TOXICITY IN PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA

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Background/Objectives: Vincristine is an important component of treatment protocols for acute lymphoblastic leukemia (ALL). However, vincristine can cause neurotoxicity, a disabling adverse effect that can affect the quality of life of the patients. This neurotoxicity can lead to dose reduction or treatment discontinuation, which can have an impact on survival. Nowadays, one of the challenges in medicine is to predict which patients are going to respond to a treatment based on their genetic characteristics in order to adjust the treatment from the beginning.The mechanism of action of vincristine is based on its binding to beta-tubulin, which causes the inhibition of microtubule assembly and cell cycle arrest. In the nervous system, the binding of vincristine to beta-tubulin leads to severe alterations in axonal microtubules, resulting in axonal swelling and nervous fiber damage that disturbs both sensory and motor functions that are characteristics in neurotoxicity. Recently, a genome-wide association study in 2 independent cohorts of childhood ALL patients found a polymorphism in the promoter region of *CEP72* that was associated with increased risk of vincristine-related neurotoxicity. *CEP72* gene encodes a centrosomal protein essential for microtubule formation, and vincristine exerts its pharmacologic effects by inhibiting microtubule formation.The aim of this study was to replicated the polymorphism of CEP72 in a spanish cohort of childhood B-ALL patients and determine if other polymorphism in microtubule-related genes are associated with vincristine neurotoxicity.
Design/Methods: DNA from blood of 152 children with B-ALL during complete remission and treated with the LAL/SHOP protocol were analyzed. 22 SNPs in 7 genes were studied.
Results: We found several polymorphisms in these genes significantly associated with vincristine toxicity.
Conclusion: Our results suggest that polymorphisms in microtubule-related genes may affect the risk of vincristine toxicity in childhood ALL. This project was supported by RETICS (RD/12/0036/0060 and RD/12/0036/0036) and Basque Government (IT661-13, 2012111053).

P-032

MORBIDITY AND MORTALITY DURING INDUCTION CHEMOTHERAPY OF PAEDIATRIC ACUTE LYMPHOBLASTIC LEUKAEMIA: REPORT FROM COMBINED MILITARY HOSPITAL RAWALPINDI, PAKISTAN

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Background/Objectives: To analyze pattern of morbidity and mortality during induction chemotherapy of paediatric Acute Lymphoblastic Leukaemia (ALL).
Design/Methods: Prospective descriptive study conducted at Paediatric Oncology department, Combined Military Hospital Rawalpindi, Pakistan. All newly registered cases of ALL between 1 to 18 years of age during three years of study from 1st January 2012 to 31st December 2014 were included.
Results: Out of 241 patients with ALL, 169 (70%) were males and 72 (30%) were females. The mean age was 6.2 years with a range from 15 months to 17 years. The mean duration of symptoms before reporting to oncologist was 41 days with a range from 3 to 305 days. Diagnosis was Pre-B ALL in 176 (73%), T-ALL in 26 (10.8%), Lymphoblastic lymphoma in 10 (4.2%) cases, 29 (12 %) cases were diagnosed as ALL on basis of morphology only. Cytogenetics was available in 72 (29.8%) cases. Only 11 (4.6%) cases had CNS disease at the time of diagnosis. The patients were treated according to standard arm of UKALL2011 protocol. One hundred and twenty seven (52.7%) cases were categorized as high risk and were treated with four drugs (regimen B induction) and 114 (47.3%) patients were of standard risk and were treated with three drugs (Regimen A). the major problems in induction were; infection in 158 (65.6%) cases, proximal myopathy in 75 (31.1%) cases, drug induced hepatotoxicity in 18 (7.5%) cases and neuropathy in 12 (5%) cases. Eighteen (7.46%) patients died during induction chemotherapy, 12 (66.6%) due to infection, 3 (16.7%) due to bleeding and 2 (11.1%) due to hepatic failure and one (5.5%) due to Anthracycline induced cardiotoxicity.
Conclusion: Infection and proximal myopathy are the major concerns during induction chemotherapy. Infection alone or in combination with other factors is the major cause of death during induction chemotherapy.

P-033

PENTOXIFYLLINE INCREASES APOPTOSIS AND REGULATES A PROAPOPTOTIC GEN EXPRESSION PROFILE IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA DURING INDUCTION TO REMISSION PHASE (STEROID WINDOW)

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Background/Objectives: Acute lymphoblastic leukemia (ALL) is the most common childhood cancer. Pentoxifylline (PTX) increases chemotherapy-induced apoptosis. A pre-treatment window clinical trial was developed to evaluate whether PTX increases apoptosis and gene expression profile in ALL during the induction steroid window phase.
Design/Methods: Thirty-two children with a new diagnosis of ALL were randomly assigned to receive prednisone (PRD 40 mg/m^2/day) only during the 7-day treatment pre-phase (PRD group, n=11) or to receive PRD with PTX (10 mg/kg/day) (PTX group, n=11); the control group included children with normal bone marrow (n=10). Bone marrow aspiration was performed at diagnosis in all groups, and at the end of PRD window for patients with ALL (PRD and PTX groups). Apoptosis was evaluated by flow cytometry using Annexin V-Flourescein isothiocyanate /Propidium iodide stains. Gene expression profile was performed by microarray and sq-PCR.
Results: Apoptotic index at diagnosis was similar in all groups. After treatment, apoptosis was significantly higher in the PTX group than in the Prednisone group ($p < 0.04$). There were no serious adverse effects observed for PTX. Expression of wide number of genes was regulated by PTX between the PRD group and the PTX group (170 and 875 genes respectably $p<0.01$). PRD and PTX groups showed a proapoptotic gene expression profile. PTX when added to PRD induced the expression of proapoptotic genes involved in the death inducing signaling complex formation (CASP8, RIPK1 and TNFIP3L). The intrinsic pathway was also affected by the BNIP3L and p53 regulator BCL11A.
Conclusion: PTX potentiates blast apoptosis induced by PRD in children with ALL during steroid window phase. Experimental reports suggest that PTX induce inhibition of NF-κB, inhibiting survival genes facilitating apoptosis. PTX promote apoptosis by inducing the expression of extrinsic as well as intrinsic pathway genes. At the present time we are conducting a study to conclude this hypothesis.

P-034

RESULTS OF HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR HIGH RISK PEDIATRIC LEUKEMIA: THE EXPERIENCE IN A SINGLE-CENTER IN MÉXICO

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Background/Objectives: Hematopoietic stem cell transplantation (HSCT) offers an opportunity to cure children with high-risk leukemia. We describe the results of this procedure in our Center.
Design/Methods: From March 2003 to May 2014, fifty-nine pediatric patients with high-risk leukemia aged 1 to 20 years underwent HSCT. Status disease were: ALL 1st CR:10, ALL 2nd CR:13, ALL 3rd CR:4 , AML: 22, CGL non responsive to imatinib:8, MMJL:1, Secondary LLA:1. All conditioning regimens were myeloablative. GVHD prophylaxis consisted in cyclosporine plus methotrexate.
Results: Stem cell sources included: Bone Marrow (BM) in 71%, Peripheral Stimulated Blood (PSB) in 12% and Cord blood (CB) in 17%. Fifty patients received Allogenic HSCT while 9 AML patients autologous HSCT. Medium infused CD34 cells/Kg for Bone Marrow group were 3ˆ6, in CB group 0.21ˆ6 and in PSB group 5ˆ6. Engraftment succeed in 53 patients, 6 patients had graft failure. Average Neutrophil engraftment occurred on day +17 in BM and PSB patients while in UCB on day +28. Platelet recovery was achieved in average at day +20 in BM and PSB patients while in UCB at day +34. Acute GVHD was diagnosed in 45% of patients being grade I-II in 60% and Grade IV in 40%. Mild cGvHD occurred in 10 patients. Currently, 61% of patients are disease free with a follow-up of 45 months. Main cause of death was Leukemic progression in 52% followed by aGVHD in 22%, CMV infection after day 100 in 9%, graft failure in 9%, sepsis in 4% and VOD 4%.
Conclusion: HSCT is a valuable treatment in high-risk pediatric leukemia, reaching 61% of cure in our series. Mean cause of death post transplantation still being leukemic relapse. In our population most cases of chronic GvHD were mild to moderate, probably because we use BM and CB a source of hematopoietic progenitors.

P-035

ACUTE LYMPHOBLASTIC LEUKEMIA PRECEDED BY STEROID RESISTANT NEPHROTIC SYNDROME – CASE REPORT AND REVIEW OF LITERATURE

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Background/Objectives: Infections, tumour lysis, leukemic infiltration and drug toxicity usually account for renal involvement in Acute Lymphoblastic leukemia (ALL). Mostly, renal disease develops following the onset of ALL.
Design/Methods: We describe the clinical course and management of a child, in whom nephrotic syndrome (NS) preceded the diagnosis of ALL, with a review of pertinent literature.
Results: A 6 year old boy presented with fever, abdominal pain, vomiting, oliguria, pallor, anasarca and hypertension. Investigations revealed deranged renal functions, albuminuria(++++) and hypoalbuminemia(1.9 g/dL). Initial blood counts showed: Haemoglobin 8.2g/dL, platelet count 1,98,000/μL, total leucocyte count 6000/μL, with a differential count of neutrophils 60%, lymphocytes 27%, eosinophils 4% and monocytes 8%. Peripheral smear showed no abnormal cells. Ultrasonography showed bilateral bulky kidneys. P-ANCA was positive by immunoenzymatic assay (repeated twice). Renal biopsy showed gross tubular necrosis with mesangial and segmental sclerosis. He showed initial improvement on steroids and intermittent hemodialysis. However, proteinuria persisted. Later, Tacrolimus was added for steroid resistant NS. During 4th month of treatment, he developed fever. Investigations showed thrombocytopenia with peripheral smear showing 11% blasts. Bone marrow evaluation confirmed precursor B-cell ALL. He was started on induction chemotherapy (BFM95 protocol). He developed sepsis on day 10 of chemotherapy, requiring antimicrobials, ventilation and inotropes. He developed intracranial haemorrhage on day 15, requiring decompressive craniotomy. He continued to receive non-myelosuppressive chemotherapy. His progressively worsening renal function required hemodialysis. Despite all, he developed septic shock, multi-organ failure and finally succumbed on day 34 of chemotherapy. Previously, 5 children were reported to develop ALL, 5 – 84 months after a diagnosis of NS. All 5 achieved remission, though renal problem persisted in all.
Conclusion: This child had no clinical or laboratory clues of malignancy at initial presentation. The exact pathogenesis for the co-incidence of these two disorders is still not clear. High index of suspicion is essential.

P-036

IMMUNOPHENOTYPIC, CYTOGENETIC AND CLINICAL FEATURES OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA: A DEVELOPING COUNTRY EXPERIENCE

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Background/Objectives: Immunophenotyping has great importance for diagnosis, classification and prognosis of acute lymphoblastic leukemia (ALL). However, with resource constraints the complete work up can not be carried out in many cases. We investigated the immunophenotypic subtype of ALL and its association with cytogenetics and clinical features.
Design/Methods: A total of 210 children with ALL were studied for their clinical presentation. Immunophenotyping was carried out in 165 children by flow cytometry using a panel of monoclonal antibodies. 56 patients were also subjected to karyotype analysis by G-banding technique.
Results: Mean age of the patients was 6.4 years .with male to female ratio of 1.6:1. 28.1% patients had cell count $>50 \times 10^9$ /L of which more than half had counts of $>100 \times 10^9$ /L. 3.3% patients had prominent musculoskeletal manifestations. 5.7% had nephromegaly. 2.9% had central nervous system symptoms. Another 3% patients had positive blats in CSF without CNS symptoms. 18.8% were identified as T-ALL and 81.2% as B-ALL. Among B-ALL, 4.4% were identified as Pro-B ALL, 69.2% as Common ALL, 24.2% as Pre-B ALL and 2.4% as mature-B ALL. Myeloid antigen (MyAg) expression was documented in7.9% of patients. Myeloid positivity was more in patients with T-ALL (12.9%) than B-ALL (6.7%). Myeloid positivity was associated with high cell count ($>50 \times 10^9$ /L). CD13 was the most commonly expressed antigen. Of the 56 patients karyotyped, 3 (5.4%) were positive for ph chromosome. 6 had hypoploidy, 2 had hyperploidy, 5 had monosomy and 7 had trisomy.
Conclusion: More number of patients showed high risk features such as hyperleucocytosis and T cell disease compared to previously reported studies from developed countries.

P-037

IMPACT OF EARLY INVASIVE FUNGAL INFECTIONS ON CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA THERAPY AND OUTCOME

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Background/Objectives: The objectives of this study were to investigate the frequency and mortality rates of invasive fungal infections and to assess the impact of these infections on the timely application of chemotherapy regimens during induction and consolidation therapy in pediatric patients with acute lymphoblastic leukemia (ALL).
Design/Methods: This is a retrospective cohort study analyzed patients below the age of 18 years with ALL, receiving chemotherapy for remission induction and consolidation therapy from January 2012 to December 2012. Patients were evaluated for frequency of invasive fungal infection (either probable or proven fungal infection). Also dates of chemotherapy that given during these phases and any changes in the schedule was reported.
Results: During the study period, 96 patients were enrolled with median age of 5 years, and male/female ratio was 1.5:1. According to Total XV St. Jude protocol, 48 patients (50%) were low risk, 47 patients (49%) standard risk, and one high risk. Infection was the most common complication during induction and consolidation as it was reported in 42 patients (43.7 %), 19 patients (19.8%) had probable fungal infection, 13 (13.5%) with documented bacterial sepsis, and 10 (10.4%) with soft tissue infections. The total deaths during induction and consolidation were 16 patients (16.70%) (All of them died during induction), the most common cause of death was sepsis (9.4%), followed by fungal infection (3.1%). Median duration of treatment delay during induction and consolidation therapy was 31 days in patients with invasive fungal infection compared to 8 days without IFI (P.valu <0.001).
Conclusion: Infectious complications during induction therapy are still a major problem affecting the outcome of the childhood ALL. High incidence and the attributable mortality rate of fungal infections during ALL induction as well as their impact on chemotherapy schedule may call for the antifungal prophylaxis during this phase of treatment.

P-038

LUNG TRANSPLANTATION OF PEDIATRIC BRONCHIOLITIS OBLITERANS PATIENTS AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION : A SINGLE CENTER EXPERIENCE

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Background/Objectives: Bronchiolitis obliterans (BO) is a lung involvement of chronic graft-versus-host-disease after allogeneic hematopoietic stem cell transplantation (HSCT). In severe progressive BO unresponsive to immunosuppressant therapy, lung transplantation (LTx) can be a treatment option for patients. There are only a few reports about pediatric LTx for BO hence we here present patients who have undergone LTx with BO in our center.
Design/Methods: We retrospectively reviewed data of patients who had allogeneic HSCT from 2008 to 2014 and developed BO. Clinical characteristics, treatment modality, imaging studies as well as results of pulmonary function test (PFT) have been collected.
Results: Among 119 patients who received allogeneic HSCT, 18 (15.1%) were diagnosed as BO. Their primary diagnosis were ALL in 9 patients, AML in 5, lymphoma in 2, Krabbe's disease in 1 and Ewing sarcoma in 1 patient. As one patient with relapsed ALL had been transferred for the BO treatment, total 19 patients were evaluated. Median duration of BO development is 7.3 months (range, 3.6-19.3) after HSCT. There were two who had been enrolled to LTx candidate and died before surgery and five patients (26.3%) with continuous falling of PFT parameters were able to received LTx. One patient expired because of pneumonia which progressed to multi-organ failure after 102 days of LTx, three has been shown improved lung function after LTx, and one patient just received LTx three weeks ago. The longest survival after LTx is 10.5 months. Among 12 patients who were not on waiting list of LTx, five patients expired, all due to direct or indirect influence of BO.
Conclusion: The mortality of BO is 42.1% in our study, 25% in LTx patients. Patients' 5 year overall survival rate is $48.0 \pm 5.4\%$. LTx could be considered as effective treatment for pediatric patients with BO, although long term follow up of patients are needed.

P-039

PEDIATRIC-INSPIRED VERSUS HYPERCVAD PROTOCOLS FOR PHILADELPHIA-NEGATIVE ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) IN ADOLESCENTS AND YOUNG ADULTS (AYA): AN NNT ANALYSIS

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Background/Objectives: ALL treatment outcomes in adolescents and young adults (AYAs, ages 16-39 years) are poorer relative to children due to age-associated cytogenetic features and treatment differences. Compared with adult protocols,

pediatric treatment protocols generally contain higher cumulative doses of nonmyelosuppressive agents including L-asparaginase. HyperCVAD is an asparaginase-free chemotherapeutic regimen widely used to treat AYAs and adults with ALL. The hyperCVAD regimen consists of 2 alternating cycles: fractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone (Cycle-A); and high-dose methotrexate and cytarabine (Cycle-B). While treatment of AYA patients with hyperCVAD is common in the US, noncomparative data suggest that outcomes may be inferior to pediatric-inspired treatment protocols, which include L-asparaginase. Objective was to calculate the number-needed-to-treat(NNT) to prevent 1 relapse or death for pediatric-inspired treatment versus hyperCVAD in AYA patients with ALL.
Design/Methods: No comparative clinical trials were found in a comprehensive review of published literature to identify outcomes for AYA patients with Philadelphia-negative ALL undergoing pediatric-inspired versus hyperCVAD first-line treatments. Progression-free survival (PFS) was estimated for these regimens based on 2 studies with similar patient populations (Kantarjian et al, *Cancer*, 2004; Storring et al, *BJH*, 2009) by fitting Weibull curves to the published PFS rates. The NNT was calculated using these estimates. NNT is the inverse of the absolute risk reduction (ARR) associated with experimental intervention relative to controls (1/ARR), where ARR equals control event rate (CER) minus experimental event rate (EER), ie, ARR=CER-EER (Laupacis et al, *NEJM*, 1988).
Results: Five-year PFS estimated from the relative survival curves were 0.44 for hyperCVAD and 0.62 for pediatric-inspired regimens, translating into an NNT of 6.
Conclusion: An indirect comparison of published literature in similar populations suggests that pediatric-inspired regimens containing asparaginase may have better clinical outcomes than treatment with the asparaginase-free hyperCVAD protocol, with an NNT of 6 (for every 6 patients treated, one relapse or death is averted).

P-040

INVASIVE CANDIDIASIS IN PEDIATRIC PATIENTS WITH HEMATOLOGIC DISORDERS

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Background/Objectives: Invasive Candidiasis (IC) is one of the major infectious complications in pediatric patients with hematologic disorders. Several techniques based on the detection of Candida species –specific DNA, circulating serum biomarkers and Candida antigens have been developed. The aim of this prospective study is to determine the incidence of IC in pediatric patients with hematologic disorders by nested PCR, Galactomannan and Beta -D- glucan Tests.
Design/Methods: All the patients were classified according to the diagnostic criteria of the European Organization for Research and Therapy of Cancer and Mycoses Study Group (EORTC/MSG) consensus revised definitions draft, presented at PMC, 2009. BDG measurement using the glucan detection kit and MN antigen using Platelia Candida Ag, were used with cut-off value of ≥80 pg/mL and ≥0.5ng/mL, respectively. Two sets of primers universal were used for Candidas identification.
Results: Between Oct. 2006 and Jun. 2008, two hundred two sera from 124 pediatric patients with hematologic disorders, hospitalized in Nemazee hospital , southern Iran, Shiraz, who were febrile, neutropenic or on chemotherapy, followed up for Invasive Candidiasis. Mean age was 9.3 years (range 1—14 years). Seventy seven were male and forty seven were female. The underlying diseases were ALL (n=43), AML (n=31), aplastic anemia (n=7), pancytopenia (n=9), CLL (n=16) and CML (n=18). The incidence of IC in the patients was 29 %(36/124), with 6/124 being proven and 30/124 probable. The sensitivity of the assays for the patients with candidemia were as follows: Candida nested PCR 88%, BDG 47%, Mannan 41%.
Conclusion: On the basis of our data, commercially available BDG and GM assays besides molecular methods such as PCR can offer diagnostic help in patients with suspected IC. Developing nucleic acid based tests and other novel technologies is warranted to promote the accuracy of IC diagnosis.

P-041

MONITORING OF MINIMAL RESIDUAL DISEASE AND IT'S SIGNIFICANCE IN DISEASE OUTCOME IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Background/Objectives: Purpose: Minimal residual disease (MRD) monitoring has become an integral part of the management of ALL in children. MRD has an essential role in predicting relapse and overall survival.
Design/Methods: Methods: It is a retrospective analysis of MRD levels and its correlation with the disease outcome in children with Acute Lymphoblastic Leukemia. We have analysed 33 children with ALL who has received treatment with from Jan 2010 to Dec 2014. All of these children were treated with BFM 95 protocol based on risk stratification. MRD levels were done by flow cytometry method at D33 of induction chemotherapy and at the end of reinduction chemotherapy.
Results: MRD at D33 of induction was done in twenty four patients out of thirty three (73%) and at the end of reinduction in twenty patients (60%). MDR at D33 was <0.01% in twenty patients out of twenty four (83%) and >0.01% in four patients (17%).In nine patients (27%) MRD level couldnot be done as two patients died during induction, and four had already received some treatment at local centres before coming to us and initial flow cytometry was not available and in three patients cost burden was the cause. All four patients with high MRD levels at D33 of induction had poor prognosis in spite of treatment intensification, two had very early relapses, one died due to progressive disease and one had late relapse.Out of twenty patients who had MRD <0.01% at D33 of induction only two had late relapses.
Conclusion: MRD monitoring has become a standard of care in the treatment of ALL in children. But in developing countries still many centers have to rely on bone marrow morphology only due to lack of facility for MRD testing and associated cost burden.

P-042

TREATMENT RESULT OF CHILDREN ACUTE LYMPHOBLASTIC LEUKEMIA IN VIET NAM NATIONAL CANCER HOSPITAL FROM 4/2006 TO 8/2010

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Background/Objectives: *Background*: Acute lymphoblastic leukemia (ALL) is the most common malignant disease in children, accounts for 30 – 35% children cancers. *Purpose*: To evaluate the result of treatment of childhood standard risk ALL by the modified CCG-1991 protocol. *Objective*: 40 children with previously untreated standard risk ALL in Peadiatric Oncology Department, Viet Nam National Cancer Hospital from April 2006 to August 2010.
Design/Methods: Prospective study, apply the protocol.
Results: After 52 months of follow - up, disease free survival rate is 65%, overall survival rate is 67,5%.
Conclusion: Treatment of childhood standard risk ALL by the modified CCG-1991 protocol has good results.

P-043

RESULTS OF THERAPY OF ACUTE LYMPHOBLASTIC LEUKEMIA IN CHILDREN ACCORDING TO PROTOCOL MB 2008 IN UZBEKISTAN

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Background/Objectives: Since 2009, Clinic Research Institute and Mr. PC have been starting to apply a protocol MB-2008 for the treatment of children with ALL.The optimization of treatment acute lymphoblastic leukemia in children on the basis of the application and effectiveness analysis of protocol ALL-MB-2008.
Design/Methods: We analyzed 222 patients with primary diagnosed ALL treated on protocol ALL-MB-2008, admitted to the hospital of the Institute of Hematology and Blood Transfusion (Tashkent) in the period from 01.01.2009 on 01.01.2014.
Results: There was held an analysis of treatment in 222 patients who received treatment according to protocol ALL-MB-2008. Frequency of induction deaths is quite high and amounts to 4.0% for all patients; with the performance of the induction of mortality did not differ between patients SRG (standard risk group) and ImRG (intermediate risk group). During the observation 11 patients of the 222 were lost to follow-up. 200 of 222 (90%) patients achieved PR. Mortality in remission differed in SRG and ImRG and amounted to 1.2% and 5.7%, respectively. In all patients who died during the remission had developed severe sepsis, bacterial and fungal etiology. In 2 patients reported the development of secondary tumors by 2.2 and 3.4 months after treatment of ALL, respectively. In 17 patients (7.6%) reported relapse of ALL. During the phases of consolidation infectious complications developed in 93 patients ImRG (80,1%), and 22 patients (18.9%) developed severe sepsis.
Conclusion: The effectiveness of the protocol ALL-MB 2008 proved to be quite high. The 5-year EFS was 72 ± 13%, OS - 75 ± 2%. Thus, patients in SRG EFS were 80,7 ± 13%, OS -82 ± 2%, in the levels of ImRG EFS and OS were 68% ± 2 and 72 ± 2%, respectively, for the patients HRG EFS were only 18.1 ± 6%, and OS - 19,7 ± 6%.

P-044

CLINICOPATHOLOGICAL PROFILE AND TREATMENT OUTCOMES IN INFANT LEUKEMIAS (IL) – A SINGLE CENTRE EXPERIENCE FROM LOW AND MIDDLE INCOME COUNTRY (LMIC)

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Background/Objectives: Infant leukemia (IL) is rare high-risk leukemia with poor but improving outcomes in High Income Countries. The aim is to study the clinicopathological profile and treatment outcomes of IL in a LMIC setup.
Design/Methods: We retrospectively studied case records of 88 patients with age<1year diagnosed as leukemia (WHO-2008 criteria) from 2005-2014 for demographic, hematological, immunophenotypic, cytogenetic and treatment outcome data.
Results: Eighty-eight patients (M:F=1.75:1; median age=9 months) of IL were studied, however 3 were excluded from further analysis due to incomplete workup. Mean hemoglobin, WBC, platelet and blast count was 9gm/dl (range:4-17gm/dl), 120×10^9/L (range:2-554$\times10^9$/L), 83×10^9/L (range:3-1077$\times10^9$/L), and 67.5% (range:2-100%) respectively. Serum LDH was raised in 81.4% cases (mean=1632U/L, range:115-6470U/L). Immunophenotyping of acute leukemias (76/85) revealed following subtypes– ALL (50/76; B-ALL=48, T-ALL=2), AML (24/76; FAB subtypes: AML-M4/M5=8; AML-M7=6; Others=10) and acute undifferentiated leukemia [AUL] (2/76). JMML was diagnosed in 9 male patients. On cytogenetics study, MLL gene was rearranged in 50% (B-ALL=20, T-ALL=1, AML-M4/M5=7, AML-M1=1, AUL=1); further subtyped as t(4;11) (20%), t(9;11) (20%), t(11;19) (3.3%) and unknown partner (56.7%). Of 76 patients of acute leukemia, only 35 (46.1%) opted for treatment (ALL-26; AML-9). Of 26 patients of ALL, 16 attained remission (4 relapsed; 12 sustained remissions), median follow-up was 24 months (range:3-91months). Factors like female sex, age<6 months, hyperleucocytosis, Pro-B phenotype and MLL-gene rearrangement correlated with adverse outcomes. Of 9 patients of AML who received treatment, 5 attained remission (2 relapsed; 3 sustained remissions), median follow-up was 17 months (range: 2-122months). Infants with JMML received only cytoreductive therapy.
Conclusion: Though 42.9% of those treated have achieved long-term remissions, in LMIC setup with limited infrastructure/resources, only the better risk patients get treated. Overall only 17.7% of our patients are in sustained remission. Hence, there is a need to explore newer treatment modalities to improve the survival of patients with IL in LMIC setup.

P-045

INTERFERON ALPHA2B PLUS RIBAVIRIN THERAPY FOR HEPATITIS C (HCV) INFECTION IN CHILDREN WITH CANCER ON CHEMOTHERAPY: EFFICACY AND OUTCOME

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Background/Objectives: To study the efficacy of interferon-alpha2b plus ribavirin for the treatment of HCV infection in children with cancer on chemotherapy.
Design/Methods: This study is a retrospective analysis of data collected on 39 children treated (2011-2014) for HCV infection, while on chemotherapy: ALL, 30; AML, 3; Hodgkin lymphoma, 2; Non-Hodgkin lymphoma, 4. Median age, 5 yrs (range 2-19); M:F, 22:17. Treatment included recombinant interferon-alpha 2b (rIFNa) or peginterferon-alpha2b (pIFN); plus ribavirin p.o in standard doses. The response was followed by HCV –RNA by PCR.
Results: At the time of diagnosis of HCV, 36 of 39 were in remission from the malignancy; the median HCV RNA was 2.26×10^6; (range 0.12 to 50.3×10^6); the median (range) AST/ ALT values were 60 (26-748) and 92 (19-708) respectively; only five patients had bilirubin values above 1.2 mg/dl. Initial treatment consisted of rIFNa in 23 and pIFN in 16. For patients without significant response to rIFNa, the treatment was changed to the pIFN and vice versa. In total, 8 of 39 (20. 5%) patients achieved a sustained virologic response (SVR); 4 responses occurred on rIFNa and the other four on pIFN. The median time to achieve negative HCV RNA was 32 weeks (range, 8-74). All eight patients continue to be negative for HCV RNA for 7 to 25 months (median, 16 months). Five of the 31 non-responders have died; one from acute liver failure; two from infections during neutropenic period; and two from relapsed malignancy. All of the 26 surviving non-responders continue to have high HCV-RNA counts, but without any clinical signs of liver failure.
Conclusion: Inteferon plus ribavirin combination offers sustained virologic response to only a minority of children with active HCV infection and on chemotherapy; thus newer more effective drug therapy should be studied in this group of patients.

P-046

SIBLING SUPPORTERS´ SUPPORT FOR SIBLINGS WHO HAVE A BROTHER OR A SISTER WITH CANCER

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Background/Objectives: Siblings of a child with cancer have rights under the United Nation´s Convention on the Rights of the Child concerning the promotion of their own welfare. For siblings it is important to get a sense of the context of what is happening from their own perspective. Given each sibling support with person-centred care, means that each child is treated respectfully regardless of its resources and to act in the child's best interests. In Sweden have sibling supporters became a part of the staff since 1990 and are included in the support group around the family. They are available at all children´s cancer centers, the child hospice, play therapy and Ronald Mc Donald house.The aim of the study was to describe both the short and long term support, sibling supporters provide for siblings with a brother or a sister who has a cancer.
Design/Methods: The study was qualitative descriptive in design. The sibling supporters were individually interviewed via Skype by two authors (MJN, SN). Data were collected during autumn 2014. Twelve Swedish sibling supporters (9 women, 3 men) participated at the time of the interview. The interviews were conducted as communication between the interviewers and sibling supporter which included 20 questions with follow-up questions. A qualitative content analysis was used to draw a systematic conclusion from the text and to extract the message.
Results: The result comprises two domains, i.e. possibilities and challenges, which were analyzed further into 11 categories.
Conclusion: This study shows the importance of having sibling supporters to support siblings, a support that provide the siblings with person-centred care and promote health.

P-047

PLASMA MIRNAS PREDICT THE CURATIVE EFFECT AND PROGNOSIS OF PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA

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Background/Objectives: To investigate the expression level of plasma miRNAs of hsa-miR-197-3p and hsa-miR-652-3p in childhood acute lymphoblastic leukemia (ALL) samples, BCP- ALL cell lines and healthy children.
Design/Methods: First, We performed micro-array analysis in 12 samples, which included 9 ALL plasma samples from new diagnosis (ND), complete remission (CR), and relapse (RE) in 3 patients and additional 3 plasma samples from healthy children. Second, we validated the results of micro-array analysis by stem-loop reverse transcriptional real-time PCR in independent samples. One set is paired bone marrow (n = 29, 12 paired ALL samples of ND and CR from the same patient, and 5 samples of RE), and the other is matched plasma samples (n=100, 30 pair ALL plasma samples of ND and CR, and 10 samples of RE).The level in REH and Nalm-6 BCP-ALL cell lines were also analyzed.
Results: The expressions levels of hsa-miR-197-3p and hsa-miR-652-3p in childhood ALL plasma exhibited a specific characteristic: healthy > CR > RE > ND. Significant differences were observed between each group ($P<0.05$). The miR-197-3p and miR-652-3p in plasma and bone marrow samples were expressed consistently ($P<0.05$). Compared to the normal adult common B cell line, the expression levels of miR-197-3p and miR-652-3p in REH and Nalm-6 were much lower ($P < 0.05$).
Conclusion: Hsa-miR-197-3p and hsa-miR-652-3p maybe act as cancer suppressor genes through leukemogenesis and progression of pediatric ALL. Furthermore, our research indicates the possibility of miRNA as the biomarker in the diagnosis, treatment and prognosis of pediatric ALL.

P-048

ROUTINE CEREBROSPINAL FLUID EXAMINATION DURING INTRATHECAL CHEMOTHERAPY IN PEDIATRIC ALL: IS IT REALLY NECESSARY?

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Background/Objectives: The success rate of pediatric ALL has reached > 95%. CNS relapse still occurs in 3 -8% of patients. Most ALL protocols recommend a routine CSF examination during the intrathecal chemotherapy. Each patient undergoes 22-25 intrathecal during the treatment. CSF analysis during all of these adds to approx INR 10,000 per patient to the cost of therapy. We wish to analyze the value of performing CSF examination during intrathecal chemotherapy in diagnosing isolated CNS relapse.
Design/Methods: Between Jan 2013 to Dec 2014, 32 patients underwent treatment for ALL in our unit. 19 (59 %) of these were on regimen A of UK ALL 2003 protocol and 13 (41%) on regimen B. The medical records of these patients were reviewed and reports of CSFexamination done during were evaluated. Patients in whom CSF was done due to CNS complaints were excluded.
Results: Total 225 CSF samples were collected from 32 patients during the study period. Out of these, 141 (63%) samples were taken from patients undergoing treatment in regimen A (n=19) and rest 84 (37%) from patients under regimen B (n=13). In regimen A, 78 (55%) samples were collected during intensive phase and 63 (44.6%) during maintenance. None of these CSF samples were found to be positive for malignant cells. In regimen B, 84 CSF samples were collected. Seventy- two (85.7%) samples were collected during intensive phase and twelve (14.2%) during maintenance. Two of these samples were detected to be positive for lymphoblasts. One patient was undergoing interim maintenance and the other was in maintenance. Bone marrow was normal in both the patients.
Conclusion: Occult CNS relapses are more common in high-risk pediatric ALL. Continued CSF surveillanceis recommended in this group of patients and can be omitted in standard risk patients.

P-049

DIFFUCULTIES IN DIAGNOSING AND TREATMENT OF INTRACRANIAL FUNGAL INFECTIONS: REPORT OF THREE CASES

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Background/Objectives: Invasive fungal infection (IFI) of the CNS is life-threatening disease in patients with malignancies.We report three IFI cases during chemotherapy.
Design/Methods: *Case 1*: Ten-year-old male patient was diagnosed T-cell ALL. At the nineteenth day of the chemotherapy, the thoracicCT revealed nodular lesions, Liposomal amphotericin B(LipAmpB)was given. At the thirty third day ofthe fungotherapy, patient had consciousness andconvulsion. The cranialMRI demonstrated several lesions localized on temporal lobe.The voriconazole was added to the therapy.In the follow up, the patient developed convulsion. The cerebrospinal fluid examination demonstrated fungal hyphes. The stereotaxic biopsy was done.The third antifungal, flucytosine, was added to dual therapy. The minimal regression on cranialMRI was observed after one month.However, bone marrow relapse occurred withinfour month and patient died.*Case 2*: Elevenyear-old female patient was diagnosed CommonB-ALL. At thirty sixth day LipAmpBwas given as galactomannan test positive.At the eighteen dayof the fungotherapy, abscess detected.LipAmpB was ceased, voriconazole started. During follow-up, regression of lesion demonstrated. Patient continues chemotherapy and is now onfifth month of treatment. *Case 3*: Fiveyear-old male patient was diagnosedCommonB-ALL. Patient developed headache at twentieth day of chemotherapy. The cranial MRI showed abscess on frontal region.LipAmpB was given. Patient developed consciousness and intracranial bleeding was detected and patient undergone urgent neurosurgical intervention. As progression of lesion was shown, the voriconazole was added to the treatment. As lesion culture demonstrated tricoderma species with characteristics of resistance to amphotericinB and sensitive to voriconazole.We began caspofungin with voriconazole administered together.Patient continues his therapy with severe neurological sequel.
Results: One of the patients performed combination therapy was died due to progressive disease, the other lives with severe neurological sequel.Our one case responded to antifungal therapy well and is followed-up regularly.Two patient undergone stereotaxic biopsy.The early stage surgical intervention could not be performed in our cases and 2 patients undergone surgery when they had hydrocephaly and intracranial bleeding respectively.
Conclusion: The Intracranialfungal infections show highmortality in patients receiving chemotherapy. There aresome studies showing positive effect of early surgical intervention on prognosis beside antifungal therapy.The combined antifungal therapy is still controversial.

P-050

HAIR, URINE AND SERUM SELENIUM STATUS IN PEDIATRIC CANCER PATIENTS

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Background/Objectives: The role of different trace elements in normal vital activities and initiation of some disease has long been known.Selenium (Se) is a trace element which has multiple functions including plays a key role in ptotecting cells against oxidative damage.Low Se amounts in serum and hair have been reported in pediatric and adult cancer patients.
Design/Methods: Eighty eight pediatric patients with newly diagnosed cancer including acute leukemia(n=58),Hodgkin's lymphoma (n=4) non-Hodgkin's lymphoma (n=12) and solid tumors(5neuroblastoma,5medulloblastoma,1 wilms,1 hepatoblastoma,1rhabdomyosarcoma and 1 osteosarcoma)admitted to the hospital.Age and sex-matched 32 healthy children(brothers or sisters of patients) were enrolled to the study as the control group.There were 51 male and 37 female (mean age: 6.79±3.88 years)in the study group and 19 male and 13 female (mean age: 6.52±2.52 years) in the healthy control group.2 ml of venous blood were collected from 120 children by using cleaned syringe and needles,into heparinized pretreated clean polypropylene tubes,carefully avoiding external metal contamination and hemolysis.Hair samples were collected by hair clippings from the back of the head and near the scalp with a stainless-steel scissor and put in clean plastic bags.Blood and urine measurements were obtained from patients and controls at 08.00 am.Serum was separated with centrifugation at 3500 rpm and stored-80 °C.Selenium levels were determined by ICP-MS spectroscopy.
Results: In this study we found that Se levels in serum and hair of children with cancer were significantly lower than those of controls.There are no differences in the leukemia, lymphoma and solid tumors group.On the other hand,Se levels of urine samples were slightly elevated in cancer patients compared with control groups.There was no marked difference in Se levels of patients who had different types of cancer.
Conclusion: Se deficiency might be associated with the development of pediatric cancer. Especially in children, additional studies are needed to define whether low levels of Se may play a role in cancer pathogenesis.

P-051

IS SERUM PHOSPHOR LEVEL ASSOCIATED WITH HIGH RISK OF MORTALITY IN PEDIATRIC FEBRIL NEUTROPENIC PATIENTS WITH MALIGNANCY?

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Background/Objectives: Phosphor is a basic intracellular anion required for many biological functions. Hypophosphatemia has been informed to be related to sepsis and has been associated with sepsis severity.There are several studies showing that severe hypophosphatemia can increase the mortality in septicemia.There is no study about serum level of phosphor in the febril neutropenic attacks (FNA) in pediatric cancer patients. In this prospective study, we aimed to determine whether hypophosphatemia associated with mortality in febril neutropenic patients with malignancy. Also we assess the relationship between serum level of phosphor and characteristics of attacks and treatment modification in cases of febrile neutropenia.
Design/Methods: The study included febrile neutropenic children with malignancy who were hospitalized during one year (2013-2014).The study group consisted of 27 female and 49 male with median age of 5 years (5months-16years).The number of febril neutropenia was 129 among 76 patients.The 23%of cases was ALL, 7% of them AML,52%of them Burkitt lymphoma,8%of them neuroblastoma and10% of cases was other solid tumors.The patients were examined,we performed the hematological and biochemical analyses including phosphor,cultures of blood and urine in febril attack. One hundred twenty nine FNA were observed in76 patients.They were were divided into 2 groups:group 1 comprised 45 attacks with severe hypophosphatemia(serum inorganic phosphate (Pi)<1 mg/dl); group 2 comprised 84 attacks without severe hypophosphatemia(Pi>1 mg/dl).

Results: In 45 attacks(35%), serum level of phosphor was under normal level,and in 84 attacks(65%) level was normal range.There is no significant differences duration of antibiotics, microbiologically documented number of attacks,number of fever with unknown origin,number of attacks with treatment modification and death between two groups.
Conclusion: Hypophosphatemia occurs in the sepsis and can be associated with the life-threatening condition.In our study,we showed that the lower level of serum phosphor did not increase the mortality and length of stay in hospital in cases of febrile neutropenia.The relationship between serum level phosphor and mortality in FEA need to be confirmed in further studies.

P-052

EXPRESSION OF CD133.2, AS A PROSPECTIVE MARKER, PREDICTING MINIMAL RESIDUAL DISEASE (MRD) LEVEL AT DAY 15, IN CHILDREN WITH CD45-DIM B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA (B-ALL)

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Background/Objectives: To address predictive value of CD133.2 receptor expression on CD45-dim B-ALL cells at initial diagnosis, in the context of minimal residual disease monitoring at day 15 in children with B-ALL.
Design/Methods: Nine newly diagnosed children with CD45-dim B-ALL were assessed for MRD levels on the day 15 of remission induction. We arbitrarily assigned the patients to either relatively 'high or low CD133.2' groups based on percentage of CD133.2 positive events at initial diagnosis. Phenotyping was performed in agreement with ALL-ICBFM-2009 recommendations using 4-color flow cytometry, with an acquisition number of at least 300.000 nucleated cells per tube and MRD of 30 cellular events was considered as positive.
Results: Among study subjects there were four males and five females with an average age of 3.1 (95%CI: 1.9 – 4.3). Median percentage of CD133.2 positive cells in 'low CD133.2' group were defined as 0.8% (Interquartile range (IQR): 0,115 – 1.70) and as 42.85% (IQR: 29,01 – 70) in 'high CD133.2' group gated on CD19+ ALL cells. Comparison between these groups revealed statistically significant difference in minimal residual disease levels at day 15 (p=0.02); Median percentage of MRD in 'high CD133.2' group was 1.75% (IQR: 1.18 – 6.6), while a median of 0.04% of residual leukemic cells (IQR: 0.04 – 0.08) was observed in 'low CD133.2' group. Correlation analyses revealed significant positive correlation between CD133.2 and CD45 receptor expression (Mean Fluorescent Intensity) at diagnosis (r^2= 0.86; p=0.029). Percentage of CD133.2 positive B-ALL cells also positively correlated with leukocyte count at initial diagnosis (r^2= 0.83; p=0.04).
Conclusion: Study showed that, CD133.2 receptor expression at initial diagnosis might be exercised as a surrogate marker to predict MRD levels at day 15 in children with CD45-dim B-ALL, although further, larger cohort studies are needed to address this question.

P-053

CLOFARABINE TOXICITY IN RELAPSED OR REFRACTORY ACUTE LEUKEMIA IN CHILDREN

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Background/Objectives: Although modern treatment of acute leukemia in children had a dramatic success during the last decades same results could not be reproduced in relapsed and refractory patients to standard chemotherapy. Clofarabine which could be used in such patients for salvage therapy is a second-generation purine nucleoside analogue inhibiting DNA synthesis and repair. Despite its efficacy when combined with other DNA damaging agents it has significant toxicity.
Design/Methods: We have given combined chemotherapy consisting of clofarabine to 4 relapsed (2 AML, 2 ALL), 6 refractory (3 AML, 3 ALL) leukemia patients for 12 times. AML patients received clofarabine combined with cytarabine whereas ALL patients had clofarabine along with cyclophosphamide and etoposide. One of the resistant AML and one of the resistant ALL patients received their clofarabine therapies after their relapses from stem cell transplantation (SCT).
Results: All of the patients experienced hematological toxicity as grade IV myelosupression, grade II/III infectious toxicity, grade II/III nausea, vomiting and mucositis. Mucositis was grade IV in 2 patients. During 6 cycles, hypokalemia which was resistant to therapy was observed with a 10 days duration. None of the patients had veno occlusive disease. One of the patients died on the 3rd day of treatment probably due to capillary leak syndrome. Two of the patients died on 40th and 45th day of after clofarabine therapy with severe intracranial fungus infection and disease progression. Of the remaining 7 patients 5 were immediately undergone SCT whereas 2 patients who received clofarabine after SCT relapse have been prepared for a second transplant.
Conclusion: Clofarabine is a potent and efficient chemotherapeutic agent in relapsed and refractory leukemic children. However due to its substantial toxicity profile it could be used as a salvage therapy bridging to SCT.

P-054

DEXTROMETHORPHAN IS A SIMPLE BUT EFFECTIVE TREATMENT AND PROPHYLAXIS FOR HIGH DOSE METHOTREXATE RELATED NEUROTOXICITY

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Background/Objectives: Methotrexate induced neurotoxicity is a frequent complication of methotrexate (MTX) therapy and can occur after intrathecal or systemic administration. The pathogenesis of MTX neurotoxicity is multifactorial, though one potential biochemical pathway leading to neurotoxicity involves the folate dependent remethylation of homocysteine (Hcy). MTX therapy is known to cause elevations of both plasma and CSF Hcy levels. Hcy is directly toxic to vascular endothelium and Hcy and its metabolites are excitatory agonists of the N-methyl-D-aspartate (NMDA) receptor. Competitive or noncompetitive antagonists might afford protection from or reversal of neurotoxicity. Dextromethorphan, a noncompetitive antagonist of the N-methyl-1-aspartate (NMDA) receptor may be able to reverse or prevent methotrexate related toxicity.
Design/Methods: 14 years old female, follow up case of Pre B ALL with previous history of seizure disorder, being treated as per the BFM 95 protocol. After the administration of high dose MTX (@ 5gm/m^2) with intrathecal MTX she developed altered behavior, agitation, insomnia within 48 hrs of therapy and had a brief seizure with unconsciousness on 7th day. She had delayed excretion of MTX resulting in rise in creatinine and acute renal injury. She was managed with leucovorin (Folinic acid) and dextromethorphan. Her MTX level was serially monitored till it was below 0.3ng/ml. In subsequent 3 cycles of high dose MTX, she was given dextromethorphan prophylaxis along with reduced dose of MTX (2gm/m^2). This regimen was tolerated well by her and prevented neurotoxicity on subsequent cycles.
Results: The patient's symptoms resolved dramatically after starting dextromethorphan in the first course and she had no further seizures, vomiting stopped and her agitated behavior settled and she could sleep well. She did not develop any signs/symptoms of neurotoxicity in subsequent 3 cycles of high dose MTX with dextromethorphan prophylaxis.
Conclusion: Dextromethorphan is an effective agent for treatment and prevention of MTX related neurotoxicity.

P-055

METABOLIC SYNDROME IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA, PRELIMINARY RESULTS

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Background/Objectives: The aim of the study was to find out the impact of metabolic syndrome (MS) on realization of program of treatment in children with Acute Lymphoblastic Leukemia (ALL).
Design/Methods: The objects of our study were two groups of patients. The 1st one consisted of 173 children with ALL treated according to the ALL-MB scheme from 01.01.2000 to 31.12.2012. The 2nd retrospective group in our study included 462 children with ALL which received treatment for the last 20 years according modified ALL-BFM scheme for period from 01.01.1994 to 31.12.1999.
Results: Among 173 children with ALL in the period of 01.01.2000 till 31.12.2012 we diagnosed MS in 57 (32,9%) patients but we did not disclose it in other 116 (67.1%). During this period 35 (20.2%) patients from the 1st group died because of disease progression or lethal complications which occurred in the course of treatment. Among died patients there were 25(71.4%) children with MS and 10 (18.6%) without it. The percentage of fatal outcomes of patients without MS was 8,6% (10/116) but it was 43,8 % (25/57) of patients with MS. The treatment of ALL was complicated by steroid diabetes in 13 (2.8%) cases from 462 and 12 of them came to children with MS. There was manifestation of complication in 12 (92.3%) cases at the repetitive courses of glucocorticosteroid drug usage where 9 (69.2%) patients took anti-relapse treatment.
Conclusion: The patients with MS have complications more often when curing ALL and these complications lead to deviations from the program chemotherapy. For that reason we should rate MS as factor which works on course and results of treatment.

P-056

CNS FUNGAL INFECTION DURING ALL INDUCTION: HOW LONG TO CONTINUE ANTI FUNGAL TREATMENT?

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Background/Objectives: Brain abscesses in children though rare, remains a life-threatening complication in those with haematological malignancies. As prognosis is dismal and with little information on the appropriate management of this complication, we reviewed literature on the management for children who developed multiple fungal brain abscesses while on anti-leukemic therapy to try and find out an ideal treatment recommendation.
Design/Methods: A six year old girl with ALL was started on UKALL 2003 regimen B (4 drug) induction. While on induction she developed prolonged febrile neutropenia and later had an episode of status epilepticus which on investigation revealed multiple brain abscesses. All the bacterial work up were negative including that for tuberculosis. Among the fungal work up only CSF galactomannan was positive in high titres. She was started on conventional Amphotericin (1.5 mg/kg/day) and Voriconazole (7 mg/kg 12 hrly) for 6 weeks and then Voriconazole alone was continued for 9 months. During the course of her treatment, a repeat titre showed decreased levels in 6 months. As she was stable, her anti-leukaemic therapy continued and she is currently in remission and receiving maintenance chemotherapy. Detailed literature review showed one study in which a child received Voriconazole for 17 months for multiple fungal brain abscesses.
Results: Our case will be the first documented survived case from the Indian subcontinent. Right antifungal treatment need to be continued until the lesions get smaller or disappear. However if the child becomes neutropenic during the treatment for ALL, that needs to be addressed aggressively.
Conclusion: We conclude that patients with ALL and multiple fungal brain abscesses can be salvaged by developing a rigorous febrile neutropenic protocol. At the moment there is no consensus about the duration of antifungal therapy in children with leukaemia and fungal CNS infection.

P-057

CRITICAL ILLNESS POLYNEUROPATHY AND ACUTE LYMPHOBLASTIC LEUKEMIA

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Background/Objectives: Muscle weakness and peripheral neuropathy is common in children with Acute Lymphoblastic Leukaemia (ALL) during induction therapy mainly due to steroids and vincristine . Critical Illness Polyneuropathy (CIPN) appears to be a common complication of severe sepsis and is thought to represent a neurologic manifestation of the systemic inflammatory response syndrome (SIRS).
Design/Methods: A 22 month old boy with Pre- B ALL, whilst on UK-ALL03 Regimen A Induction (3 drugs) presented to us on day 22 of induction with Right sided pneumonia and septic shock . He required multiple fluid boluses (150 ml/kg), packed red cell (30ml/kg), platelet transfusion, inotropic support (for 72 hours). He was on mechanical ventilation under sedation for 5 days. Two attempts at extubating him on day 6 and 13 of ventilation were unsuccessful. It was due to poor muscle tone and power. He has had generalized hypotonia & areflexia with muscle power of <2/5 in upper and lower limb muscle groups. As he was well and this onset of hyptonia happened following the septic shock a possibility of CIPN was considered. The other differential diagnosis such as vincristine induced neuropathy, steroid myopathy, Guillaine Barre Syndrome (GBS) and malnutrition aggravating the pathology were thought of. On day 21 he was successfully extubated to non invasive BiPAP. He was treated with antibiotics, antifungal and IV IgG medications.
Results: Many toddlers with ALL during induction period stop walking due to muscle weakness. It would be difficult to differentiate between CIPN, drug induced neuropathy and GBS. Following the regular physiotherapy, vitamin and nutritional support, his muscle tone and power is improving.
Conclusion: CIPN is seen in children who are admitted in intensive care units especially with septic shock. Following multidisciplinary team approach we would be able to manage these children.

P-058

TREATMENT OF TUMOUR LYSIS SYNDROME RELATED HYPERPHOSPHATEMIA; ROLE OF SEVELAMER HYDROCHLORIDE

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Background/Objectives: Tumour lysis syndrome (TLS), the commonest oncological emergency seen in children, is associated with high levels of uric acid, phosphate and potassium along with low levels of calcium and abnormal renal function needing dialysis in some cases.The standard treatment of hyperleukocytosis with TLS in majority of the centres in India are hyper hydration, alkalinisation of urine and allopurinol.In some cases haemodialysis is performed to improve the renal function and control the high uric acid and phosphate levels. Calcium based phosphate binders are not used due to increased chance of developing calcium phosphate crystals. Sevelamer hydrochloride, an oral phosphate-binder is used in the treatment of hyperphosphatemia in children and adults on haemodialysis for chronic kidney disease.
Design/Methods: We hereby report two cases of T-cell ALL who presented with a high white cell count (49000cells/cc and 375000cells/cc), bulky disease and proceeded to spontaneous tumour lysis syndrome.Both cases received Rasburicase and Sevelamer hydrochloride which reduced the serum uric acid and phosphate level respectively.
Results: In both cases serum phosphate levels were high (12.5 mg/dl and 22 mg/dl) enough to initiate haemodialysis, however, performing haemodialysis in newly diagnosed ALL with TLS is challenging in view of low platelet counts. In both these cases received hyperhydration 5lit/m2 and urine output was achieved with regular diuretics, however their serum creatinine levels were abnormal (1.9 mg/dl and 2.4 mg/dl) for the initial 72 hrs. Following the introduction of Sevelamer hydrochloride we successfully avoided hemodialysis and reduced the serum phosphate levels within 48 hrs.
Conclusion: In developing countries like India children with these diseases present late when the disease has progressed to an advanced stage with a high tumour load. Sevelamer hydrochloride appears to be effective and safe treatment for hyperphosphatemia associated with tumour lysis syndrome.

P-059

IMPACT OF ALLERGY TO L-ASPARAGINASE ON OUTCOME OF ACUTE LYMPHOBLASTIC LEUKAEMIA (ALL) IN CHINESE CHILDREN

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Background/Objectives: L-asparaginase (L-asp) is standard anti-leukaemia agent for treatment of ALL. Allergy to L-asp is common and associated with antibody production. Patients allergic to native E Coli L-asp need alternative L-asp preparations. Outcome of patients recruited into two Hong Kong PHOSG ALL protocols with or without allergy to L-asp was analysed.
Design/Methods: From 2002 to 2008, 159 patients were recruited into IBFM-IC ALL 2002 Study, and 132 patients into the CCLG 2008 Study from 2008-2012. First line L-asp was leunase, 2nd line was PEG-asp (Oncaspar), Erwinia asp (Erwinase) was 3rd line. Induction, early intensification and consolidation treatment was similar in both protocols. In 2002 Study, standard risk (SR) patients were randomized to 1 or 2 delayed intensification (DI), Intermediate Risk (IR) to 1 or 3 DI, high risk (HR) patients received 3 pulse blocks and 2 DI. In 2008 study, SR patients received 1 DI, IR received 2 DI and HR received 6 blocks and 1 DI. All the DIs and blocks included L-asp treatment.
Results: L-asp allergy developed in 28.9% patients (17.6% in 2002, 42.4% in 2008 Study). HR patients had significantly higher incidence of allergy (HR 59.3% vs IR 20.6% vs SR 23.8%, $p<0.001$). Relapse risk was similar in those with/without allergy (10.7% vs 15%), there was no difference in EFS (78.6% vs 78.6% in 2002 Study, and 92.9% vs 85.5% in 2008 Study). According to risk groups, there was no difference in EFS for those with/without allergy in SR and IR (SR 83.3% vs 85.7%, IR 89% vs 80.6%) but better EFS in HR (90.6% vs 68.2% , $p=0.021$).
Conclusion: More exposures to treatment phases with L-asp increased incidence of allergy. Switching from leunase to alternative L-asp did not affect outcome nor increased risk of relapse. Oncaspar with higher dose activity may overcome silent asp-antibody with good outcome.

P-060

IS IT REALLY USEFUL AS A PROGNOSTIC FACTOR THE ABSOLUTE LYMPHOCYTE COUNT AT THE END OF INDUCTION THERAPY IN IN PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA?

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Background/Objectives: Several recent studies have suggested that the prognostic utility of absolute lymphocyte count (ALC) may be a prognostic indicator in children with hematologic malignancies, with low ALC associated with adverse outcome. We studied whether the ALC at the end of remission induction in children with acute

lymphoblastic leukemia (ALL) treated on two consecutive protocols have been useful as a prognostic factor, independent with respect to minimal residual disease (MRD).
Design/Methods: We reviewed 96 newly diagnosed cases of pediatric ALL treated on the Hospital Universitario de Cruces enrolled in two trials: ALL SHOP-99 (August 1999-April 2005) and ALL SHOP-2005 (May 2005-May 2013). Variables analyzed included: age and gender at diagnosis, initial leukocyte count, lineage, cytogenetics, risk group, MRD status at the end of remission induction therapy (MRD-34) only in the ALL SHOP-2005 trial, and ALC at day +34 of induction (ALC-34) in both trials.
Results: Thirty six cases were treated with ALL SHOP-99 and sixty with SHOP-2005. The mean age at time diagnosis was 5 years (range 1-15); 59 males (61.5%) and 37 females (38.5%). The initial leukocyte count was ≥50,000/mm^3 in 24%. ALL linage: B; 82.4% (n: 79), T; 15.6% (n: 15), and biphenotypic; 2% (n: 2). Cytogenetic negative; 54%, and alterations in the rest; being the most common TEL-AML (19%). The risk groups were: standar risk (29%), high risk (52%) and ultra-high risk (19%). Overall survival (OS) was 91% in ALL SHOP-99 and 88.3% in SHOP-2005, and event-free survival (EFS) 85.3% and 83.3% respectively. In our patients, 1,250/mm^3 in was the median ALC-34 value for patients who relapsed or died (53.5%; <1,000/mm^3). All of relapse cases in ALL SHOP-2005 trial; has negative MRD-34.
Conclusion: In our study, the ALC and MRD at the end of induction were not significant and independent prognostic factor in childhood ALL comparing the number of cured cases.

P-061

HIGH INCIDENCE OF HYPERTENSION IN YOUNG CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA DURING INDUCTION REMISSION

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Background/Objectives: High doses of corticosteroids form the backbone of acute lymphoblastic leukemia (ALL) induction therapy and contribute to most of the non-life threatening side effects. Steroid induced hypertension is an often under-reported toxicity. We report high incidence of hypertension in young children.
Design/Methods: Induction data of 133 consecutive pediatric ALL patients treated per BFM95 protocol, between January 2011 and December 2013, was retrieved from physician notes, blood pressure (BP) records and medication orders. All patients received prednisolone at 60 mg/m2 for 7 days and 40 mg/m2 for 21 days. Hypertension was defined as BP measurement of more than 95th percentile for age, sex, height (3 separate occasions). Statistical analysis was done using SPSS version 21.
Results: Demographic and disease characteristics revealed median age 6 years (4months-18years), male preponderance (102/133,77%), extramedullary disease in (6/133,4.5%), B immunophenotype (115/133,86%) and unfavourable (t(9,22),t(4;11)) molecular genetics in (10/133,7.5%) patients. BFM standard, moderate and high risk occurred in 31/133(23%), 71/133(54%) and 31/133(23%) cases respectively. Hypertension was observed in 51/133(39%) patients, requiring one (42/51) or more(9/51) antihypertensive drugs. Most patients were asymptomatic. Incidence did not vary by sex (males 36/102, females 15/31) or risk group. Incidence of hypertension in children <1year, 1-9 years and >9 years was 0/3, 42/89 and 8/43 respectively (p,0.02). The odds ratio of having hypertension in 1-9 year age group was 10.7 and all patients requiring 2 or more antihypertensive agents belonged to this group. Malnourished (WHO, BMI <3,>85 percentile) patients were more likely to have hypertension as compared to normally nourished (BMI >3,<85 percentile) patients (22/36,61% versus 20/53,38%;p0.03) with an odds ratio of 5. Complete remission rate was 95%(126/133) with an induction mortality of 2/133(1.5%).
Conclusion: Hypertension during ALL induction is common. Children aged 1-9 years and those with under-/over-nutrition are more predisposed. Frequent and careful monitoring of blood pressure is recommended as this condition can be managed medically.

P-062

LONG-TERM FUNCTIONAL OUTCOMES OF HYPERFRACTIONATED RADIATION ON CHILDHOOD ALL SURVIVORS: A PILOT STUDY

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Background/Objectives: Cranial radiation in acute lymphoblastic leukemia (ALL) has irreversible neurocognitive effects. A hyperfractionated radiation (HFX) strategy was randomized against conventional radiation (CFX) in the DFCI 87-01/91-01 trials attempting to minimize these effects. Neurocognitive test results 8 years after therapy demonstrated no difference, and this strategy was abandoned. The objective of this pilot study was to evaluate whether patients who received HFX as part of the DFCI 87-01/91-01 trials have better late functional outcomes than those who received CFX.
Design/Methods: This retrospective study reviewed all patients treated according to the DFCI 87-01/91-01 trials at the McMaster Children's Hospital in Hamilton, Canada. Inclusion criteria required that patients were <18 years at diagnosis and have attended at least one follow-up visit since Jan 1, 2000. Data were collected from patient charts. The primary outcomes examined were functional outcomes. IQ test results were examined for trends. Demographics and outcomes were presented with descriptive statistics.
Results: We identified 57 DFCI 87-01/91-01 trial participants; 14 received HFX, 29 CFX and 14 had no radiation. There were no demographic differences between the HFX and CFX groups. Survivors who received HFX were more likely to be living independently (64% vs 28%, p=0.02) and to be engaged in long-term relationships (57% vs 25%, p=0.04) than those who received CFX. Non-statistically significant trends suggested HFX survivors may be more financially independent (67% vs 36%, p=0.09), employed full-time (57% vs 34%, p=0.16), and less likely to have experienced educational difficulties in school (23% vs 45%, p=0.30). Patients who received HFX also had a trend toward higher scores on neuropsychological IQ testing.
Conclusion: ALL survivors who received HFX appeared to have better overall long-term functional outcomes than those who received CFX. A wider study involving all patients enrolled on DFCI 87-01/91-01 protocols should be done to reconsider radiation protocols for ALL.

P-063

MORTALITY IN CHILDREN WITH ALL: A 10-YEAR REVIEW

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Background/Objectives: Despite improvements in cure rates of children with acute lymphoblastic leukemia (ALL), 15-20% die of disease or treatment-related complications (TRC). We aimed to analyze cause of death in children with ALL.
Design/Methods: Retrospective review of clinical data of children who died between Jan'05-Dec'14 in a Pediatric Oncology Unit (POU) that admits about 30 ALL annually, 0-15y, using DFCI 2005 as first-line protocol.
Results: Forty children with ALL died, representing 12.6% of all deaths. Most were boys (26/40) and B-lineage (22/40). Fifteen died after a TRC (G1) and 25 from incurable disease (G2). Most children were high or very-high risk (G1-11/15, G2-17/25). Genetic abnormalities were rare (G1-6/15, G2-5/25), including 1 trisomy-21 and 1 ataxia-telangiectasia in G1. Almost all (G1-13/15, G2-25/25) were under intensive cycles (levels 3/4 of the *Intensity of Treatment Rating Scale 2.0*). In G1 6/15 died during induction, 3/15 first consolidation, 1/15 second consolidation, 2/15 maintenance, 3/15 second-line protocol. Cause of death was infection (9/15), organ toxicity (3/15), graft-versus-host disease (2/15) and anaphylaxis (1/15). Within infections, 5/9 occurred in aplasia; primary site was blood (5/9), gastrointestinal tract (2/9), lung (1/9), skin (1/9). Pathogens were identified in 6/9 (3 Gram- bacteria, 4 fungus, 1 virus), 2 co-infections (bacteria+fungus). In G2, 22/25 died under second or third-line protocols, 2/25 with a second malignancy (glioblastoma, rhabdomyossarcoma) and 1/25 in first consolidation. Median interval between diagnosis and death was 0.8y in G1 (IQR 0.2-2y) and 2.9y in G2 (IQR 1.3-6.7y). In G1 11/15 children died in intensive care units (ICU), 3/15 at home, 1/15 in the ward. In G2 12/20 died at home, 5/20 in ICU, 3/20 in the ward.
Conclusion: Despite improvements in supportive care, TRC remain a major challenge for POU. Many deaths are potentially preventable and efforts must be directed towards educating professionals and patients at risk.

P-063A

DE NOVO MYC AND BCL2 DOUBLE-HIT B CELL PRECURSOR ACUTE LYMPHOBLASTIC LEUKEMIA (B-ALL) IN PEDIATRIC PATIENTS AND YOUNG ADULTS ASSOCIATED WITH POOR PROGNOSIS

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Background/Objectives: MYC and BCL2 translocations in B cell lymphomas are defined as "double-hit" associated with poor prognosis. Such double-hit events are extremely rare in B cell precursor acute lymphoblastic leukemia (B-ALL), especially in pediatric patients or young adults. This study is to investigate the clinical manifestation of double-hit B-ALL in young patients.
Design/Methods: This study was designed to perform a retrospective data review and to identify the patients with de novo double B-ALL. Flow cytometry immunophenotypic, cytogenetic, pathologic, immunohistochemistry and clinical outcome data are collected and summarized. Additional literature cases were reviewed.
Results: Three patients were identified and there were two females and one male, with 15, 18 and 24 years of age, respectively. All patients had an unremarkable medical history before presenting with extensive bone marrow and central nervous system

involvement at diagnosis. Flow cytometry immunophenotypic analysis showed an immature BCP-cell immunophenotype in all cases (CD10+, CD19+, TdT+, surface Ig-) and immunohistochemistry showed high expression of MYC and BCL2 in all cases. All patients showed complex karyotypes associated with 8q24 abnormalities in the form of t(8;9)(q24;p13) or t(8;14)(q24;q32) and t(14;18)(q32;q21). Fluorescence in situ hybridization confirmed MYC and BCL2 rearrangements. Two patients died of refractory disease or disease progression 7 and 13 months after initial diagnosis, respectively, and the third patient was treated with protocol AALL0232 under the Children's Oncology Group study, achieved complete remission and remained in remission for 53-month at last follow-up. Combining our cases with previous documented cases in literature, we found that the de novo double-hit B-ALL occurs predominately in young patients with a medium age of 27 years.
Conclusion: Our study showed that MYC and BCL2 double-hit rearrangements exist in pediatric or young adult patients with B-ALL and, such double-hit events associated with complex karyotypes and poor prognosis. Younger patients may benefit from intensified chemotherapy.

P-064

HEALTH RELATED QUALITY OF LIFE, DEPRESSION, ANXIETY AND SELF-CONCEPT IN CHILDHOOD ALL SURVIVORS IN TURKEY

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Background/Objectives: With the advance in childhood acute lymphoblastic leukemia (ALL) survival rate, long-term side effects of the treatment which contains high doses of asparaginase, vincristine, and corticosteroids have become more important. As previously reported ALL treatment might adversely affect health-related quality of life. Besides health related quality of life our aim was to investigate, depression, anxiety and self-concept among ALL survivors.
Design/Methods: 50 patients who have been diagnosed Pre B ALL at least 4 years ago and their siblings were enrolled (n=100). Kovacs depression scale, State-Trait anxiety inventory, Offer Self Image Questionaire, Quality of life scale for children and adolescent were used for collecting data. The data were collected in a single session.
Results: There are significant differences between Quality of life scores among groups. The physical health ($p< 0.05$), psychological health ($p<0.03$) and total scores of the scale ($p<0.05$) of ALL survivors were significantly lower than the score of the siblings and reported significantly lower self-concept ($p<0.00$) than controls. ALL survivors have significant difficulty in the impulse control, level of emotion, body and self-image, social relations, professional purposes, sexual attitudes, family relationships, mental health and environmental compliance. Finally the results show that ALL survivors have significantly higher depression ($p<0.00$) and anxiety ($p<0.00$) symptoms when compared with their siblings.
Conclusion: A continuous diagnostical and interventional mental health services might be necessary for possible emotional side effects of treatment during and after the treatment. Adequate rehabilitation and follow-up programmes should be implemented for children during the treatment and after remission from ALL. When consedering parents child interaction is reciprocal, parents should recieve mental /psychological counseling too.

P-065

LEUKEMIA INITIATING CELLS IN ACUTE LYMPHOBLASTIC LEUKEMIA ARE ENRICHED IN EARLY CELL CYCLE AND CHARACTERIZED BY LOW CELLULAR ENERGY METABOLISM

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Background/Objectives: In acute lymphoblastic leukemia (ALL), the nature of leukemia initiating cells (LIC) remains undefined, although of key clinical relevance since LICs need to be eradicated in order to cure the disease. The hierarchical concept with few LIC being able to propagate leukemia upon transplantation onto immunodeficient mice has been challenged by data showing LIC-activity also in committed cells supporting a stochastic model. As a common strategy, these studies are based on defining sub-populations by distinct surface marker profiles. In order to alternatively characterize and define LIC in ALL, energy metabolism and cycle phases were addressed in patient derived xenograft B-cell precursor (BCP) ALL samples.
Design/Methods: ALL cells were analyzed for levels of reactive oxygen species (ROS) along with DNA and RNA staining allowing determination of cell cycle phases. Repopulating activities of sorted cellular sub-fractions were investigated upon transplantation onto NOD/SCID mice.
Results: All cell cycle fractions showed LIC-activity and led to NOD/SCID/huALL engraftment. However, cells of early G0/G1 cell cycle phases showed increased repopulation activity compared to later/G2-M cell cycle phases. Interestingly, a low oxidative state (ROS^{low}) was identified in cells of early cell cycle in contrast to ROS^{high} cells originating from later cell cycle suggesting that the ALL cells' oxidative state is indicative for its leukemia initiating activity. To functionally address this hypothesis, sorted ROS^{high} and ROS^{low} cells were transplanted. Interestingly, ALL cells of low oxidative state (ROS^{low}) cells showed higher repopulating activity with short leukemia free survival of recipients compared to ROS^{high} ALL cells leading to significantly prolonged leukemia engraftment.
Conclusion: Our data indicate that all cells in ALL show LIC activity, with cells of early cell cycle and low energy metabolism representing the driving leukemia initiating cell compartment, thus pointing to redox modulation as a potential therapeutic target in ALL.

P-066

INFECTIONS DURING HIGH DOSE METHOTREXATE THERAPY IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA (ALL)

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Background/Objectives: High-dose methotrexate (HDMTX) therapy as an effective therapy for childhood ALL, which is frequently associated with side effects like infection in our centre . It prolongs hospital stay, delays chemotherapy and causes more economic burden on patients.Objective of this study is to identify the incidence, risk factors , and severity of infection during HDMTX therapy.
Design/Methods: This prospective observational study included fifty patients, aged 1-15 years scheduled to receive HDMTX 2.5gm/m^2 in B cell leukemia and 5gm/m^2 in Tcell leukemia at Department of Pediatric Hemato-oncology of BSMMU .With the approval of the local institutional review board, study was done over a period of six months from January,2012 to June 2012. Baseline investigations were done prior to therapy .Follow-up was done in daily basis from day of infusion upto recovery or 7 days after discharge from hospital. Demographic, clinical, pathological and microbiological data were collected according to a pre-defined Patient Data Form.
Results: Out of 50 patients, infection occurred in 19 (38%) patients. Gastro intestinal tract (GIT) was the most common site 8(42.11%). Microbiologically documented infections found in 9 occations, where Gram negative bacilli - E.coli 4(44.4%), Pseudomonus 3(33.33%) were predominant organisms. The rate of infection is significantly higher (P value =0.01) in children <5 yr(78.94%). Male child 15(78.94%) are more prone to infection then female child 4 (21.05%) (P value =0.01). Total 3 patients died during study period due to infection, the mortality rate was 6%.GIT symptoms as vomiting, mucocitis, diarrhea were the commonest features after HDMTX administration.
Conclusion: Infection (38%) as well as fatality rate (6%) is high with HDMTX chemotherapy, specially in younger children. Gram negative organism (E. coli, Pseudomonus) are the main pathogen in our center.

P-067

THE EFFECT OF CNS INVOLVEMENT AND CNS IRRADIATION ON SURVIVAL IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Background/Objectives: Central nervous system irradiation (CNS-RT) has been an important modality in the treatment of acute lymphoblastic leukemia (ALL). Nevertheless, most recent ALL protocols have omitted CNS-RT due to concerns regarding the long-term late-effects. Our aim was to estimate the effect of CNS involvement and CNS-RT on survival in children with ALL.
Design/Methods: In total, 2735 children aged 1-14.9 years with pre-B and T-cell ALL were treated according to the NOPHO ALL-92 and 2000 protocols. Patients stratified as High Risk, were included in the study (n=836). Prophylactic CNS-RT was prescribed to a subgroup of HR-patients older than 5 years. We evaluated the effect of CNS status at diagnosis and CNS-RT on the risk of death (overall survival, OS) and any event (event-free survival, EFS). Outcome estimations were calculated with the Kaplan-Meier method, Poisson regression and competing risks regression.
Results: CNS involvement was detected in 56/836 HR-patients (6.7%). Complete remission rate was similar in patients with or without CNS involvement. The central nervous system was more frequently involved at relapse if CNS positive at diagnosis. There were no differences in the OS (69.3% vs. 74.4%), EFS (60.6 vs. 61.9%) and

cumulative incidence of relapse (30.5% vs. 30.8%) at 10 years in patients with or without CNS involvement. CNS-RT was given to 170 patients. Overall survival was similar in patients with or without CNS-RT (84.4 ± 2.8% and 88.3 ±1.5%) but the hazard ratios in the irradiated patients for relapse, CNS-involving relapse and isolated CNS relapse were 0.36 ($p<0.001$), 0.35 ($p<0.01$) and 0.22 ($p<0.05$), respectively.
Conclusion: CNS involvement at diagnosis is a strong risk factor for CNS involving relapses, especially CNS involving relapses but is not an independent risk factor for overall survival or event-free survival. CNS-RT does not increase overall survival in general but decreases the risk of relapse and CNS involving relapses.

P-068

SECONDARY MALIGNANT NEOPLASMS AMONG CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA PATIENTS TREATED USING THE KYUSHU-YAMAGUCHI CHILDREN'S CANCER STUDY GROUP PROTOCOLS: A RETROSPECTIVE STUDY

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Background/Objectives: To investigate the cumulative incidence of secondary malignant neoplasms (SMN) and related factors among childhood acute lymphoblastic leukemia (ALL) patients treated using the Kyushu-Yamaguchi Children's Cancer Study Group (KYCCSG) protocols.
Design/Methods: A retrospective cohort study including 509 children diagnosed with ALL and registered in 3 consecutive multicenter KYCCSG protocols between June 1988 and July 2002 was conducted. The cumulative incidence of SMN and related factors including treatment protocol, irradiation, stem cell transplantation, and other features of primary ALL, were analyzed. Approximately two-thirds of patients (n=338) received cranial irradiation, and 90 patients received stem cell transplantation.
Results: Fifteen of 509 patients were diagnosed with SMN, including acute myeloid leukemia (AML)/ myelodysplastic syndrome (MDS) (n=7), brain tumor (n=5), malignant schwannoma (n=2), and basal cell carcinoma (n=1), within a median follow-up duration of 12.7 years. The cumulative incidence of any SMN was 2.5% (95% CI, 1.7-3.3%) at 10 years and 4.3% (95% CI, 3.1-5.5%) at 20 years, respectively. The standardized incidence rate ratio (SIR) of all SMN was 28.6. The SIRs of AML/MDS and brain tumor were 13.4 and 6.3, respectively. Univariate analysis revealed that cranial irradiation had a tendency to be associated with an increased risk of all SMN (chi-square=3.0, p=0.08). However, we an increased risk was not found for the type of protocol or stem cell transplantation.
Conclusion: Despite exposure to intermediate chemotherapy and cranial irradiation (including stem cell transplantation in some patients), the cumulative incidence of SMN was unexpectedly low. However, the SIR of SMN in childhood ALL was significantly higher than that of the age-matched general population. Risk-based follow-up and health check education for ALL survivors, and collaboration between the survivors' physician and a clinical oncologist should be encouraged for prevention and early detection of SMN.

P-069

BONE MINERAL DENSITY DEFICIT IN ADULT SURVIVORS OF CHILDHOOD CANCER: A SYSTEMATIC LITERATURE REVIEW

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Background/Objectives: Childhood cancer treatment may lead to diseases of the skeleton characterized by low bone mineral density (BMD), and a consequent increased fracture risk. A comprehensive review on the occurrence of BMD deficit, and its risk factors in childhood cancer survivors (CCS), has never been pursued.
Design/Methods: An electronic literature search was performed using PubMed, Medline, Scopus and Web of Science databases. Studies were included if survivors of childhood cancer (median age at diagnosis ≤18 years) were at least a median period of 5 years after stop therapy and had a median age of ≥18 years old at BMD measurement. Outcome measures were total body BMD (BMD_{TB}), lumbar spine BMD (BMD_{LS}) and hip BMD (femoral neck (BMD_{FN}), total hip (BMD_{TH}), expressed as Z-scores or Standard Deviation Scores (SDS).
Results: Literature search revealed 29 studies. All studies were retrospective and most of them used samples with less than 50 survivors; only 5 studies included more than 100 survivors. Most studies measured BMD in survivors of pediatric acute lymphoblastic leukaemia (ALL); fewer studies assessed BMD in survivors of solid tumors. The majority of the studies found lower BMD values in survivors in comparison with healthy peers. In one large study, the percentage of all survivors with BMD<-1 SDS was about 40%. Especially, survivors of ALL and acute myeloid leukemia (AML), brain tumor, and osteosarcoma seemed to have a high risk of a BMD deficit. Lower body weight at adult age, cranial radiotherapy and treatment with glucocorticosteroids or chemotherapeutic agents seemed risk factors for BMD deficit.
Conclusion: Long-term childhood cancer survivors are prone to BMD deficit already at a relatively young adult age. These results indicate that greater awareness is needed, especially in survivors of leukemia, brain tumor and osteosarcoma, who have underweight and were treated with cranial radiotherapy or glucosteroids.

P-070

HIGH INCIDENCE OF HYPERDIPLOIDY AND BETTER PROGNOSIS FOR HIGH HYPERDIPLOIDY IN OUR COHORT OF PEDIATRIC B-ACUTE LYMPHOBLASTIC LEUKEMIA: FLOW CYTOMETRY BASED STUDY FROM NORTHERN INDIA

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Background/Objectives: *Introduction*: DNA ploidy assessment forms an important method to detect numerical genetic abnormalities in B-ALL and patients are categorized into favorable or unfavorable risk groups based on high hyperdiploid (>51 chromosomes) or hypodiploid (<46 chromosomes) DNA index respectively. *Aims & Objectives*: To standardize and note the frequency of DNA ploidy abnormalities in pediatric B-ALL and to correlate the same with early response to chemotherapy.
Design/Methods: DNA ploidy assessment was done in 40 pediatric B-ALL cases confirmed on bone marrow and immunophenotyping before start of chemotherapy. 40 non-leukemic controls were run with each sample. Samples were processed using DNA ploidy kit reagents (Cycletest DNA ploidy kit; BD biosciences) and analysis was done on a flow cytometer (LSR-II; BD biosciences). The DI (DNA index) was calculated using the Mofit software. The results were compared with standard risk criteria and chemotherapy outcome (modified UK-ALL protocol).
Results: A hyperdiploid cell line was noted in 33/40 (82.5%). 7/40 (17.5%) cases had diploid cell line. None of the cases showed a hypodiploid population. DI of 1.01-1.15 (Hyperdiploid A) was seen in 17/33 (51.5%), DI between 1.16-1.6 in 11/33 (33.3%) and 4/33 (15.2%) had a DI>1.90 (tetraploidy range). Cases with DI >1.16 had significantly better response to treatment than with those having diploid DI or DI between 1.06-1.16 ($P<0.05$). Significant prognostic factors on Cox analysis were DI>1.16, age between 2-9 years, WBC count< 50,000 and Hb<9.0.
Conclusion: There is a relatively high frequency of hyperdiploidy cell line in our cohort of B-ALL patients. Cases with DI>1.16 and WBC count <50,000 at presentation are likely to respond better to chemotherapy with less risk of relapse. However, prospective studies on a large cohort of B-ALL cases in our population are needed to derive definitive conclusions and make individualized treatment decisions.

P-071

STUDYING T-CELL ACUTE LYMPHOBLASTIC LEUKEMIA (T-ALL) MINIMAL RESIDUAL DISEASE (MRD) USING TEN COLOR FLOW CYTOMETRIC ASSAY

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Background/Objectives: MRD is a well establish prognostic factor in the management of T-cell acute lymphoblastic leukemia (T- ALL) and flow cytometry (FC) is easily available and widely used for MRD evaluation. Currently standardized FC based MRD assays are 4 to 6-color assays and have analytic limitations leading to decreased efficacy. With aim to overcome these limitations and to improve sensitivity and specificity, in this study we standardized a 10-color FC T-ALL MRD assay.
Design/Methods: We studied 68 MRD tests in 50 pediatric T-ALL patients from January 2014 to January 2015 at different time points. Of these 50 were post-induction (day 33), 15 were post-consolidation (day 78) and three maintenance samples. T-ALLs were diagnosed as per WHO 2008 criteria using a comprehensive antibody panel. Ten-color T-MRD assay was standardized and all the samples were analyzed by the Navios flow cytometer (Beckman Coulter) using Kaluza analysis software Antibodies for T-MRD panel included CD5-BV421, surfaceCD3-BV510, CD8-FITC, CD7-PE,

cytoplasmicCD3-ECD, CD34-PCcy5.5, CD16+CD56-PC7, CD4-APC, CD45-AF700, CD38-AF750, and Syto13 for nuclear staining.. MRD results were correlated with other high risk factors.
Results: Fifty T-ALL cases (M:F ratio 7.3 :1) including 5 early precursor T-ALLs (ETPALL) were studied. Seventeen (34%) of 50 post-induction and 3 (17.5%) post consolidation samples were MRD positive (mean - 0.78%, median - 0.1% & range - 0.002% to 24.5%). Two (40%) of 5 ETPALLs were positive post induction but negative post consolidation. Lowest level of MRD detected by this assay was 0.002%, which indicates very high sensitivity (2 in 10^6) of 10-color FC-T-MRD as equal to MRD by molecular assay.
Conclusion: Ten-color T-ALL MRD assay provides high level of sensitivity and helps in better monitoring of response to therapy.

P-072

OUTCOME OF TREATMENT OF PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA IN DOWN AND NON DOWN SYNDROME. EXPERIENCE AT A SINGLE TERTIARY CARE CENTER

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Background/Objectives: Outcome of Acute Lymphoblastic Leukemia (ALL) in children with Down syndrome (DS) remains poor mainly because of high relapse rate and treatment related toxicities.
Design/Methods: Medical records of 34 DS patients with ALL between 1997 and 2013 were reviewed. Data extracted included those related to clinical characteristics of patients and their outcome.
Results: Twenty One patients were males (61.76%). Median age at diagnosis was 60.96 months (range17.16-162.24). Thirty one patients were below the age of 10 years (91%). Mean WBC count was 33.95(range 1-500), CBC blasts mean was 40.51. Twenty Five patients were CNS1, Five were CNS2 and one patient was CNS 3. Thirty three patients had precursors B- (97%) and one had Biphenotype ALL. Three patient had additional trisomy (9.6%). Twenty eight patients were evaluated for BM response. Twenty five (89.28%) achieved remission at day 14 while 28(100%) achieved remission at the completion of induction. Seven Patients (20.5%) relapsed (4 on therapy and 3 off therapy) at a median time of 20.22 months (range 3.57-86.59). Fourteen patients (41.1%) died, 10 due to progressive disease and 4 due to infections. Twenty three patients developed chemotherapy related infectious toxicities in induction and 22(64.8%) in post induction phase. OS was 50.1% and EFS was 48.8% compare to OS of 85% and EFS of 71.9% in non-DS ALL patients who received treatment at our institution during the same period. Age at diagnosis, gender, WBC count and Blasts in CBC did not significantly affect the probability of OS and EFS in our cohort.
Conclusion: Our results show a relatively poor outcome in DS ALL patients which is comparable to published data.

P-073

IS NUTRITIONAL STATUS AT DIAGNOSIS RELATED TO CLINICAL OUTCOME IN ACUTE LYMPHOBLASTIC LEUKEMIA?

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Background/Objectives: Undernutrition is considered to be an adverse prognostic factor in the outcome of treatment in patients with acute lymphoblastic leukemia (ALL), influencing the course of the disease and chances of survival. This analysis was performed to evaluate the effect of undernutrition on outcome in children with ALL.
Design/Methods: We analyzed 286 children treated for ALL from January 2010 to December 2012. Weight for age, height for age, BMI (WHO classification) and serum albumin at diagnosis were recorded. Anthropometric parameters were correlated with outcome.
Results: Mean age: 5.82 ± 3.14 years. There were 199 boys and 87 girls. Standard risk (NCI): 177, Intermediate/High risk: 108. Weight < -3 z score: 11.8%, between -3 & -2 z score: 14.6% and normal weight: 73.5% children. Height < -3 z score: 8.3%, < -3 & -2 z score: 8.3% and normal height: 83.4%. BMI < -3 z score: 12.3%, between < -3 & -2 z score: 12.3% and normal BMI: 66.4%. Serum albumin < 3 gm/dl: 33.4% of patients. Event free survival (EFS) is 63.9% (Events: relapse, death, default). Event free survival was not affected by weight (65.1% vs. 60.5% in underweight patients p=0.513); height (65% vs. 58.3% in stunted children p=0.710); BMI (EFS being equal in both groups) Hypoalbuminemia had a significant effect on EFS (56.1% vs. 68.4% p=0.035). Weight, height and BMI did not affect death independently (p= 0.386, 0.207 & 0.6) No difference in undernutrition, stunting and BMI was observed across gender and the standard/intermediate/high risk groups of disease.
Conclusion: There are conflicting results as to the outcome in undernourished children with cancer. There is a trend towards a lower outcome in undernourished children, with hypoalbuminemia at diagnosis having significantly lower EFS. Collaborative prospective studies using a common algorithm for assessment are needed to assess the impact on morbidity and mortality.

P-074

COGNITIVE OUTCOME IN CHILDREN AND ADOLESCENTS IN REMISSION FROM ACUTE LYMPHOBLASTIC LEUKAEMIA, TREATED WITH CHEMOTHERAPY ONLY

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Background/Objectives: The cognitive functioning in survivors of childhood acute lymphoblastic leukaemia (ALL) treated with chemotherapy only protocols has been evaluated by comparison to different groups, but results have been inconclusive. Studies that compare to matched healthy controls are still scarce. The aim of the present study was to assess cognitive outcome in children and adolescents in remission from ALL, treated with chemotherapy only, compared to healthy controls.
Design/Methods: Thirty-five children and adolescents, between the ages of 8-15 years and in long-term remission from ALL, 4-12 years post diagnosis, without relapse and no prediagnosis history of neurodevelopmental disorder, were compared with 35 healthy controls matched for gender and age. The survivors of ALL were recruited from Oslo University Hospital and St. Olav's University Hospital in Trondheim, Norway.The Wechsler Intelligence Scale for Children-Third Edition (WISC-III, Wechsler, 1989, 2004) was used to test cognitive outcome.
Results: All but two of the ALL survivors treated by chemotherapy only, obtained WISC-III Total Intelligence Quotient (IQ) scores in the normal range (M = 95.3). However, their scores were significantly below levels for their matched controls and below normative standards for WISC-III. The difference between the patient and controlgroup was significant at the $p < 0.001$ level for the measures Total IQ, Verbal IQ, Verbal Comprehension Index, Freedom from Distraction Index and three verbal subtest scores.
Conclusion: The results indicate impairment in global cognitive functions. They also indicate that verbal function, processing speed, as well as attention and complex visual-spatial problem-solving may be affected in the group of children receiving only chemotherapy, and should be taken into account by schools and health care providers. Therefore, it will be essential to implement adequate rehabilitation and follow-up programs for children in remission from ALL.

P-075

NEUROPSYCHOLOGICAL OUTCOME IN CHILDREN AND ADOLESCENTS AFTER TREATMENT FOR ACUTE LYMPHOBLASTIC LEUKAEMIA WITH CHEMOTHERAPY ONLY

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Background/Objectives: The main treatment for children with acute lymphoblastic leukamia (ALL) is chemotherapy only (CTO), however the cognitive functioning over time in long-term survivors has been inconclusive. Further evaluation and records of their neuropsychological function are scarce. The aim of the present study is to examine neuropsychological differences between survivors of childhood ALL treated with CTO compared to matched healthy controls.
Design/Methods: Neuropsychological performances in 36 children and adolescents, age 8.4 - 15.3 years, in long-term remission from ALL, 4.3 -12.4 years post diagnosis, without relapse and no pre-diagnosis history of neurodevelopmental disorder, were compared with the performance of 36 healthy controls matched for gender, age and the parents socio-economic status. The former patients and the healthy controls completed an extensive battery of standardized neuropsychological tests. The children and adolescents treated for ALL, were recruited from Oslo University Hospital and St. Olav's University Hospital in Trondheim, Norway. The treatments were initiated from May 1992 through 1999, in accordance with protocols developed in 1992 by the Nordic Society of Pediatric Hematology Oncology-ALL (NOPHO-1992).
Results: Survivors treated by CTO obtained significantly lower scores than healthy controls on tests of visual-spatial construction, working memory, memory span and

processing speed in tactile stimuli. The ALL survivors obtained a steeper rising learning slope with lower scores after single-trial memory and problem solving tasks, but catches up with the controls when the stimuli were repeated.
Conclusion: The results indicate neuropsychological long-term sequelae in ALL survivors limited to specific domains, especially processing novelty. Intervention programs and school programs should take into account the deficit in processing new information, and a focus on repetition may prevent that survivors fall behind their peers.

P-076

LONG TERM FOLLOW-UP OF 6-THIOGUANINE-INDUCED HEPATOTOXICITY IN CHILDREN TREATED ON UKALL 97/99 PROTOCOL; THE ROYAL MARSDEN EXPERIENCE

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Background/Objectives: The use of 6-thioguanine (6-TG) for treatment of ALL during UKALL 97/99 was associated with hepatotoxicity in a small subset of patients treated at the Royal Marsden hospital. We report the long term follow-up of these children with regard to their hepatic status.
Design/Methods: The case sheets and follow-up records of all these childrenwere revisited and data retrieved. Conventional descriptive statistics was used to analyse the data.
Results: Of the 11 children (boys-8, girls-3) with documented 6-TG induced hepatotoxicity in our database, 6 became symptomatic during treatment whereas 5 presented after a median of 24 (range 1-72) months from the end of therapy. The former group (n=6) presented with features of veno-occlusive disease (4) and transaminitis (2), whereas the latter group (n=5) had low counts with hepatosplenomegaly (4) or isolated splenomegaly (1) at presentation. After a median follow-up of 132 (72-168) months, 8 of 11 children had persistent problems; isolated splenomegaly was noted in 6 and hepatic involvement as evidenced by altered hepatic echo-texture on ultrasound was seen in 7 of these 8 patients. Of the 5 patients who underwent upper gastrointestinal endoscopy, 4 had oesophageal varices and 1 required banding. Liver biopsy performed in 4 of these 8 children showed nodular regenerative hyperplasia in all 4. Thrombocytopenia, present in 7 of these 8 children was associated with menorrhagia and pregnancy loss in 1.
Conclusion: Hepatic involvement in the majority of the patients with 6-TG induced hepatotoxicity in this cohort progressed to chronicity, highlighting the importance of continuing long-term hepatology and haematology follow-up in these patients.

P-077

FOLATE DEFICIENCY AND NEED FOR SUPPLEMENTATION DURING MAINTENANCE THERAPY FOR CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) - A PILOT STUDY

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Background/Objectives: Folate deficiency is common in children from resource limited settings. We had previously observed the association of folate deficiency with increased complications during maintenance chemotherapy for ALL. This prompted us to supplement folic acid in deficient children during maintenance, the effects of which are being reported.
Design/Methods: All children currently undergoing maintenance chemotherapy for ALL in our centre were enrolled, provided they had completed at least one cycle (84 days). Folate levels were assessed prior to each cycle or following unexplained cytopenias. Children were supplemented with 2.5 mg folic acid daily for 7days whenever their levels fell below <4ng/ml. The clinico-haematological parameters were recorded and analysed.
Results: Sixty-three children were included with a mean follow-up of 15.45(±9.69) months. 285 cycles of maintenance were studied. Folate deficiency was noted in the beginning of 51 cycles where folic acid was supplemented upfront. Folate deficiency was documented following screening for unexplained cytopenia in another 18 cycles (out of the 25 cycles screened). A higher incidence of febrile neutropenia (10 of 18 vs. 8 of 51; p=0.02) and longer duration of chemotherapy interruption (15.49±6.32 vs. 8.45±1.49 days; p<0.001) were noted in children of the latter group during a given cycle despite supplementation than children who were detected deficient and supplemented on routine screening. Ten deaths were seen during maintenance, of which 8 occurred in folate deficient children and 5 of these during episodes of unexplained cytopenias (p=0.04). None of the children studied had relapse of disease till last follow-up.
Conclusion: Folate deficiency was common in children during maintenance therapy of ALL and was a common cause of unexplained cytopenias in them. Pre-emptive detection of folate deficiency by frequent periodic screening and supplementation may decrease the incidence of complications and improve the outcome of maintenance therapy in these children, particularly in the resource limited countries.

P-078

MICRORNA EXPRESSION IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA: IDENTIFICATION OF MICRORNAS INVOLVED IN LEUKEMOGENESIS AND PROGNOSIS

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Background/Objectives: Abnormal microRNAs expression has been shown to play an important role in development and progression of different human cancer, but data in pediatric acute lymphoblastic leukemia (ALL) are limited. The present study aimed to evaluate the differential expression of miRNAs in children with ALL and correlate the expression levels with features of diagnosis and clinical outcome.
Design/Methods: We aimed to evaluate the miRNAs expression profile by microarray using the Human miRNA Microarray Kit (V3, 8×15K, Agilent) in 81 consecutive bone marrow samples from children with ALL at diagnosis (39 T-ALL and 42 CD10 B-lineage ALL). Changes in miRNA expression levels were detected using empirical Bayesian approach corrected by False Discovery Rate. Ten miRNA of the most differentially expressed were chosen to be validated by qRT-PCR using TaqMan probes in the 81 ALL samples and 8 pediatric non-neoplastic bone marrow (BM). The difference in expression between the groups was analyzed by Mann-Whitney test and event free survival (EFS) and overall survival (OS) by Kaplan-Meier plots and log-rank test, median of the expression values were used as cut-off and $P < 0.05$ considered as significant.
Results: The unsupervised hierarchical clustering evidenced two main clusters clearly identifying B-lineage and T-ALL. From the 10 validated mIRNA 5 were down-expressed (miR-148, -151, -550, - 497 and -765) and 1 overexpressed (miR-213) in ALL when compared with non-neoplastic BM. When compared B-lineage vs T-ALL overexpression was observed to miR-151, -455 and -574, and down-expression to miR-141, -148, -213 and -765. Overexpression of miR-455 and -574 were associated with death in B-lineage ALL. A higher expression level of miR-574 in B-ALL was also associated with lower EFS and OS. In children with T-ALL overexpression of miR-141 was associated with higher EFS.
Conclusion: The present results suggest a role of miRNAs in leukemogenesis and their potential prognostic in childhood ALL.

P-079

EFFECT OF THE INHIBITION OF THE XPO7 GENE IN RESPONSE TO METHYLPREDNISOLONE IN A CORTICORESISTANT T ACUTE LYMPHOBLASTIC LEUKEMIA CELL LINE

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Background/Objectives: In a previous study we observed a higher expression of *XPO7* gene at diagnosis in children with acute lymphoblastic leukemia (ALL) and poor response to induction treatment. The present study aimed in to investigate the effect of the silencing of *XPO7* gene by shRNA and the response to methylprednisolone (MPRED) in a T-ALL cell line.
Design/Methods: The corticoresistant CCRF-CEM T-ALL cell line was transduced by the RNA interference (shRNA) using 5 specific lentiviral clones to XPO7. After verification of gene knockdown (by qRT-PCR) and protein inhibition (by western blot), treatments were made with MPRED at different concentrations (1, 5, 50 e 100 μg/mL) at the times 24, 48, 72 and 96 hours of exposition followed by in vitro functional studies. Cytotoxicity was evaluated by the method of resazurin at all times and apoptosis by flow cytometry using anexin and propidium iodide at 96 h.
Results: Due to the resistance of the cell line to MPRED the IC50 was not possible to be evaluated, once 73% of the cells were viable with 100 μg/mL of MPRED. After silencing, there was a significant decreased of the proliferation with the dose of 100μg/mL in 24 h when compared with the pLKO non-silenced control ($P<0.05$). Interestingly the opposite occurred at the times 48, 72 and 96 h with increase of proliferation compared to control. No differences were observed with the other

concentrations used. A significant increase of apoptosis was observed with the dose of 100μg/mL at 96 h (P<0.05).
Conclusion: The inhibition of *XPO7* can be an interesting target for the treatment of corticoresistant T-ALL.

P-080

CNS-DIRECTED TREATMENT AND ITS EFFECT ON VISUOMOTOR CONTROL IN THE SURVIVORS OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKAEMIA: A PRELIMINARY RESULT

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Background/Objectives: Central nervous system(CNS)-directed treatment is an integral part of childhood ALL protocol, leading to marked improvement in prognosis and survival over the last few decades. However, major chemotherapeutic agents used as CNS prophylaxis have central neurotoxic side effects, thus, evaluations to determine the late effects of the treatment to the survivors were of great concern.
Design/Methods: A single centre, cross sectional study was conducted in Paediatric Oncology Unit, UKMMC from 1st May 2014 until 28th February 2015 to evaluate the effect of chemotherapy on visuomotor control in survivors of childhood ALL. A total of 40 survivors who were off-treatment for at least 1 year and were in remission, and 40 healthy controls were enrolled into the study. Three subtests from Amsterdam Neuropsychological Task(ANT) program were administered to assess the subjects' visual reaction time (baseline speed) and their cognitive control/processing(tracking and pursuit).
Results: Majority of the patients recruited were treated using the UKALL 97(99) protocol (87.1%, n=34) while the rest were treated using UKALL 2003 protocol. Median age at diagnosis was 3.87 years (IQR 2.95-5.45) while mean duration off-treatment was 6.03 years (SD±2.76). Twenty five patients (62.5%) were of Standard Risk group and 15 patients were High Risk group. Four patients had relapse while 2 patients had CNS involvement and received craniospinal irradiation. There were statistically significant difference between the survivors of childhood ALL and healthy controls on the measures of tracking accuracy($p = 0.020$) and pursuit stability($p = 0.035$). Higher cumulative intrathecal Methotrexate dose predicted poorer performance for the pursuit stability. There were no significant correlation between gender and age at diagnosis with the visuomotor deficit in our study cohort.
Conclusion: Survivors of childhood ALL in our centre showed components of visuomotor control deficits compared to healthy controls. Remedial actions should be offered to improve the survivors' neuropsychological performances.

P-081

URINARY TRACT INFECTIONS IN PEDIATRIC ONCOLOGY PATIENTS – SINGLE CENTER EXPERIENCE

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Background/Objectives: Infectious complications of chemotherapy are common and potentially severe, especially in neutropenic patients. Urinary tract infection (UTI) is one of the most prevalent bacterial infection in pediatric oncology patients. But most febrile neutropenic patients had any sign and symptoms of inflammation. Aims of this study are to find distinguishing characteristics of UTI in pediatric oncology patients.
Design/Methods: UTI was defined as a positive urine culture in the absence of another focus in a febrile patient. Urine culture was considered positive if >105 CFU/ml of single urine pathogen was found in a clean catch urine sample or by clean catheterization. Nine episodes of UTI on 9 patients enrolled in this study (UTI group). Control group consists of febrile neutropenia with negative urine culture, and 34 episodes of 24 patients were enrolled in this group. We compared clinical features, lab findings between two groups and analyze characteristics of UTI group.
Results: Compared to controlgroup, UTI group shows high level of total IgG, lower creatinine level, and have shorter duration of fever. In UTI group, E. coli was the most common pathogen. In UTI group, patients with pyuria tend to appear abnormal finding in renal Doppler and DMSA.
Conclusion: Urinalysis and urine culture should be obtained routinely as part of the diagnostic evaluation of patients with fever and neutropenia.

P-082

SIGNIFICANT PROGNOSTIC VALUE OF MINIMAL RESIDUAL DISEASE DETECTED BY MULTICOLOR FLOW CYTOMETRY DURING INDUCTION TREATMENT IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Background/Objectives: The study aimed at assessment of prognostic value of multicolor flow cytometric MRD detection during induction treatment of childhood ALL according to ALL-IC BFM 2002 protocol.
Design/Methods: The study group consisted of 371 children treated for ALL in centers of the Polish Pediatric Leukemia/Lymphoma Study Group. Bone marrow samples obtained at initial diagnosis were analyzed with multiparameter flow cytometry according to the EuroFlow protocols. Based on the immunophenotype at diagnosis, the 2-3 flow cytometric 6-8 color tubes were selected to detect MRD in bone marrow samples obtained at day 15, day 33, and at week 12. The median follow-up for the whole group was 5.4 years. Equality of continuous variables was analyzed by Mann-Whitney's U test. For multivariate analysis, the Cox regression model was applied. The probability of event-free survival and of overall survival was determined by Kaplan–Meier analysis. $p < .05$ was considered significant.
Results: On day 15 MRD levels were <0.1% in 31% of patients. Only 2 patients in this group relapsed. Moreover, in 14.2% of patients MRD was undetectable at D15. None of the MRD-negative children relapsed. In 34 patients (12.4%) MRD at D15 exceeded 10%. At D33 MRD was detectable in 40.2% of patients. In 42 patients MRD levels were > 0,1%, which was associated with unfavorable events in 15 patients. At week 12 MRD was present in 15.9% of patients; 8 MRD+ patients experienced unfavorable events. Event-free survival was significantly influenced by leukocyte count at diagnosis (p<0.001), prednisone response (p<0.05), MRD D15 (p<0.001) and MRD D33 (p<0.001). Age and leukocyte count at diagnosis (p<0.05), steroid response (p<0.05), MRD D15 (p<0.001), MRD D33 (p<0.001) and MRD at week 12 (p<0.05) were significantly associated with overall survival.
Conclusion: MRD detection based on multicolor flow cytometry gives significant prognostic information and can be applied for improved risk group assignment in pediatric ALL.

P-083

LOW COST INNOVATIONS IN SUPPORTIVE CARE IN CHILDREN UNDERGOING HIGH DOSE CHEMOTHERAPY

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Background/Objectives: Low cost innovations in supportive care will result in improved outcomes in children undergoing cancer chemotherapy in developing countries.
Design/Methods: Our study included all children from 0 to 18 years of age diagnosed at our centre treated for a malignancy from 2002 to 2014. Their outcomes in terms of rates of sepsis, mortality and durable remission rates were analyzed.
Results: The first intervention was with respect to neutropenic diet based on the fact that translocation of gut bacteria resulted in systemic sepsis especially hospital acquired resistant bacteria like Klebsiella. Neutropenic children were put on a strict diet program including double boiled rice, vegetables, pulses, yogurt and lactose free milk supplements. Wheat, lactose and meat products were eliminated from the diet. This intervention has resulted in decrease in infections rates from 22% down to 8 %. The second intervention was related to central line associated blood stream infections (CLASBI). Biopatch placed over the central line entry site has decreased rates of CLASBI by 32% and central line dressing is done only once in 5 days. The cost of the biopatch is 500 Indian rupees, while the cost incurred on antibiotics for treatment of CLASBI amounts to over 12,000 Indian rupees a day for a 15kg child. The third intervention was related to the universal use of Peg Asparaginase for all children with acute lymphoblastic leukaemia regardless of their economic background. Two or three children shared the cost of each vial (Rs 120,000), ensuring availability of this expensive

yet highly efficacious chemotherapeutic drug to all children irrespective of their economic condition.
Conclusion: Effective use of simple low cost innovations in supportive care of our children help reduce rates of hospital acquired infections and ensure equitable treatment for all children with improved survival.

P-084

PAEDIATRIC STEM CELL TRANSPLANTATION: A SINGLE CENTRE EXPERIENCE FROM THE DEVELOPING WORLD

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Background/Objectives: To review paediatric patients who underwent allogeneic haematopoietic stem cell transplant (AHSCT) at Groote Schuur/University of Cape Town Private Academic Hospital Transplant Unit with post-transplant care at Red Cross War Memorial Children's Hospital from December 1999 to December 2014.
Design/Methods: A retrospective analysis of paediatric patient charts who underwent AHSCT between December 1999 and December 2014.
Results: Fifty children received AHSCT. Indications varied: 25 for haematologic malignancies, 13 for bone marrow failure syndromes, 8 for transfusion dependant haematological disorders, 3 for life threatening immunodeficiency and 1 for adrenoleukodystrophy. There were 31 male (median age 93.9 months range 1.67-135.9 months) and 19 female (median age: 104.6 months range 9.2-141.5 months) patients. Thirty three received HLA identical mobilised peripheral blood stem cell (PBSC) graft from a sibling and 1 a maternal haplo-matched bone marrow (BM) graft. Eight received 10/10 HLA matched unrelated grafts: 6 were PBSC grafts and 2 were BM grafts. Eight umbilical cord blood (UCB) transplants were performed. Only 3 of the unrelated PBSC grafts were from local donors. The cords were all from international registries. Five patients died of complications of graft versus host disease (GvHD) and 1 due to graft failure. Two patients died due to severe infections within 6 months of transplant. 3 patients died of relapsed leukaemia after transplant. Thirty nine patients are alive in remission (sixteen oncology patients and 23 non-oncologic patients). Three patients are living with chronic graft versus host disease (GvHD) necessitating ongoing immunosuppression.
Conclusion: Fifty children underwent AHCST, 25 for haematological malignancies and 25 for benign haematological conditions. The majority of stem cells were from siblings. These results are promising for a resource limited setting especially for patients transplanted for benign diseases.

P-085

ERWINIA ASPARAGINASE USE IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKAEMIA ALLERGIC TO PEGASPARGASE

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Background/Objectives: Asparaginase is an effective drug and essential part of the combination treatment of children with acute lymphoblastic leukaemia (ALL) and the 5-year survival rate has increased significantly since it was introduced into treatment protocols. Failure to complete treatment with asparaginase leads to poorer outcomes and it is therefore important to identify patients with clinical and subclinical allergy. In the UK, patients receive between 3 and 8 doses of pegaspargase 1000IU/m^2/dose intramuscularly (IM) depending on their risk stratified treatment group. UK Protocols (UKALL 2003, Interim guidelines and UKALL 2011) all advise to change each dose of pegaspargase to 6 doses of 20,000IU/m^2 IM Erwinia Asparaginase in case of systemic allergy. Prior to November 2005 Erwinia asparaginase was not available in the UK and patients allergic to pegaspargase discontinued asparaginase treatment altogether.
Design/Methods: We retrospectively identified and evaluated patients (aged 1-24 years) with a systemic pegaspargase allergy who were treated for ALL from October 2003 to March 2015 at The Royal Marsden Hospital. A systemic allergy was defined as Grade 2 or more using the common terminology criteria for adverse events.
Results: During this time 453 patients received treatment for ALL as per UKALL 2003, 2011 Interim Guidelines and UKALL2011 trials. We identified 24 (5.3%) patients with pegaspargase allergy who needed to switch to Erwinia asparaginase. The severity of the reactions varied from a generalised rash to full-blown anaphylaxis. There were no deaths related to the allergic reactions.
Conclusion: The incidence of children who developed pegaspargase allergy was 5.3%. No children reacted to Erwinia asparaginase after switching.

P-086

A STUDY OF SERUM AND CSF METHOTREXATE LEVELS FOLLOWING HIGH DOSE METHOTREXATE INFUSION IN ACUTE LYMPHOBLASTIC LEUKEMIA AND ITS CORRELATION TO RELAPSE

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Background/Objectives: High dose methotrexate is a major component of most contemporary acute lymphoblastic leukemia (ALL) treatment protocols as a CNS-directed therapy.
Design/Methods: We describe a retrospective analysis of ALL cases diagnosed between January 2007 to December 2013. 114 children (378 cycles) who received high dose methotrexate infusion were analyzed. Children were treated using two ALL protocols (BFM- 95 protocol(5 gm/m^2/cycle x 4) and UK ALL XI (6 gm/m^2/cycle x 3)) at our center during this period. Serum and CSF methotrexate levels were measured at the end of 24 hours, with additional serum levels at 48 and 72 hours as required.The data was analyzed for the correlation of serum and CSF methotrexate levelsachieved to occurrence of medullary and extramedullary relapse.
Results: Median age at diagnosis was 4 years (1 – 18). 12 patients had T cell, rest had B cell lineage. Median 24-hour and 48-hour levels achieved were comparable between both protocols. Significant variability was noted in the 24-hour values. 48-hour serum level and CSF level remained homogenous. There was good correlation observed between 24-hour serum level and CSF level. >90% patients achieved a protective level of Mtx in the CSF in all cycles. A total of 7 relapses (2 CNS, 2 medullary, 3 medullary + testes) occurred during a median follow up of 3.7 years. There was no statistically significant difference in the any serum or CSF drug level between patients who relapsed and those who did not. In patients who relapsed CSF and serum levels were significantly less than average. None developed any major complications during HDMtx cycles.
Conclusion: HDMtx is definitely feasible in India. Although our follow up is short, it has definitely helped us in reducing the incidence of CNS relapse. 48 hour Methotrexate values were homogenous and close to statistical significance in preventing relapse.

P-087

POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME TREATMENT BASED ON SYMPTOMS AND IMAGING FINDINGS IN PEDIATRIC PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Background/Objectives: Posterior reversible encephalopathy syndrome (PRES) is an uncommon side effect of some chemotherapeutic agents, particularly methotrexate. The clinical presentation depends on the area of brain hypoperfusion. To date there is no standardized treatment, but a myriad of drugs and procedures have been proposed. The purpose of this study is to report our experience in the treatment of this síndrome in patients with acute lymphoblastic leukemia (ALL).
Design/Methods: We performed a retrospective chart review and included patients with lymphoblastic leukemia with neurologic focal symptoms two weeks after methotrexate treatment regardless route of administration. The study period was from October 2004 to December 2014.The demographic and clinical characteristics are described as means or proportions according to variable type.
Results: We reviewed 176 charts of eligible patients, of which eight (4.5%, 4 female, 4 male) had PRES. The average age was 11.2 years. Seven patients had high-risk ALL (87.5%) and 1 (12.5%) standard risk ALL. The onset of symptoms started at an average of 7.3 days after intravenous (n=6; 75%), or intrathecal (n=2; 25%) methotrexate. None of the cases had simultaneous routes of administration.Patients with localized ischemia (n=3) were treated citicoline (10-20 mg/kg/d) for 5-7 days, with seizures (n=2) were treated with valproate for 6 months (15 mg/kg/d); and with areas of brain edema were treated with dexametasone (0.5 mg/kg/d) for 5 days. All patients with brain ischemia without seizures (n=3) were treated with hyperbaric oxygen therapy. Five patients had multiple simultaneous therpay according to clinical and imaging characteristics. Symptoms recovery was present at 10 days postreatment average. None of the patients had permanent neurological sequelae.
Conclusion: According to our findings, complete recovery of PRES can be achieved if therapy is started early based on symptoms and MRI findings. If no contraindication is present, multiple simultaneous therapy can be safely prescribed.

P-088

IS IT REASONABLE TO USE HIGH INTENSITY PROTOCOLS FOR ACUTE LYMPHOBLASTIC LEUKEMIA IN COUNTRIES WITH LIMITED RESOURCES? EXPERIENCE WITH ST JUDE HOSPITAL TOTAL XV PROTOCOL

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Background/Objectives: Implementing high intensity protocols in pediatric patients with Acute Lymphoblastic Leukemia (ALL) in countries with limited resources has been debated. We analyzed the survival of our patients using the Total XV St Jude protocol in SOLCA Hospital.
Design/Methods: We reviewed medical records and POND online database for a 9 year period from January 2006 to December 2014.
Results: A total of 191 patients were diagnosed with ALL; from these, 138 were elegible. We excluded patients previously treated in other hospitals, with prior malignancies and infants. There were 63 females and 75 males. Common ALL (97) was the predominant lineage, T-cell (18), early pre B (8), bilineal (T&B) 8, and biclonal 7 (AML/ALL). Hyperleukocytosis (>100.000/mm3) was identified in eleven patients (7.9%). Twenty-nine (21%) had translocations: t(1;19), t(12;21) and t(9;22) were the most common. Fourty-two (30.4%) were considered low risk patients, 81 (58.7%) standard risk and 15 (10.9%) high risk according to the stratification used in the original protocol. Twenty patients (14.5%) relapsed. Bone marrow and isolated Central Nervous System (CNS) were the most common sites, from these, 10 are alive in treatment or post stem cell transplant. Twelve patients (8.6%) abandoned treatment. Thirty-three (24%) patients died. Overall survival is 76% and if we exclude abandonment, 83%. Ten patients (7%) died during induction. One with CNS hemorrhage and nine with bacterial (6) or fungal (3) infections.
Conclusion: High intensity protocols can be used in middle income countries if the hospital provides a multidisciplinary team, Intensive Care Unit, broad spectrum antibiotics, antifungals, blood products, and if protocols are implemented for management of febrile neutropenia. We have to find strategies to decrease the abandonment of treatment and improve the education of parents for early arrival to the hospital in emergencies.

P-089

PHONE-BASED PALLIATIVE CARE FOR CHINESE PEDIATRIC PATIENTS WITH CANCER

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Background/Objectives: More than 60000 pediatric patients in China were diagnosed cancer each year. However, only few cancer patients can receive palliative care even though almost 25% of them are incurable. With the development of China, more and more patients and families have the demand of palliative care especially at the end of life.
Design/Methods: From Nov. 2013 to Dec. 2014, patients with incurable cancer were received palliative care by a multidiscipline team in hematology/oncology center of Beijing Children's Hospital. The support was operated by experienced nurses and oncologists. Phone support is the main method to communicate with families.One phone call by nurses every two weeks if patient was stable. Updating of the patients' condition, quality of life evaluating, pain management and psychological counseling were the majority of calls. For sure parents could call back to team at anytime they need. A routine round by team members were held every month in order to discuss patients' situation and make plans for the next step.
Results: 38 patients with incurable cancer were enrolled.Patients' average age was 5.96±5.16 years, 75% patients were leukemia, 22.5% were solid tumor.52.6% (20/38) patients experienced pain which could be controlled by team. 30 patients died peacefully by now, the median survival time was 30 days, the average score of quality of life was increased 21.08% during hospice care. 93.3% (28/30) families could accept children's death without long term depression, .all families satisfied with palliative support.
Conclusion: Because of the different culture background, parents would like to bring incurable children back to hometown, phone-based palliative care can be the important and effective method in China.

P-090

DETERMINE THE GENOMIC BREAKPOINT OF TEL-AML1 BY NEXT GENERATION SEQUENCING

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Background/Objectives: The most common chromosomal translocation observed in childhood acute lymphoblastic leukemia (ALL) is t(12;21)(p13;q22), which leads to an ETV6-RUNX1 gene fusion and associated with favorable prognosis following conventional therapeutic strategies. To TEL-AML1 positive leukemia, the genomic breakpoint and flanking sequence from the translocation of chromosome 12 and 21 is one of the best markers of minimal residual disease (MRD) monitoring by quantitative real-time polymerase chain reaction (QRT-PCR).
Design/Methods: In this study we established the next-generation sequencing (NGS) based TEL-AML1 translocation capturing and sequencing method. Moreover, we compared patient-specific breakpoint and flanking sequence on paired diagnostic and relapsed samples.
Results: We found patient-specific breakpoints in 24 cases of childhood ALL samples. Besides, we found the three-way translocation including TEL-AML1 in 5 patients, and 4 of them relapsed on the late or after the cessation of treatment. In contrast, 19 patients without three-way translocation were still in remission (P<0.0001). The three-way translocation may reflect the degree of genetic instability or gene damage. Moreover, by comparing patient-specific breakpoint and flanking sequence on paired diagnostic and relapsed samples, we also found that relapsed clone mainly derived from primary leukemia clone at diagnosis.
Conclusion: The three-way translocation maybe an important risk factor of TEL-AML1 positive leukemia relapse, and this method could be further developed and become a new MRD monitoring method.

P-091

COMPLETE BLOOD COUNTS AND PERIPHERAL SMEAR REVIEWS IN YOUNG CHILDREN WITH AND WITHOUT ACUTE LEUKEMIA

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Background/Objectives: The proportion of young children with leukemia but without blasts found on peripheral smear review is unclear as are results on the automated complete blood count (CBC) that best differentiate between those with and without acute leukemia.
Design/Methods: We recorded the clinical presentations, and results of CBC, and peripheral smear reviews in 87 consecutive children aged <5 years with acute leukemia. We then compared the CBC results to those from 739 consecutive outpatients of the same age.
Results: In patients with acute leukemia 77% (95% CI – 67.1%-84.6%) had blasts found on the peripheral smear review, and those without blasts had a bone marrow examination because of combinations of presenting symptoms and findings on the automated CBC. Retrospectively, we found that a combination of four criteria had the best sensitivity and specificity in differentiating patients with and without acute leukemia; 94.3% (95% CI- 87.2-97.5%) of the young children with leukemia but in only 2.3% (1.4-3.7%) of those without leukemia had at least one of four criteria (a white blood cell count $>30 \times 10^9$ cells/L, an absolute neutrophil count $< 1 \times 10^9$ cells/L as well as a platelet count less than 120×10^{12} /L, or a hemoglobin value < 80 gm/L). All the children not identified by at least one of the four criteria had clear clinical indications for a bone marrow examination.
Conclusion: A significant number of young children with leukemia will not have blasts found on the peripheral blood smear review, and physicians should rely on the automated CBC test results and the presenting symptoms to determine the need for a bone marrow examination. Prospective studies with larger numbers of young children are warranted to confirm these preliminary findings that suggest automated CBC criteria that are most helpful in determining the need for a bone marrow examination.

P-092

AUTOPHAGY-DEPENDENT RESTRICTION OF GLUCOSE METABOLISM IN PRIMARY ACUTE LYMPHOBLASTIC LEUKEMIA CELLS

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Background/Objectives: Clinical evidence indicated that favorable Glucocorticoids (GCs) sensitivity of childhood acute lymphoblastic leukemia (ALL) tended to associate with high periodic acid-Schiff (PAS) scores for glycogen staining, inhibition of glycolysis, and activation of autophagy.
Design/Methods: To investigate whether GC-induced cytotoxicity was influenced by autophagy and manifested by the interruption of glycogen metabolism and glycolysis, primary cells were isolated from patients and tested for glucose utilization under cultured conditions, without or with rapamycin pretreatments. The levels of IL-1β secretion in vitro, as well as in the plasma of original patients, were examined by ELISA. The cellular existence and distribution of glycogens was evaluated by PAS scores, and cross-examined with transmission electron microscopy (TEM).
Results: Rapamycin treatments were able to activate autophagy and restrict the glucose utilization in cultures from patients with different PAS scores. However, there seemed to lack the direct correlation between levels of autophagy activation and the *morphological changes of glycogens. Interestingly, the IL-1*β levels in poor GC-responsive group with low autophagy activities were higher than others with statistical significance.

Conclusion: As autophagy was increasingly recognized as a key process to regulate glucose metabolism, the approach of using primary cultures for probing the autophagy activation capacity could be an attractive and practical method for clinical outcome evaluations. Despite no direct association between the glycogen and autophagy activation of ALL cells was established from this study, the discovery of IL-1β for the indication of glucose metabolism changes implied potential diagnostic values. The dependence of IL-1β secretion to the activation of autophagy has enabled IL-1β as a candidate marker of autophagy in other tissue types, its application potential in leukemia remained to be further investigated.

Posters: Bone Tumours

P-093

EWING SARCOMA AND PRIMITIVE NEUROECTODERMAL TUMORS OF THE CHEST WALL IN CHILDREN: HACETTEPE EXPERIENCE

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Background/Objectives: Ewing sarcoma/primitive neuroectodermal tumor (ES/PNET) is the most common malignant tumor of chest wall in children. We aimed to review our institutional experience to document clinical and pathological characteristics and treatment results of our cases.
Design/Methods: Hospital files of 36 children with chest wall ES/PNET diagnosed between 1972-2014 were reviewed. Demographic characteristics, presenting symptoms, physical examination findings, laboratory and radiological data, extent of disease, treatments and outcome were analyzed.
Results: Median age was 9.8 years (2-17; male/female: 20/16). Most common presenting complaints were chest wall masses and pain, respiratory problems followed; fever and weight loss were less common. Primary tumor sites were ribs in 33/36, soft tissues in 3/36 cases. Histopathology was PNETs in 16/36 (45%), ES in 20/36 (55%). Eleven cases (30.5%) had distant metastases (lungs 9, bones 3). Primary tumor resection was performed in 12 cases (33%) at our hospital or outside; in 13 cases (36%) tumors were resected following chemotherapy; in 11 cases (31%) surgery was not attempted. All cases received multiagent combined chemotherapy regimens depending on year of diagnosis. Twenty-five cases (70%) received external irradiation to primary tumor sites. In the follow-up, 25 cases (70%) experienced tumor recurrence or progression mostly in primary sites, recurrences in lungs or bones were less frequent. A boy who had a recurrence 44 months after initial diagnosis received further treatment and was in remission for 7 years. At a median follow-up of 76 months, 23 cases died, 5 were lost to follow-up and 8 cases were under follow-up (6 disease-free). Five-year event-free and overall survival rates were 22.7% and 30.2%, respectively.
Conclusion: Most patients had advanced disease and complete resection wasn't possible in the majority. Local and/or distant failures were frequent. Preoperative chemotherapy may facilitate total resection. More intensive standard chemotherapies and effective local therapies, especially surgery, should be encouraged to improve prognosis.

P-094

IMPACT OF GENTAMICIN USE ON CISPLATIN-INDUCED HEARING LOSS IN PATIENTS WITH OSTEOSARCOMA

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Background/Objectives: Patients treated with the ototoxic anticancer drug cisplatin often receive aminoglycosides to treat febrile neutropenia or gram-negative infections. The additional impact of the use of aminoglycoside on the hearing loss risk of patients who already receive cisplatin for cancer treatment is not fully resolved yet.
Design/Methods: We investigated the use of gentamicin in 20 patients with osteosarcoma (aged 9-24 years, median: 15.4 years). Patients received 120 mg/m^2 cisplatin per cycle as a continuous infusion over 72h according to the COSS96 (6 patients) or EURAMOS-1 (14 patients) protocol. Ototoxicity was graded according to the Muenster Classification for Early Detection of Cisplatin-Induced Hearing Loss (MS).
Results: Patients were classified in hearing loss ≥ MS grade 2b (9 patients, group A) and <MS grade 2b (11 patients, group B). Among group A, 5 of 9 patients were treated according to COSS-96, while only 1/11 patients of group B received COSS-96 (p=0.05; Fisher's exact test). The cumulative cisplatin doses ranged between 240-480 mg/m^2. Patients of group A tolerated significantly less cisplatin until onset of hearing loss compared to patients of group B (group A: median: 240 mg/m^2; range: 120-360 mg/m^2 vs. group B: median: 480 mg/m^2; range: 360-480 mg/m^2, p<0.001 Mann-Whitney Rank Sum Test). Seventeen of 20 patients received gentamicin for supportive care (8/9 in group A und 9/11 in group B). Two of 9 patients in group A already developed ototoxicity before any gentamicin was administered. Altogether no significant differences were observed between group A and B with respect to tolerated gentamicin administrations and cumulative gentamicin doses. However, the interval between ototoxic medications (cisplatin/gentamicin) was significantly shorter in patients of group A (group A: median: 26.5 days; group B: median 40.3 days) (p=0.002, Mann-Whitney Rank Sum Test).
Conclusion: Regarding the long half-life of aminoglycosides their ototoxic impact has to be considered in the course of platinum treatment of patients with osteosarcoma.

P-095

CLINICOPATHOLOGIC CHARACTERISTICS AND OUTCOME OF CHILDHOOD EWING'S SARCOMA IN CENTER OF TUNISIA

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Background/Objectives: Ewing sarcoma (ES) is the second most common tumor of bone in childhood. Survival of patients with ES has increased since 1970.
At present 5 year overall survival rate of localized disease is approximately 75%. The aim of this study is to evaluate clinicopathologic characteristics and outcome of ES in children in center of Tunisia.
Design/Methods: Thirteen patients under 18 years with documented pathology of ES referred to Farhat Hached center through 2002 to 2013 were enrolled in this retrospective study. Overall survival and disease free survival and prognostic factors were evaluated.
Results: The median age at the time of diagnosis was 12 years (range, 3–17 years).The sex ratio was 2. 25. Primary tumor sites were flat bone and log bone respectively in 54% and 31%. The median size of primary tumor was 16 cm (range, 5cm-49cm). Seven patients (54%) presented with localized disease and 6 patients (46%) had metastatic disease at presentation, including 2 patients (33.3%) with multiple metastatic sites. All children achieved partial responses with induction chemotherapy. Complete surgical resection was done in 84.6 %. Histological good response was obtained in 27.2 %. Four patients (50%) received radiation therapy after surgery. Eight relapses (61.6%) have occurred (five metastatic and three local).The overall 5-year year survival was 60%.
Conclusion: Marked improvements in survival have been reported during the past 40 years for patients with localized disease with chemotherapy combined with local treatment. However, lesser improvements have been seen for patients with metastatic or recurrent disease. A better understanding of the complex biology of Ewing's sarcoma may lead to the successful development of biologically targeted therapies.

P-096

FACTORS RELATED TO YEARS POTENTIAL LIFE LOST IN CHILDREN WITH OSTEOSARCOMA OF THE VALLEY OF TOLUCA, MEXICO

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Background/Objectives: In Mexico, infant mortality due to cancer is a public health problem. Osteosarcoma is a tumor with high probability of premature death, so it is important to study its causes. Potential years of life lost (YPLL) index compares the relative importance of the causes of more relevant deathObjective: To assess factors related to potential years of life lost in children with osteosarcoma treated in the Valley of Toluca, Mexico.
Design/Methods: Material and methodsIn a retrospective study, we included patients with diagnosis of osteosarcoma in the Toluca Valley, We estimated the YPLL and clinical and paraclinical factors related were studied in bivariate analysis.
Results: Of were evaluated 30 of 36 patients with diagnosis of osteosarcoma which 20 died. The YPLL estimated was 1502 years (0-78) average of 50 ± 36, median of 73. The age, the gender, histological type, type of chemotherapy were not correlated with greater or lesser number of YPLL, the presence of bulky disease as well as lung metastases at diagnosis and localization at sites other than the femur increased the years lost. Treatment with amputation it seems to reduce years of life lost.
Conclusion: The rate of YPLL estimated in patients with osteosarcoma in our environment is extremely high, despite high costs exerted by social protection in health schemes, should be considered for planning new programs of care, define priorities for action and research that include actions aimed at early diagnosis and to establish strategies to improve treatment such as the use of biological therapies whose cost limits

their use in our country. YPLL related factors are mainly secondary to late diagnosis and reference.

P-097

METASTATIC EWING SARCOMA TREATED WITH MIFAMURTIDE. A CASE REPORT FROM MEXICO CITY

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Background/Objectives: Ewing sarcoma (ES) belongs to the family of malignant, small, round cell neoplasms of soft tissue or bone origin. The treatment is characterized by multi-disciplinary collaboration. Outcomes for patients with metastatic ES remains poor. Mifamurtide is an orphan drug approved for the treatment non-metastatic osteosarcoma. We present the case of a child with Ewing sarcoma and pulmonar metastasis that was treated with multiagent chemotherapy and mifamurtide, with good response.
Design/Methods: We report the case of a 6 year old male, with a femur bone lesion and pulmonary metastases. Pathological anaylisis was consistent with Ewing sarcoma. The patient received neoadyuvant chemotherapy with posterior limb-salvage, and we added mifamurtide to the adyuvant chemotherapy. The pulmonary metastasis were considered unresectable .After 24 months of treatment, we resected the pulmonary metastasis with pathological report of necrosis.
Results: Last image study PET-CT was reported without tumoral activity.Mifamurtide is currently an investigational agent that holds orphan drug status for the treatment of osteosarcoma,it is an immunomodulator with antitumor effects that appears to be mediated via activation of monocytes and macrophages, so its main use remains in pulmonary metastasis. Even though it is only used in osteosarcoma we presume that it can also be used in metastatic solid tumors.
Conclusion: Mifamurtide had a manageable safety profile. So we consider that this drug can be used in other solid tumors with pulmonary metastatic disease. More experience is needed to prove efficacy.

P-098

18F-FDG-PET / CT AND DIFFUSION MRI IN BONE SARCOMA: HISTOLOGIC AND IMAGING CORRELATION

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Background/Objectives: 18F-FDG-PET/CT and diffusion-weighted MRI were used for predicting response to treatment in patients with bone sarcomas in this study. Correlation between PET and MRI parameters with histopathological response and clinical outcome was assessed.
Design/Methods: Sixteen patients (5 osteosarcoma, 11 Ewing's sarcoma) aged between 5-16 years were included in study. All patients underwent 18F-FDG-PET/CT and diffusion MRI before (PET1 and MR1) and after preoperative chemotherapy (PET2 and MR2) to assess the radiological tumor response. The number and localization of 18F-FDG involvements, "maximum standardized uptake" value (SUVmax), metabolic tumor volume (MTV) and total lesion glycolysis (TLG) in 18F-FDG-PET/CT, and tumor volume and diffusion coefficients (ADC) from three separate areas within tumor on MRI were measured. Changes in parameters before and after treatment were compared with histopathological tumor response.
Results: PET/CT at diagnosis revealed 18F-FDG uptake in 1-32 different anatomical regions. Median SUVmax1 and TLG1 values were 6.0 (ranged between 2.6-9.4) and 127.0 (ranged between 8.2-573.3), respectively. Eight patients with good histologic response had lower median post-chemotherapy FDG-PET/CT parameters compared to those with poor response (1.7 vs 3.0 for SUVmax2 and 5.0 vs 62.5 for TLG2, respectively). The correlation coefficients between tumor necrosis and SUVmax2 and TLG2 were -0,647 and -0,656 respectively, $p<0,05$).Based on ROC curve analysis, SUVmax2 and TLG2 predicted a good pathological response. The optimal cut-off values for SUVmax2 and TLG2 were 2,25 and 43,85 which yielded a sensitivity/specificity of 0,83/0,75 and 0,67/100 respectively.Median diffusion MRI ADC changes were found 27.6 and 46.9 in poor and good responders, respectively ($p>0.05$, 8 patients).
Conclusion: PET/CT can be used for identification of metastasis in patients with bone tumors on diagnosis and can predict the histopathological response after neoadjuvant therapy. Although statistically non-significant, due to small number of patients, diffusion MRI may predict tumor response.

P-099

DEMOGRAPHIC PROFILE AND PREDICTORS FOR CHEMO TOXICITY IN OSTEOSARCOMA: A TERTIARY CARE CENTER EXPERIENCE FROM INDIA?

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Background/Objectives: Osteosarcoma is the most common primary malignant bone tumor in children. There is sparse data from India regarding the disese characterstics and is worth exploring.
Design/Methods: This prospective study evaluated demographic profile and risk factors for chemotoxicity in patients enrolled on OGS-12 regimen comprising DD-CT with Doxorubicin, Ifosfamide, & Cisplatin. Baseline tumor burden and nutritional parameters were studied and correlated with chemotoxicities. CT response was evaluated with histological-necrosis (HN) grading. Good responders (GR) were defined as those with ≥ 90% HN.
Results: There were 325 patients enrolled between December 2011 and December 2014, out of which 86(26%) were metastatic and 239(74 %) nonmetastatic.Median age was 17(6-56) years.There were 164(69%) male and 75(31%) female patients. In the nonmetastatic cohort,baseline median values of Albumin-4.4gm/dl, Iron-57mcg/dl, TIBC-329mcg/dl, Transferrin saturation 17%, Vitamin B12 172pg/ml, BMI 17, LDH 233U/L, SAP 332U/L.At presentation, 74% were malnourished (higher or lower BMI), 38% anemic, 57% iron deficient, and 57% were B12 deficient. Mean lesion size was 11cm, all had high LDH and 37% had high SAP.Most common histologic varient was conventional(82%), followed by chondroblastic(11%).Most common site of disese was lower end femur (42%) followed by upper end Tibia(28%).There were 60% good responders to chemotherapy.Incidence of grade III/IV chemotoxicity was febrile-neutropenia (FN) (30%), thrombocytopenia (18%), GI-toxicity (6%), and cardiac (4.7%), however there was no toxic death.Chemo toxicity was found to be correlated with the variables like serum levels of SAP, LDH and Albumin which were identified as predictors for GI toxicity. For thrombocytopenia, SAP was found as predictor.
Conclusion: The study underlines the challenging to treat population in developing world with features of higher tumor burden at presentation with coexisting malnurishment. Chemotoxicity could be predicted by LDH, SAP and Albumin at baseline, and these novel markers merits further exploration.

P-100

LIMB SALVAGE FOR OSTEOSARCOMA: FUNCTIONAL EVALUATION IN PEDIATRIC PATIENTS

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Background/Objectives: To evaluate the quallity of life in patient with limb preservation surgery, to compare the local relapse betwen these group and the mutilation one and its influence on the survival, in patients with osteosarcoma treated at "Hospital de niños Ricardo Gutiérrez".
Design/Methods: We retrospectively evaluated the medical records of patient with osteosarcoma admitted between January 1990 and December 2013. Patient were evaluated with an adapted version of the functional system accepted by the Musculoskeletal Tumor Society (MSTS).
Results: Total 2349 patients were admitted with a diagnosis of solid tumors, 127 patients with osteosarcomas The average age was 176 months (range 23 a 236 months), H / M 1.3/1.The most frequent location was: femur (67) (52.7%), tibia (25) (19.6%), humerus (12) (9.44%), fibula (5) (3.93%), other locations (18) (14.1%). Localized stages (98) (77.1%) non metastatic (29) (22.8) Surgical intervention received were: disarticulation (12) (9.44%), amputation (32) (25.1), salvage surgery (63) (49.6%) refused to receive treatment or were lost to follow-up (20) (15.7 %).). neo adjuvant chemotherapy (122) (96.1%), adjuvant (5) (3.9%). Local relapse was: patients with conservative surgery (5) (8%), disarticulated patients (2) (10%), in amputed patients (3) (10%). Five of the patients initially treated with conservative surgery that relapsed locally, were amputed. And three of the them are alive Funtional results in patients with conservative surgery were good: 84%.
Conclusion: The functional results with conservative surgery are good.The local recurrence rate is comparable to non-conservative surgeries with the possibility of rescue patients with a second surgery.Our results are accord with publish dates.

P-101

IMPACT OF RECOMMENDATIONS FROM THE INTERDISCIPLINARY TUMOR BOARD OF THE CESS GROUP ON THE OUTCOME IN PATIENTS TREATED WITHIN THE EUROEWING99 TRIAL

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Background/Objectives: The prognosis in patients with Ewing sarcoma localized disease has improved up to 70%. While the value of systemic treatment is systematically analyzed in clincial trials, a systematic investigation on the value of different local treatment approaches is lacking. Local treatment in Ewing Sarcoma is a crucial step in the treatment and must be planned carefully and individually. The trial office of the cooperative Ewing sarcoma study group offers the support of an interdisciplinary tumor board (ITB).
Design/Methods: Between 2006 and 2009, 1,234 patients were discussed in the ITB in Münster. Of these, 696 were not registered into the EuroEWING99-trial (EE99). 538 (43.6%) of these patients participated in the EuroEWING99 study and were included in our analysis. Fiftyseven patients were excluded because of missing information or missing follow up (N=481).
Results: Median age at diagnosis was 15 years. The ITB discussedmore patients with metastases at the time of diagnosis than with localized disease (39.5% vs 34.1%; p=0.149). A combined local therapy was done in 45.6% of the patients who were discussed in the ITB vs 33.7% in patients who were not discussed in the ITB (non-ITB) (p=0.010). The ITB had no significant impact on the survival of the patients: non-ITB (N= 307) 3y-EFS: 0.57 (SE=0.03); ITB (N=174) 3y-EFS: 0.58 (SE=.04); p=0.948. Neither in patients with primary localized disease non-ITB (N= 217) 3y-EFS: 0.70 (SE=0.03) ITB (N=114) 3y-EFS: 0.73 (SE=0.04) ; p=0.966) nor in patients with metastases at the time of diagnosis the ITB had an impact on the survival non-ITB (N= 90) 3y-EFS: 0.25 (SE=0.05); ITB (N=60) 3y-EFS: 0.31 (SE=0.06) ; p=0.353.
Conclusion: The recommendations given by the ITB had no impact on the event free survival. A detailed subgroup analysis has been undertaken, in order to analyze additional clinical prognostic factors such as site, size, number of metastases and histological response.

P-102

POOR PROGNOSTIC FEATURES AND METASTATIC DISEASE AT PRESENTATION CONTRIBUTION TO LOW SURVIVAL RATE OF CHILDREN WITH OSTEOGENIC SARCOMA IN JOHANNESBURG

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Background/Objectives: Survival rates of South African children with osteogenic sarcoma (OS) are known to be poor. An audit was performed at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) to assess the prognostic features and survival rates in patients treated at one centre.
Design/Methods: A retrospective folder review was conducted of all children with documented OS at CMJAH over a 20 year period. Kaplan-Meier survival analysis, Pearson's chi square and Cox regression tests were performed.
Results: Sixty four patients with histologically proven OS were identified, representing 3.3% of the total paediatric malignancies. Ten files were excluded as records were incomplete. The ratio of male to female was 1:1. The majority of patients (40/55) were black. The mean duration of symptoms was 90 days (range 21 to 180 days). Most patients presented with poor prognostic features: 47(85%) has masses larger than 8cm diameter; 55(100%) presented with high alkaline phosphatase and 46(83.6%) had elevated lactate dehydrogenase (LDH). Histology included osteoblastic (37/55) and chondroblastic OS (24/55). Thirty five of the patients were underweight for age at presentation (63.6%). Forty one patients were treated with ifosfamide, doxorubicin, methotrexate and cisplatinum, while 14 (25%) did not receive chemotherapy (6/14 declined chemotherapy while 8/14 were treated palliatively). Four patients refused surgery. The intent-to-treat 5 year survival rate was 42%. Causes of death included disease (22/41) and treatment complications (5/41). The following factors were found to impact significantly on survival: nutrition (p=0.05), LDH (p= 0.05), stage (0.048) and response to chemotherapy (p=0.05).
Conclusion: The poor survival rate in this population may be improved by increased attention to modifiable factors such as nutrition and diagnostic lag time. Delayed presentation is common in the South African setting; lag time is longer than in high income countries and this study will be used to increase awareness of OS to be part of a broader education programme.

P-103

SKIP METASTASIS IN OSTEOSARCOMA: EXPERIENCE FROM A SINGLE INSTITUTION

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Background/Objectives: Skip metastasis (SM) is defined as synchronous regional bone metastasis. Using new imaging modalities, detection of SM is easier and possibly more common. We reviewed patients with SM and compared their characteristics and outcome to other patients with osteosarcoma (OS) treated at our center.
Design/Methods: We reviewed retrospectively children (<18years) with newly diagnosed high grade OS who presented from July2006 until December2014. Patients' characteristics, treatment modalities, and outcome were analyzed. All cases were discussed in multidisciplinary clinic that included two experienced radiologists.
Results: We identified 60 patients diagnosed with OS; among them 10 patients (16%) had SM detected by MRI. Patients with SM had a median age at diagnosis of 9.8 years (range, 7.4-17). Three patients had metastasis at diagnosis (2 had lung only and 1 had lung and bone). Bone scan was positive for the skip lesion in three patients only. Nine patients underwent primary tumor resection after neo-adjuvant chemotherapy (amputation in three, limb salvage surgery in six). One patient did not have local control due to disease progression. Resection margin was negative in all but one, and four had post chemotherapy necrosis ≥90%. Two patients relapsed (one local and one in the lung) and died of disease.Compared to the rest of the patients, those with SM were younger at diagnosis (median age 9.8 vs.14.2 years, P=0.0052) but otherwise had similar clinical features. Outcome was similar in the two groups with no significant differences in EFS and OS (P=0.84 and 0.86, respectively).
Conclusion: In this study, we identified higher than expected number of patients with SM, possibly due to improved sensitivity of imaging studies. Bone scan detected only 3 skip lesions (out of 10) and only 1 patient had combined distant bone metastasis. Patients with SM were younger; otherwise had similar clinical features and outcome to the rest of our patients.

P-104

OSTEOSARCOMA IN CHILDREN RETROSPECTIVE STUDY IN THE CENTER OF TUNISIA

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Background/Objectives: Osteosarcoma (OS) is the most common malignant bone tumor in children. Survival for these patients was poor with surgery and/or radiotherapy. The introduction of multi-agent chemotherapy improved the outcome of these patients with a PFS of 60%-70%. This study was conducted to investigate presentation, treatment, and outcome in young children with OS.
Design/Methods: We retrospectively analyzed the data of 26 consecutive children with high-grade bone OS, with histological confirmation treated with RosenT10, OS94 or OS2005 protocol, through a period of 10 years (2002-2013). Epidemiologic and therapeutic result was analyzed with SPSS software and Kaplan Meier method.
Results: The median age at diagnosis was 13 years (range, 6-17 years). The Sex ratio was 2.25. The majority of the tumor was located in the long bones of lower limb (60%). Most of them had conventional OS histology (77%). The median size of primary tumors was 24 cm (range, 3cm-56cm). Tow patients had metastasis at diagnosis. All patients received primary chemotherapy. Of the 26 patients, 7 patients underwent limb salvage surgery (35%), 13 underwent amputation (65%). Only 20% analyzed tumors responded well (>95% necrosis) to neo adjuvant chemotherapy. On follow-up, 7 patients were still alive at last clinical contact. Four patients never achieved a complete remission and 8 developed recurrences (local, N=01; metastatic, N=07) and 07 died. The overall 04-year survival was 40%. Metastasis at diagnosis *was* associated with poorer outcome. Better survival was correlated with good response to chemotherapy.
Conclusion: A lot of progress has been made in the treatment of the OS over the last 30 years, due to introduction of chemotherapy and multi-disciplinary collaboration.

Relapsing and refractory tumor, need new effective drugs, new therapeutic targets and new strategies.

P-105

HEMATOPOIETIC STEM CELL TRANSPLANTATION IN RELAPSED OR REFRACTORY EXTRACRANIAL PRIMITIVE NEUROECTODERMAL TUMOR OF CHILDREN AND ADOLESCENTS: A MULTICENTER SURVEY STUDY

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Background/Objectives: The objective of this study was to evaluate the outcomes experienced by children with relapsed or refractory extracranial Primitive Neuro-Ectodermal Tumor (rr-ePNET) following high-dose chemotherapy and hematopoietic stem cell transplantation (HSCT).
Design/Methods: We retrospectively analyzed the outcomes of 44 patients with rr-ePNET. Of 44 patients underwent HSCT, 18 had high-risk, non-relapsed disease and 7 had primary refractory disease. At the time of transplantation, only 66% of the patients were chemosensitive. The majority of patients received busulphan+melphalan for conditioning (28/44), and peripheral blood (41/44) was used as a source of stem cells.
Results: After a median follow-up period of 18 months, 20 patients were alive. At 2 years, the probabilities of overall survival (OS), event-free survival (EFS), progression-free survival (PFS), the cumulative non-relapse mortality (NRM) and the crude relapse rate (RR) were 35.6±8.8%, 35.3±8.2%, 43.2±8.4%, 14.6±8.2% and 52.3%, respectively. The probability of PFS in chemosensitive and chemoresistant patients at 2 years was 63.7±10.0%, and 13.3±8.8%, respectively (p=0.001). Although patients with only lung metastases had better OS than those with other or combined metastases (2-year OS 53.6±18.0% vs 40.0±13.9%), it did not reach statistical significance. Multivariate analysis showed that chemoresistant disease at the time of transplantation was the factor predicting limited PFS (odds=2.739, p=0.026).
Conclusion: HSCT increased PFS in a significant proportion of children with rr-ePNET. Survival rates were better for patients with chemosensitive disease at the time of HSCT.

P-106

POSTOPERATIVE CARE AFTER TUMOR ORTHOPEDIC SURGERY ON A PEDIATRIC ONCOLOGY WARD

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Background/Objectives: Purpose: In the Department of Pediatric Oncology at University Children´s Hospital Muenster, 130 newly diagnosed pediatric cancer patients are admitted per year. Of these patients, 20 to 25 are children and adolescents with malignant bone sarcomas (Ewing sarcoma, Osteosarcoma) and require bone replacement surgery. Limb saving surgery is possible in the majority of patients, but around 10% still require amputation. Postsurgical complications under continuing, adjuvant chemotherapy include delayed wound healing, local infections and phantom limb pain. Here we address how the Pediatric Oncology nursing team can support patients in this situation.
Design/Methods: Method: Among the members of an interdisciplinary team, including orthopedic and pediatric oncology nurses, wound care experts, physiotherapists, occupational therapists, social workers, psychologists and physicians (pediatric oncologists and orthopedic surgeons), we designed and evaluated a nursing care plan for the postoperative management of patients continuing chemotherapy following tumor orthopedic surgery.
Results: Close interdisciplinary cooperation allows to optimize wound management and overall patient care in this specific situation. Written standards of care are helpful for the training of less experienced nurses and enhance an overall feeling of safety among both the members of the nursing care team and the patients and their families.
Conclusion: The experienced and standardized care and management of a patient readmitted to a pediatric oncology ward after bone tumor surgery is a critical prerequisite for an optimal recovery and quality of life, especially under conditions of continuing chemotherapy, and to allow transition towards rehabilitation and a normal daily life. Close cooperation of various disciplines is essential to meet the general and individual challenges of this situation.

P-107

EXTRASKELETAL OSTEOSARCOMA AFTER BONE MARROW TRANSPLANTATION

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Background/Objectives: Hematopoietic stem cell /bone marrow transplant (HSCT/BMT) recipients carry a risk for developing secondary malignancies, either lymphoproliferative disorders or solid tumors. There has been only seven osteosarcoma cases reported as second malignancies after HSCT/BMT to date.
Design/Methods: Retrospective case and literature review.
Results: A 17-year-old girl presented with a three-month history pain and one-month history of swelling in the right lower thigh. She had underwent allogeneic HSCT from his full-match donor, his brother for MDS when she was 4 years old. Imaging studies (x-ray, MRI) revealed a mass surrounding the femur. A trucut biopsy revealed osteosarcoma. She underwent limb sparing surgery after thre courses of neoadjuvant chemotherapy consisting of ifosfamide, cisplatin, pirubicin, followed by three more courses of the same regimen and mifamurtide. She is followed up with no evidence of disease 17 months after termination of chemotherapy.
Conclusion: Children treated for maignancies should be followed-up for late effects, including second malignancies. Osteosarcoma as a secondary malignancy after MDS is very rare. Treatment as primary osteosarcoma seems to be effective.

P-108

SIX COURSES OF NONMETHOTREXATE 3-DRUG CHEMOTHERAPY AND SURGERY IN OSTEOSARCOMA IS EFFECTIVE: 25 YEAR EXPERIENCE

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Background/Objectives: Chemotherapy and surgery are the mainstay of osteosarcoma (OS) treatment. Using 2-4 drugs and short/long duration in chemotherapy protocols have been evaluated in various trials. A metaanalysis (Anninga JK, 2011) has reported, 3-drug regimen is better than 2, not inferior than 4-drug. Our study aims to evaluate the outcome of Osteosarcoma (OS) patients treated with a nonmethotrexate 3-drug regimen and surgery.
Design/Methods: Children and adolescents with oteosarcoma treated between January,1990 - January, 2015 at Istanbul University, Oncology Institute were retrospectively evaluated for demographic features and outcome. Patients recieved 6 courses of a 3 drug regimen comprising of ifosfamide 1.8 g/m2/d x 3 days, epirubicin 90 mg/m2/d and sisplatinum 100 mg/m2/d administered 3-pre and 3-postoperatively. Methotrexate was not in the protocol because drug levels could not be monitored in the 1990's at our center. Since 2012, mifamurtide was added to the protocol postoperatively for nonmetastatic patients.
Results: 189 children (105M, 84F), median age 12 years (3-18yrs) were evaluated. 151 (80%) were non-metastatic. Median follow-up was 3,6 years (1mo.-24 yrs). 91.5 % had limb salvage surgery. Relapse/progressive disease was observed in 69 patients at a median 15 months (1mo-63 mo). The 5 and 10-year survival and event free survival for all were (OS) 63.1% and 60.5%, and (EFS) 58.8% and 57% respectively. In non-metastatic and in metastatic patients, 5-year OS was 73.8 and 23.9%, 5-year EFS was 69.4% and 20.8%; respectively ($p = 0.0001$). In 25 nonmetastatic patients recieving chemotherapy and mifamurtide 2-year OS and EFS were 90.9% and 85.5% respectively at a median of 20 months.
Conclusion: A 3-drug combination of cisplatin,epirubicin,ifosfamide given for 6 courses is an effective, well tolerated regimen for osteosarcoma; and with surgery results in survival rates comparable in the literature. Longer follow up is needed to assess the

contribution of mifamurtide on outcome. Presence of metastasis is associated with poor outcome.

P-109

CHILDHOOD EWING SARCOMA FAMILY TUMORS: 25-YEAR EXPERIENCE OF A SINGLE CENTER IN TURKEY

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Background/Objectives: Our study aims to evaluate the demographic features and survival outcome of Ewing sarcoma family tumors (ESFT) treated in a tertiary pediatric oncology center.
Design/Methods: Patients, under 19 years old, with the diagnosis of ESFT treated between January 1989 and January 2015 at Istanbul University Oncology Institute were retrospectively evaluated in terms of demographic features and survival outcomes.
Results: One hundred ninety-seven children (100 boys, 97 girls) with a median age of 12.3 years (0.4-18 yrs) were evaluated. There were 119 (60%) non-metastatic and 78 metastatic patients. Primary localisation was in the extremities in 136 (69%) patients, in other sites in 61 patients. Initial treatment consisted of 3 or 4 courses of neoadjuvant alternating IE/VAC chemotherapy given every 3 weeks, followed by surgery and or radiotherapy (RT) to the primary site and adjuvant chemo for a total of 1 year. Surgery was performed to 121 (61%) patients; RT was given to 125 (63%) patients as the local therapy. Median follow-up time was 3 years (2mo.-25 yrs). Relapse or progressive disease was observed in 53 patients (27%) at a median of 17 months (1mo-70 mo.). Presence of metastasis was significantly associated with poor prognosis in terms of overall survival (OS) and event free survival (EFS) (p=0.0001). OS at 2yrs and 5 yrs were %80 and %71.1 in the nonmetastatic group and %61.3 and %30.4 in the metastatic group. EFS at 2 yrs and 5 yrs were %70.2 and %60 in the nonmetastatic group; %50.3 and %24.1 in the metastatic group.
Conclusion: Survival of our study group is consistent with the other studies in the literature. Presence of metastasis was significantly associated with poor outcome both in EFS and OS.

P-110

MIFAMURTIDE (L-MTP-PE) IN CHILDREN WITH OSTEOSARCOMA: THE TURKISH EXPERIENCE

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Background/Objectives: Mifamurtide (liposomal muramyl tripeptide), activates macrophages, provides antitumor effect in lungs. Mifamurtide+chemotherapy improved survival in nonmetastatic osteosarcoma patients, in phase III study. After EMA approved mifamurtide for nonmetastatic osteosarcoma, it could be used off-label by the approval of the Ministry of Health on a patient basis, in Turkey. This multicentric study aims to evaluate the demographic characteristics, adverse effects, outcome of adding mifamurtide to chemotherapy in children with osteosarcoma in Turkey.
Design/Methods: From September 2011-January 2015, in 45 nonmetastatic, 4 metastatic (after metastasectomy) osteosarcoma patients, mifamurtide was added to chemotherapy after surgery in 8 centers in Turkey. Chemotherapy regimens used were epirubicin/ifosfamide/cisplatin in 29 patients (Istanbul University Oncology Institute-IUOI) and other in 20 (MayoPilotII, EURAMOS, ICE etc.). Mifamurtide was given i.v.2 mg/m^2, twice weekly for 12 weeks, followed by once weekly for 24 weeks.
Results: Median age was 14 years (4-17 years). The most frequent adverse affects were chills and fever especially in initial doses. Median follow-up time for all was 23 months (5-57mo.). Twenty-seven of 45 (60%) nonmetastatic patients completed mifamurtide. Thirty-three patients have no evidence of disease (NED) at median 23mo. (5-38 mo.). Twelve relapsed at median 15 months (9-26mo.), 2 are dead of disease, 8 are alive with disease; 2 NED. Two of 4 metastatic patients died (28, 57 months). For nonmetastatic patients 2 year event free survival was 71.3%, overall survival was 92.1%.
Conclusion: In this multicentric study, mifamurtide could be administered safely with no major side effects. The experience with mifamurtide in patients with nonmetastatic osteosarcoma is promising; a longer follow up is needed to make further conclusions for survival benefit.

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IL-6 SECRETED BY EWING SARCOMA TUMOR MICROENVIRONMENT CONFERS ANTI-APOPTOTIC AND CELL-DISSEMINATING PARACRINE RESPONSES IN EWING SARCOMA CELLS

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Background/Objectives: The prognosis of patients with Ewing sarcoma (ES) has improved over the course of the last decades. However, those patients suffering from metastatic and recurrent ES still have only poor chances of survival and require new therapeutic approaches. Interleukin-6 (IL-6) is a pleiotropic cytokine expressed by immune cells and a great variety of cancer cells. It induces inflammatory responses, enhances proliferation and inhibits apoptosis in cancer cells, thereby promoting chemoresistance.
Design/Methods: We investigated expression of IL-6, its receptors and the IL-6 signal transduction pathway in ES tumor samples and cell lines applying reverse transcriptase PCR, immunoblot and immunohistochemistry. The impact of IL-6 on cell viability and apoptosis in ES cell lines was analyzed by MTT and propidium iodide staining, migration assessed by chorioallantoic membrane (CAM) assay.
Results: Immunohistochemistry proved IL-6 expression in the stroma of ES tumor samples. IL-6 receptor subunits gp80 and gp130 were expressed on the surface of ES cells. Treatment of ES cells with rhIL-6 resulted in phosphorylation of STAT3. rhIL-6 protected ES cells from serum starvation-induced apoptosis and promoted migration. IL-6 blood serum levels were elevated in a subgroup of ES patients with poor prognosis.
Conclusion: These data suggest that IL-6 contributes to ES tumor progression by increasing resistance to apoptosis in conditions of cellular stress, such as serum starvation, and by promotion of metastasis.

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ASSOCIATION OF VITAMIN D RECEPTOR GENE POLYMORPHISM WITH OSTEOSARCOMA RISK AND PROGNOSIS

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Background/Objectives: Vitamin D receptor (VDR) plays an important role in a wide variety of cellular process. Polymorphisms in VDR gene have been linked to risk of various cancers and their prognosis. We conducted a case-control study to analyze relationship of VDR gene polymorphisms with occurrence and prognosis of osteosarcoma.
Design/Methods: Fifty-eight osteosarcoma patients diagnosed in Ankara Oncology Training and Research Hospital and 75 sex- and age-matched healthy controls were included the study. Single nucleotide change polymorphism in *Cdx2, FokI, BsmI, ApaI, TaqI* regions of VDR gene were examined by SNAPshot mini-sequencing technique. Allele and genotype frequencies in patient and control groups were compared. Association of polymorphic genotypes with osteosarcoma was evaluated. Relationship of prognostic parameters and survival rates with the presence of polymorphisms were also analyzed.
Results: Allele frequencies in *Cdx2, FokI, BsmI, ApaI* and *TaqI* regions of VDR gene of patients and controls were not different. The differences in genotype frequencies of patient and control groups were not significant. The VDR gene *Cdx2, FokI, BsmI, ApaI* and *TaqI* polymorphisms were not associated with osteosarcoma risk. Tumor volume was greater (p=0.041), metastases was more common (p=0.042) and histopathological response to chemotherapy was worse (<90%)(p=0.044) in patients having *Cdx2* polymorphic allele. All patients carrying *BsmI* homozygote polymorphic genotype had more than 90% necrosis after induction chemotherapy (p=0.037). Median follow-up time was 46 months. The three-year event free survival rate significantly higher in the

presence of homozygote polymorphic *ApaI* than heterozygote polymorphic and wild type (87.2% vs. 51.2% p=0.015). The other polymorphic genotypes have not an effect on survival rates.
Conclusion: Although an association of VDR gene polymorphisms with various cancer risks has been described, we did not find any relationship in osteosarcoma risk. We showed the relationship of *Cdx2* polymorphism with bad prognosis, *BsmI* polymorphism with good prognosis and *ApaI* polymorphism with better survival rates.

P-113

EVEROLIMUS/SORAFENIB DRUGS COMBINATION IN TREATMENT OF REFRACTORY CHILDHOOD OSTEOSARCOMA: SINGLE CENTER EXPERIENCE

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Background/Objectives: The results of treatment refractory childhood osteosarcoma are not satisfactory. According to the data of different pilot trials progression-free survival (PFS) curves dramatically tend to zero with a median follow-up in 6-8 months. Possibility of using these drugs combination in children is unknown.
Design/Methods: From May 2013 to March 2015 eight children and adolescents with refractory osteosarcoma were included in this pilot trial. Male/female ratio was 1/1. Median age - 12.7 years (range from 7 till 17). T2bN0M0 stage was revealed in 3 patients, T2bN0M1a stage – in 5 patients. All patients had received first-line chemotherapy PHOI-OS-2006, second-line therapy - high-dose ifosfamide and third-line therapy – gemcitabine/docetaxel before they were enrolled in this trial. Sorafenib was administered orally at the starting dose 150 mg/m^2 (with following possible escalation up to 200 mg/m^2) every 12 hours, everolimus - orally at the starting dose 2.5 mg/m^2 (with following possible escalation to 5 mg/m^2) once a day for consecutive 28-day cycles until disease progression or unacceptable toxic effects. The primary endpoint was 6 month PFS.
Results: The most common toxicity was skin syndrome, oral mucositis. Hematological toxicity was not more than grade I-II. Three out of 6 patients were progression free at 6 months. Maximum PFS was 12 months, a median follow-up was 4.3 months (range from 1,3 till 12,5).
Conclusion: The combination of sorafenib and everolimus showed therapeutic effect as a further-line treatment for children and adolescents with refractory osteosarcoma.

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ROLE OF HIGH DOSE METHOTREXATE (HD MTX) IN PEDIATRIC OSTEOSARCOMA: A RETROSPECTIVE STUDY

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Background/Objectives: The four major chemotherapeutic agents used for treatment of Pediatric Osteosarcoma are Doxorubicin, Cisplatin, Ifosfamide and High dose Methotrexate. MTX seems to be the most active agent however this had not been unambiguously proven. *Objectives*: To compare the survival, percentage of tumour necrosis and rate of complications in patients with Osteosarcoma receiving chemotherapy regimens with and without HD MTX.
Design/Methods: Case notes of 23 children with Osteosarcoma who were treated at a tertiary cancer hospital in Bangalore, India were retrospectively analysed. Details about symptoms, signs, chemotherapy, surgery, complications and survival were collected. These were compared between patients who received chemotherapy regimens with and without HD MTX.
Results: M:F ratio was 1.8:1 with mean age of 14.78 years (8-18 years). Pain and swelling were the most common symptoms and distal femur was the most common site. 35% were metastatic. Forty percent of children received chemotherapy with HD MTX containing MAP (Cisplatin, Doxorubicin, and HD MTX) regimen. Other received regimens which did not contain HD MTX. The percentage of tumour necrosis was more than 90% in 77.7% in HD MTX receiving children as compared to 37.5% with other protocols. Overall survival in localized Osteosarcoma was better in children receiving HD MTX compared to those receiving regimens without HD MTX 60% vs 40%. Overall survival in metastatic Osteosarcoma was better in children receiving HD MTX compared to those receiving regimens without HD MTX 50% vs 0%. Rate of admissions for febrile episodes (88% vs 57%) and need for PRBC (66% vs 50%) and platelet transfusions (66% vs 57%) were more in children receiving HD MTX.
Conclusion: HD MTX improves the survival and percentage of tumour necrosis in pediatric patients with Osteosarcoma.

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METHOTREXATE AND ALL-TRANS RETINOIC ACID COMBINED TREATMENT FOR INDUCTION OF OSTEOSARCOMA CELL LINES DIFFERENTIATION IN VITRO

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Background/Objectives: Induced differentiation of tumor cells into mature phenotypes is a promising strategy in cancer therapy. All-trans retinoic acid (ATRA) and its derivatives can induce cell differentiation in many types of hematological malignancies and solid tumors including osteosarcoma. Methotrexate (MTX; amethopterin; 4-amino-10-methylfolic acid), a structural analogue of folic acid, is still one of the most effective compounds used in osteosarcoma treatment. MTX is an inhibitor of enzyme dihydrofolate reductase (DHFR) which catalyses the reduction of folate to tetrahydrofolate. The inhibition of DHFR results in tetrahydrofolate depletion, leading to the inhibition of purine and pyrimidine precursor synthesis. Besides these cytostatic and cytotoxic effects of MTX, there is also an evidence of differentiation effect of this compound. MTX was found to be a potent differentiation inducer in HL-60 human promyelocytic leukaemia cells.
Design/Methods: We studied the potential of ATRA and MTX to induce differentiation of osteosarcoma cell lines *in vitro* and further we studied if MTX is able to modulate ATRA induced differentiation. The detection of the activity of mitochondrial dehydrogenases by MTT assay was used for the evaluation of cell proliferation. The expression of cell differentiation markers and genes involved in ATRA signalling (e.g. RAR, RXR, CRABP) was assessed using qPCR. The level of extracellular matrix mineralization was evaluated using Alizarin Red S staining.
Results: Treatment with ATRA alone enhanced the expression of the middle and late differentiation markers and ATRA alone enhanced the extent of mineralization. Combined application of ATRA and MTX slightly increased the effect of ATRA in terms of differentiation.
Conclusion: Our results suggest that MTX and ATRA could be a new promising combination in treatment of osteosarcoma.
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P-116

EXPERIENCE IN THE TREATMENT OF EWING'S SARCOMA OF THE PELVIS IN CHILDREN. EAST EUROPEAN SARCOMA GROUP

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Background/Objectives: The aim of our study was to determine treatment outcomes in two protocols: 1) using high-dose chemotherapy and autologous peripheral blood stem cell transplantation (HDCT/autoPBSCT) and 2) protocol with decreasing doses of chemotherapy in pediatric patients with Ewing's sarcoma of pelvis treated at the East European Sarcoma Group (Russian oncology research center N.N.Blokhin).
Design/Methods: We retrospectively analyzed the data of patients with Ewing's sarcoma of pelvis between 1997-2011. All patients receive the same mode neoadjuvant chemotherapy regimens 5 courses (VAC and IE).
Results: The first group included 31 children. Metastatic disease was found in 42% of patients. The average tumor volume was 345ml. Middle age was 11.5 y.o. The second group included 21 patients with a reduction in drug dosage. Metastatic disease was found in 33% of patients. The average tumor volume was 298ml. Middle age was 12.7 y.o. Overall 1-,3-,5-y survival after HDCT/autoPBSCT were 70%, 39%, 39%. Median was 17.2 months in first group. With metastatic disease overall 1-,3-,5-y survival were 46%, 7%, 7%. Median was 10.2 months. With non metastatic disease overall 1-,3-,5-y survival were 88%, 64%, 64%. Median not reached. Overall 1-,3-,5-y survival in the second group were 100%, 70.5%, 58.8%. With metastatic disease overall 1-,3-,5-y survival were 100%, 68.5%, 34.2%. With non metastatic disease overall 1-,3-,5-y survival were 100%, 71.4%, 71.4%. Median not reached. Data is valid (p=0.008).
Conclusion: Although we obtained the best survival data in the second group than the first using HDCT/autoPBSCT, are different by selection the data volume of the primary tumor and rate of metastatic disease. Requires further study and monitoring of patients undergoing treatment for Ewing's sarcoma of the pelvis.

P-117

IDENTIFICATION OF CANCER STEM CELLS IN OSTEOSARCOMA CELL LINES: CHARACTERIZATION OF CANCER STEM CELL MARKERS EXPRESSION AND IN VIVO TUMORIGENICITY

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Background/Objectives: Despite modern treatment protocols, survival for patients with metastatic or relapsed osteosarcoma remains poor. Recent studies found that cancer stem cells (CSCs) are present in osteosarcoma and could be the cause of observed clinical pattern. However, reported proportions of CSCs vary between the studies as different groups used different marker or method singly to identify CSCs.
Design/Methods: To evaluate the relevance of putative CSCs markers in osteosarcoma, we examined their expression in 8 osteosarcoma-derived cell lines and 1 established osteosarcoma cell line SAOS-2. Immunofluorescence, flow-cytometry and RT-PCR were employed to analyze expression of following markers: CD133, ABCG2, CD117, ALDH1A1, nestin, Oct3/4, Sox2 and Nanog. All 9 cell lines were tested for the presence of CSCs using *in vivo* tumorigenicity test. In the xenograft assay, 1 million unsorted cells of each cell line were injected in triplicate into NSG mice.
Results: Only 1 of 9 tested osteosarcoma cell lines was able to form xenograft tumors – OSA-13. The presence of CSCs in OSA-13 was further confirmed in serial xenotransplantations. Unexpectedly, we identified high expression of at least some of the putative CSCs markers among all of the examined cell lines. However, only OSA-13 cells expressed all of the examined CSCs markers including Sox2, which has been recently reported as crucial for self-renewal and tumorigenicity of CSCs in osteosarcoma. Moreover, OSA-13 cells expressed CSCs markers at overall higher level compared to other non-tumorigenic cell lines.
Conclusion: Our results indicate that use of previously reported osteosarcoma CSCs markers singly is limited because even high expression of the single marker does not necessary reflect the tumorigenic phenotype of the cells. CSCs are more likely characterized by simultaneous expression of multiple markers, including Sox2, and multi-marker strategies should therefore be applied for their identification in osteosarcoma.
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METHOTREXATE INDUCES EPIGENETIC ALTERATIONS IN OSTEOSARCOMA CELL LINES

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Background/Objectives: Methotrexate (MTX) is one of the most frequent chemotherapeutic drug and is still used in the treatment of osteosarcoma. MTX is able to inhibit dihydrofolate reductase, but it also interferes with the enzymes methylenetetrahydrofolate reductase, methionine synthase and methionine S-adenosyltransferase. It is therefore probable that MTX can be involved in reduction of S-adenosylmethionine level which subsequently leads to depletion of 5-methylcytosine. Moreover, it was shown that MTX can act as inhibitor of histone deacetylases due to its shared structural similarity with some other histone deacetylase inhibitors.
Design/Methods: In this study we used MTT assay for basic assessment of MTX cytotoxicity. Gene expression was measured using qPCR after MTX treatments. Differences of DNA methylation resulting from MTX and 5-aza-2'-deoxycytidine (the DNA demethylating agent) treatments were studied using ELISA assay. Histone acetylation levels were detected by ELISA and western blotting.
Results: MTX treatments influenced expression of some genes involved in drug metabolism and transport. In several cell lines MTX was able to decrease level of 5-methylcytosine in DNA and MTX was almost as effective as 5-aza-2'-deoxycytidine at the same concentration. In some cells MTX also increased level of acetylated histone H3.
Conclusion: To conclude, MTX alone is able to modify gene expression and epigenetic determinants in osteosarcoma cell lines. Acknowledgements: This study was supported by grant IGA MZCR NT14327-3 and by the European Regional Development Fund and the State Budget of the Czech Republic (RECAMO, CZ.1.05/2.1.00/03.0101).

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STEM CELL RESCUE FROM IRRADIATION OF TUMOR SITES COMBINED WITH HIGH-DOSE CHEMOTHERAPY YIELDS LONG TERM SURVIVAL IN PATIENTS WITH ADVANCED PEDIATRIC SARCOMAS WITHOUT MARROW INVOLVEMENT

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Background/Objectives: Ewing's sarcomas (ES), metastatic to more than one bone or marrow or early relapse as well as stage IV rhabdomyosarcomas (RMS) have poor prognosis. We assessed toxicity, relapse free survival (RFS) and overall survival (OS) of advanced ES and RMS patients treated with the MetaEICESS protocols.
Design/Methods: From 1992 to 2014, 20 patients, 18 with advanced ES (AES, ≥ three bones/organs or marrow involved at diagnosis, n=4 or relapse <24 months after diagnosis, n=3) and 2 with stage IV RMS, were enrolled in the two subsequent MetaEICESS 1992 and 2007 protocols consisting of induction-chemotherapy, whole-body MRI or MRI/PET directed radiotherapy to the primary tumor and to all metastases, as well as surgery, tandem high-dose chemotherapy with autologous rescue (both groups) plus allogeneic stem cell transplantation (allo-SCT, only MetaEICESS 2007). OS was also compared to outcomes of 26 historical AES patients treated with conventional protocols. Data was censured on March 1st 2015.
Results: 11/20 patients are surviving in CR. This is significantly better than historical controls. CR rates did not differ between MetaEICESS 2007 (5/9) versus MetaEICESS 1992 (3/11). 4/9 patients in the MetaEICESS 2007 group had bone marrow (BM) involvement in contrast to 3/11 in the MetaEICESS 1992 group.
Altogether, 11/14 patients without BM involvement survived in contrast to 0/7 patients with marrow involvement. There were 3 DOC, all in MetaEICESS 1992. When patients suffering DOC were excluded (n=3), 6/6 patients who had BM involvement at diagnosis had died of disease, whereas 3/11 patients without BM involvement had died of disease, leaving 8/11 patients in CR (median: 66 months).
Conclusion: The MetaEICESS protocols yield long term survival in patients with advanced ES/RMS. Allo-SCT was not associated with DOC increase. Given the higher incidence of BM involvement in the allogeneic transplant group, it remains open whether the addition of allo-SCT improves the prognosis.

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IMPACT OF PATHOLOGICAL FRACTURES ON THE PROGNOSIS OF PRIMARY MALIGNANT BONE SARCOMAS IN CHILDREN AND ADULTS. A SINGLE CENTER RETROSPECTIVE STUDY

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Background/Objectives: The purpose of this study was to investigate whether a pathological fracture (PF) has an effect on the prognosis of patients with osteosarcoma and Ewing tumor regarding 5-year survival, occurrence of metastases and local recurrence.
Design/Methods: We retrospectively analyzed 205 patients with the histological diagnosis of either osteosarcoma or Ewing sarcoma. Survival analysis was performed for all patients and differentiated for adult and pediatric (<18 years at diagnosis) patients.
Results: Out of all patients, 127 were diagnosed with osteosarcoma and 78 with Ewing tumor. At time of diagnosis, 51% of all patients were under the age of 18 years. The age ranged from 3 to 79 years (median age 17). In 20% a pathological fracture was observed. Patients with PF showed lower survival rates with 5-year survival rates of 64% compared to 83% without PF (p= 0.023). The difference in development of metastases between patients with and without PF was not statistically significant. Local

recurrence occurred in 7% of the patients without and in 24% with PF (p= 0.023). In pediatric patients, the 5-year survival rate was 87% in patients without and 77% with PF (p= 0.806). The rate of local recurrence was not different in children with and without PF (10% vs. 11%, p= 0.573). In contrast, the survival rate in adults with PF fracture decreased from 78% to 51% (p= 0.004) and local recurrence increased from 13% to 42% (p= 0.001). None of the subgroups showed a statistically significant correlation between pathological fractures and metastases.
Conclusion: The present study suggests that the overall occurrence of PF in primary malignant bone sarcomas has a negative impact on survival rates and implicates an increased risk of local recurrence. Of note, in pediatric patients, PF did not have prognostic impact.

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INHIBITION OF DNA-REPAIR ENZYMES (DNA-PK AND PARP) TO SENSITIZE EWING SARCOMA TO CHEMO-AND RADIOTHERAPY

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Background/Objectives: Exposure to DNA-repair inhibitors can render malignancies more susceptible to chemo- and radiotherapy. DNA dependent protein kinase (DNA-PK) and poly(ADP-ribose)polymerase (PARP) inhibitors are in clinical trials, both as single agents and in combinations. Metastatic and relapsed Ewing sarcoma is associated with a poor outcome and there is an urgent clinical need to improve treatment strategies. Recently, ETS transcription factors, such as EWS-FLI1, were described as biomarkers for PARP-inhibitor sensitivity in Ewing sarcoma, which had previously been limited to homologous recombination repair (HRR) deficient tumours.
Design/Methods: We assessed DNA-PK (NU7441) and PARP-1/-2 (rucaparib) inhibitors as single and as chemo- or radiosensitising agents in 3 Ewing sarcoma cell lines by performing growth inhibition and clonogenic assays, and evaluating cells for their ability to repair DNA double strand breaks by HRR. Single agent rucaparib (10 mg/kg i.p. daily) was evaluated in an *in vivo* orthotopic model with serial bioluminescent imaging.
Results: NU7441 caused chemosensitisation (etoposide, doxorubicin) and radiosensitisation (2-7 fold increase in cytotoxicity). Chemosensitisation of rucaparib was profound for temozolomide (15-29 fold) and modest for camptothecin and ionizing radiation (1.4–2 fold). Depending on the type of clonogenic assay used, single agent rucaparib activity differed with LD_{50} values ranging from 0.5-1 μM to 5-8 μM (continuous versus 24h drug exposure, respectively). After induction of DNA double strand breaks, the cells showed a significant increase in rad51 foci formation indicating intact HRR. *In vivo* testing of rucaparib was non-toxic but failed to show any tumour responses or survival advantages.
Conclusion: Ewing sarcoma cell lines are functional for HRR but nevertheless sensitive to PARP-1/-2 inhibition. Despite *in vitro* activity, monotherapy with a PARP inhibitor was not efficacious *in vivo*. Given the chemo- and radiosensitising effects of both inhibitors, our findings strongly support further evaluation of these agents in combination with chemo– or radiotherapy in preclinical models and clinical trials.

Posters: Brain Tumours

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EXPLORING POTENTIAL DRIVER MUTATIONS IN PEDIATRIC SOLID TUMORS

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Background/Objectives: Brain tumors are the most common solid malignancies in children. Over the past few years we have seen a dramatic change in the field of pediatric neuro-oncology, largely because of the emergence of unbiased high-throughput genome-wide analyses. Pediatric brain tumors have molecular features very unique compared to their adult counterparts. One example is Pilocytic astrocytomas driven by MAPK activation abnormalities, most often through KIAA1549:BRAF fusions or BRAFV600E mutations. These features may serve as diagnostic or prognostic markers or even as targets for novel therapy. The aim of this study was to genetically characterize a pediatric brain tumor set from western Sweden, and next, to explore the functional relevance of novel mutations identified.
Design/Methods: We are currently cloning the novel gene mutation transcripts, which will be further transfected into neural cell lines (HEK293, RES-186, SK-N-AS) to study cell proliferation, clonal expansion, cell adhesion, migration and invasion capabilities. The localization, binding partners, and effect of the mutated proteins will be studied through live-cell imaging, co-immunoprecipitation, and gene expression analysis. If our study demonstrates a transforming capability *in vitro*, we will move on with *in vivo* studies using a xenograft mouse model.
Results: Through RNA-sequencing and Exome-sequencing we have identified novel point-mutations and gene fusions linked to the Rab-pathway. There is increasing evidence that Rab regulators have an important role in tumor progression, but this is the first time that Rab-associated mutations are linked to pediatric brain tumors.
Conclusion: In conclusion, increased knowledge of downstream effects and pathophysiologic roles of driver mutations will facilitate the development of subgroup or tumor-specific therapeutics. The BRAF inhibition agent Vermurafenib enacts an example of personalized therapeutic potential of CNS tumors. These and other targeted agents provide hope for the treatment of advanced and incurable tumors and may radically improve current therapy.

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EMBRYONAL TUMOR WITH ABUNDANT NEUROPIL AND TRUE ROSETTES (ETANTR): LONG TERM SURVIVAL IN A CHILD TREATED WITH INTENSIVE CHEMOTHERAPY AND PERIPHERAL BLOOD STEM CELL RESCUE

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Background/Objectives: Embryonal central nervous system tumors are classified into three subtypes: medulloblastoma, atypical teratoid/ rhabdoid tumor (ATRT) and primitive neuro-ectodermal tumor (PNET).Embryonal tumor with abundant neuropil and true rosettes (ETANTR) was initially described as a subtype of PNET. Recently, described as a distinct malignant CNS tumor with dismal prognosis despite aggressive treatment.Histologically ETANTR is characterised by presence of undifferentiated neuroepithelial cells resembling classic PNET along with well differentiated neuropil and ependymoblastic rosettes arising from paucicellular regions of neoplastic neuropil. ETANTR has a specific genetic alteration, amplification of the miRNA cluster *C19MC* at 19q13.42.
Design/Methods: We report a 33 months old girl with increasing irritability, balance disturbance and neck pain. MRI scan showed a massive right occipital tumor originating in the posterior fossa, infiltrating through the tentorium up into the cerebral hemisphere with significant mass effect. MRI spine and CSF cytology were negative for metastatic disease.She underwent right occipito- parietal and sub occipital posterior fossa craniotomy with intention of gross total resection. Post surgical MRI showed small residual tumor. Histopathological diagnosis was consistent with ETANTR. FISH analysis showed heterogeneous pattern of distribution with 3-6 copies of the 19q13.41 in 30% nuclei, 10-15 copies in 8% nuclei and normal signal in the remaining cells. She received three cycles of induction chemotherapy (vincristine, etoposide, cyclophosphamide and cisplatin) followed by three cycles of thiotepa and carboplatin with peripheral blood stem cell rescue. She had second look surgery to remove small residual tumor post induction. No radiation was given.
Results: She tolerated her chemotherapy well. She is 3 years post treatment and has no significant concerns.
Conclusion: Some children with ETANTR may do well with intensive chemotherapy. Prognostic factors for variable outcome need to be identified, in particular with regard to the heterogeneous distribution of 19q13.41 signal in our patient.

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THE ROLE OF SURVEILLANCE IN FAMILIES WITH BIALLELIC MISMATCH REPAIR DEFICIENCY SYNDROME: CASE REPORT OF TWO SIBLINGS WITH MULTIPLE COLON ADENOCARCINOMA AND BRAIN TUMOR

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Background/Objectives: Biallelic mismatch repair deficiency syndrome (BMMRD) is a distinct childhood cancer predisposition syndrome caused by biallelic germline mutations in one of the four mismatch repair (MMR) genes *MLH1, MSH2, MSH6*, or *PMS2*. BMMRD predisposes children to haematological, brain and gastrointestinal malignancies. Surveillance protocol was developed for these children and applied where possible.
Design/Methods: We report two siblings with BMMRD homozygous bi-allelic *MSH6* mutation with focus on implementation of surveillance. Fifteen year-old male with

cleidocranial dysplasia presented with weight loss, chronic bloody diarrhea and hypoalbuminemia. Clinical features were suggestive of NF-1 and familial adenomatosis polyposis (FAP). Endoscopy revealed extensive polyposis coli. He underwent laparoscopic protocolectomy with end ileostomy. Pathology revealed multiple colonic adencarcinoma. He was treated with oxaliplatin and 5FU for 24 weeks with complete remission. Molecular and genetic diagnostics were negative for *APC* and *MUTYH* genes but all colonic cancers had microsatellite instability. Tumour cells and adjacent normal mucosa stained negative for *MSH6* and positive for *MLH1, MSH2* and *PMS2 suggestive of BMMRD*. A homozygous pathogenic *MSH6* mutation was identified (c.3202C>T). This is the first reported BMMRD with CHRPE that fits clinical criteria for both NF-1 and FAP. After diagnosis of BMMRD, 12 years old sister underwent genetic workup and found to have homozygous for *MSH6* mutation. While awaiting surveillance imaging she developed headache and diplopia. MRI revealed large frontal tumor. She underwent incomplete resection of a glioblastoma multiforme (GBM) followed by radiation therapy and retinoic acid. Colonoscopy showed numerous large polyps with adenomatous changes and high grade dysplasia.
Results: The GBM progressed rapidly and she died within 9 months of diagnosis. Her brother continue surveillance with recent resection of second rectal carcinoma.
Conclusion: High index of suspicion of BMMRD in children with colon cancers and early implementation of surveillance protocol may improve survival for individuals with this highly penetrant syndrome.

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MALIGNANCY IN THE CHROMOSOME 22Q11.2 DELETION SYNDROME (DIGEORGE SYNDROME/VELO-CARDIO-FACIAL SYNDROME)

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Background/Objectives: We aim to describe the correlation between malignancy and the 22q11.2 Deletion Syndrome (22q11.2DS), of which DiGeorge Syndrome (DGS) is one of its clinical phenotypes.
Design/Methods: A 10 year old boy with a pineoblastoma was treated in our center. Due to his past history of developmental delay, genetic analysis was done, which detected a 2.4 Mb deletion on 22q11.21, leading to the diagnosis of 22q11.2DS. To evaluate the correlation between 22q11.2DS and malignancies we performed an extensive pubmed search over the last 40 years.
Results: Although a link between pineoblastoma and DGS was not described before, several other malignancies were found in patients with 22q11.2DS including xanthoastrocytoma, thyroid adenoma, hepatoblastoma, neuroblastoma, renal cell carcinoma, lymphoma and wilms tumor (table overview at poster).
Interestingly, a remarkable amount of patients with a rhabdoïd tumor were described. In this group, genetic analysis consistently showed deletions distal to the ´Typically Deleted Region´ in 22q11.2DS. It is referred to as the Distal 22q11.2 Syndrome, which was recently concluded to be a separate entity from the common 22q11.2DS even though clinical overlap was described. It must be emphasized that DGS has a broad variety in clinical manifestations. Hence, children with clinical similarities to the common 22q11.2DS might benefit from additional tests to evaluate possible distal deletions, considering its clinical relevance.
Conclusion: Given the high frequency of DGS, it´s important to define the risk of malignancy. The analysis of literature, concerning malignancy in 22q11.2DS, has led us to postulate that the overall risk of malignancy might be increased in 22q11.2DS. We suggest that caregivers of these patients should be vigilant regarding cancer diagnosis.

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UTILIZATION OF 18F-DOPA-PET IMAGING FOR NEUROSURGICAL PLANNING AND TARGET DELINEATION IN THE TREATMENT OF PEDIATRIC GLIOMAS

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Background/Objectives: Delineation of at-risk sites is critical for radiation planning and surgical treatment of gliomas. MRI/CT imaging is the 'gold standard', but this may not reflect the true extent of disease. Anaplastic tumors can present as heterogeneous lesions on MRI, and reliance on contrast-enhanced images alone can lead to non-diagnostic biopsy and inaccurate grading of tumor. The tracer 3,4-dihydroxy-6-[18F]fluoro-l-phenylalanine (FDOPA) has a high sensitivity for gliomas and may improve radiation planning and neurosurgical site selection. This study compares FDOPA-PET/CT to conventional CT/MRI imaging utilized for radiotherapy and resection planning in pediatric patients.
Design/Methods: MR/CT and FDOPA-PET/CT images were obtained in 5 pediatric patients with malignant gliomas. The region of interest (ROI) was defined based on areas of enhancement on MRI and increased FDOPA uptake. Ratios of maximum tumor standardized uptake value (SUVmax) normalized to mean SUV (SUVmean) of normal brain tissue (T/N) were determined using the SUVmax from each biopsy coordinate and the SUVmean from the volume of contralateral normal brain tissue contoured at the corresponding level.
Results: An average of 5 biopsies were obtained from each patient. The FDOPA-PET images were utilized to guide biopsy site selection in four patients, and one patient did not require biopsy after FDOPA-PET failed to show evidence of increased uptake. Regions of increased FDOPA uptake extended beyond those identified with MRI in two patients, and biopsy sites correlated with the region of highest uptake in 3 patients. Average tumor SUV_{max} was 2.135 (range 2.92-1.27), and the average T/N ratio was 1.6 (range 1.92-1.18). Biopsies were consistent with Grade III or Grade IV astrocytoma in three patients. Biopsies obtained from one patient demonstrated infiltrating glioma, but were undiagnostic for grade.
Conclusion: FDOPA-PET imaging has utility in guiding biopsy selection and may assist with identifying regions of higher-grade disease in patients with astrocytomas.

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QUALITY OF LIFE IN PEDIATRIC SURVIVORS OF CENTRAL NERVOUS SYSTEM TUMORS. EXPERIENCE OF A THIRD LEVEL HOSPITAL IN A LOW INCOME COUNTRY

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Background/Objectives: *Background*: **Long-term survivorship is a reality for an increasingly number of children with cancer, and it is very important to understand and take care of their quality of life (QoL), since many of them may experience a lot disturbances (physical,social,cognitive and psychological). Central Nervous System tumors (CNS) are the most common solid tumors in children with lot of morbility among survivors.** *Objective*: **To explore the QoL of survivors of brain cancer in the Pediatric Oncology Service in a third Level Hospital.**
Design/Methods: This descriptive, cross-sectional study was conducted in a tertiary medical center in Mexico City, and involved a total of 16 pediatric survivor patients who had CNS tumors. They performed a validated quality of life scale for Mexican children ($PedsQL^{MT}$).
Results: We graded each area (emotional, cognitive, physical and social) using the PedsQL scale. In a general way, QoL in our survivors is good. Emotional and cognitive functioning of PedsQL were the most affected areas, something important was that most of our patients felt anger. The physical area was also affected. Survivors of brain tumors suffer from numerous endocrine and metabolic consequences, majority of them developing within the first 5 years after brain tumor therapy.
Conclusion: An active follow-up aiming for early diagnosis and therapy is essential for improvement of quality of life in these patients. These data support an ongoing specific interest in the QoL of long-term cancer survivors and suggest the need for further study of multidimensional functioning in this population, especially in brain tumor survivors.

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OUTCOME OF CHILDREN WITH MEDULLOBLASTOMA: RESULTS FROM A SINGLE CENTER IN IRAN

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Background/Objectives: Childhood primary central nervous system (CNS) malignancies are one of the most important concerns in pediatric oncology. Therefore, study on the outcome of Medulloblastoma as one of the most common primary CNS malignancies in childhood can be helpful to find a better therapeutic approach for these malignancies.
Design/Methods: In this historical cohort, forty nine patients with medulloblastoma treated in Ali-Asghar Children's Hospital between 1999 and 2008 were evaluated for age, gender, type of treatment, and survival.
Results: The records of twenty female (40.80%) and twenty nine male (59.20%) patients were included. The mean age was 6.8 ± 3.39 years (6 months to 14 years). Complete resection, radiotherapy, and chemotherapy were done in 59.2, 91.8, and 100 percent, respectively. Estimated 5 years overall and event-free survivals (EFSs) were 69.50% [standard error (SE) =7.40] and 37.40% (SE= 7.80), respectively. The patients with complete resected tumors had significantly better outcome ($p = 0.013$).
Conclusion: The poor EFS with consideration of high number of progressive disease among our patients suggests that children in Iran with CNS tumors had high quality of care but availability of advanced treatment protocol and sharing of cooperative trial study is essential for survival improvement. In addition to use more advanced methods and equipments of radiotherapy and chemotherapeutic drugs, we should seriously consider development of better surgical techniques to increase the rate of complete resection of malignant CNS tumors.

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RHABDOID COMPONENT EMERGING AS A SUBCLONAL EVOLUTION OF PEDIATRIC LOW-GRADE GLIONEURONAL TUMORS

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Background/Objectives: Low-grade glioma with a rhabdoid component and loss of BAF47 were reported in 4 pediatric cases up to now. Patients were usually young, with a median age of 4 years, and their prognosis dismal (3 patients died).
Design/Methods: We report 5 cases of pediatric patients presenting low-grade gliomas harboring either at diagnosis or during evolution a rhabdoid component and a homozygous deletion of *SMARCB1*.
Results: Age at diagnosis ranged from 13 months to 12 years. All tumors were located in the fronto-parietal region, and presented an avid and heterogeneous enhancement, with edema but no necrosis. Histology of the low-grade component (LGGC) was a ganglioglioma for two patients, an association between a ganglioglioma and an oligodendroglioma for one patient, a pleomorphic xanthoastrocytoma for one patient, and an unclassifiable tumor for one patient. A BRAF V600E mutation was detected in none of the patients but the pleomorphic xanthoastrocytoma one. The rhabdoid component (RC) was evidenced at diagnosis for 4 patients. It appeared at relapse for one patient while he was treated by BRAF V600E inhibitor. All cells in the RC showed a typical BAF47 loss of expression. Comparing array-CGH from the LGGC and the RC in two patients clearly showed the similarity of the two profiles. However, SMARCB1 deletion was hemizygous in LGG and homozygous in RC, demonstrating that RC was a subclonal evolution of LGGC. Overall 3 patients died, one within 24 hours after diagnosis, two patients 6 months and 2 years after diagnosis, including the patient with deletion of *SMARCB1* at relapse, and 2 patients are in complete remission 2 years and 4.5 years after the initial diagnosis.
Conclusion: This short series brings evidence that a subset of pediatric glioneuronal tumors may secondarily transform as rhabdoid tumors. CGH-profiling shows a hemizygous *SMARCB1* deletion that may underline potential aggressive transformation of such benign tumors.

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TREATMENT OUTCOME AND PATTERNS OF FAILURE IN PATIENTS OF SUPRATENTORIAL PRIMITIVE NEUROECTODERMAL TUMOUR: CLINICAL EXPERIENCE FORM A REGIONAL CANCER CENTER IN NORTH INDIA

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Background/Objectives: Supratentorial primitive neuro-ectodermal tumours (SPNET) are high grade, embryonal tumours, which account for 2–3% of paediatric brain tumours.
Design/Methods: We assessed the clinical features and treatment outcome in patients of SPNET by retrospective chart review from 2003-12. Overall survival (OS) and recurrence free survival (RFS) were analyzed by Kaplan-Meier method.
Results: Thirty two patients met the study criterion (male: female=21:11). Median age at presentation was 12 years.Tumour location was pineal in 17 and hemispheric in 15 patients. Median KPS was 80. Surgical resection was gross-total in 12(37.5%), near-total in 2, subtotal in 10(31.25%) and limited to biopsy in 7(21.88%) patients. Histopathology showed sheets of small round blue cell tumour immunopositve for synaptophysin, class III ß-tubulin and neuron specific enolase (NSE). Median MIB-1 labelling index was 35%. At presentation, 6(18.75%) patients had leptomeningeal dissemintation. Radiation therapy was delivered in 29(90.63%) patients with majority(75%) receiving craniospinal irradiation(CSI)(36Gy/20fractions/4weeks) followed by local boost of 20Gy/10fractions/2weeks. Systemic chemotherapy (median 6 cycles), given in 27(84.38%) patients, included VAC(vincristine,adriamycin,cyclophosphamide) alternating with IE (ifosfamide,etoposide) regimen in non-pineal tumours and EP (carboplatin and etoposide) regimen in pineal tumours. After a median follow-up of 29.22 months (mean 30.35 months), seven (21.88%) patients had died (6-disease progression and 1-neutropenic sepsis). Recurrence was noted in 13(40.63%) patients (local-3, leptomeningeal-5 and both-5 patients). Median OS was not reached (actuarial rate of OS at 3 years-75.7%) and estimated median RFS was noted to be 5.49 years (actuarial rate of RFS at 3 years- 59.5%). On univariate analysis, there was a trend towards inferior RFS in patients with M+ disease (median-2.19 years) compared to those with M0 disease (median-6.38 years) (P=0.06).
Conclusion: Maximal safe resection followed by CSI and chemotherapy with 6 cycles of VAC/ IE (in non-pineal tumour) or EP (in pineal tumour) is a reasonable treatment strategy in patients of SPNET in a developing nation.

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AN UNUSUAL CASE OF RHABDOID MENINGIOMA

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Background/Objectives: Meningioma accounts for approximately 1% of primary paediatric central nervous system tumours, making these a relatively uncommon diagnosis in childhood. Within the paediatric population, a higher than expected proportion of these tumours are of a malignant subtype (papillary, rhabdoid, anaplastic). We present the case of an 11 year old girl diagnosed with rhabdoid meningioma, diagnosed incidentally during investigations following a traumatic head injury.
Design/Methods: We reviewed the patient casenotes, identifying the patients initial presentation, imaging results, management plan and final pathological diagnosis.
Results: Previously asymptomatic, the patient developed symptoms of headache, vomiting, photophobia and neck stiffness over a one week period following a witnessed fall which resulted in head injury. Whilst the CT and MRI demonstrated an extra axial lesion, the remaining imaging phenotype was atypical for a meningioma with areas of diffusion restriction, lack of enhancement and areas of haemorrhage, with significant mass effect. This patient was treated with a macroscopic complete resection (Simpson grade 2). Histologically, this tumour was composed of sheets of enlarged eosinophilic cells, with eccentric nuclei and a high proliferative index (10-15%). Thickened dura was noted to extend beyond the mass. Immunohistochemical staining with INI1 confirmed the diagnosis. She is currently receiving adjuvant focal radiotherapy.
Conclusion: The results of investigations performed are in keeping with an aggressive malignant meningioma of the rhabdoid subtype. This histological diagnosis is extremely rare in children.

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THE RESULTS OF TREATMENT OF RECURRENT ANAPLASTIC EPENDYMOMAS (AE) IN CHILDREN

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Background/Objectives: To evaluate the survival of patients in relapse of AE, and there survival depending on the treatment scheme.
Design/Methods: We observed 57 children with AE progression after initial treatment, 39 boys and 18 girls at the age from 1 month to 19 years (median 4 years). The tumor was located initially supratentorial in 29 patients (50.9%) and subtentorial - in 28 (49.1%). 34 patients (59.7%) had stage M0, 2 (3.5%) - M1, 2 (3.5%) - M2, 4 (7.0%) - M3, in 15 patients (26.3%) stage was not determined. As a first-line therapy 30 patients (52.6%) received surgery+RT+PCT, 14 (24.6%) - surgery+PCT, 9 (15.8%) - surgery+RT, and 4 (7.0%) - only surgery.28 patients (47.8%) had a relapse as the progression of the disease (PD), 15 (26.3%) - continued growth, 11 (19.3%) - Mts, 3 (5.3%) - relapse+Mts, 1 (1.7%) - continued growth+Mts. The median time before PD

was 17 months (3-48 months).37 patients (65.0%) was obtained as a therapy of the 2nd line Protocol HIT REZ 2005 with TMZ, 6 (10.5%) - only surgery, 4 (7.0%) - surgery+RT, 4 (7.0%) - only RT, 6 (10.5%) - various non-protocol treatment.
Results: The median of follow-up after PD - 15 months (1-110 months). 5-year PFS after 2nd line therapy - 0.30. Median PFS - 25 months. Alive 35 patients (61.0%), 17 of them finished treatment.5-year PFS in patients treated with the protocol HIT REZ 2005 with TMZ - 0.34, in patients receiving only surgery and / or radiotherapy - 0.24, non-protocol with treatment - 0.23, $p = 0.56$.
Conclusion: The best results were obtained in the group of patients treated with the protocol HIT REZ 2005 with TMZ.

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CEREBELLAR ASTROCYTOMA IN A REGIONAL NEURO-ONCOLOGY CENTRE; EVALUATING THE NEED FOR POST-SURGICAL IMAGING SURVEILLANCE

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Background/Objectives: Cerebellar astrocytomas constitute around 15 % of CNS neoplasms in childhood. Surgery, with the aim of complete resection, is the principal treatment modality, although need for and duration of post-surgical MRI surveillance is not well defined. In this respect, we conducted an evaluation of the outcome of cerebellar astrocytomas at our regional paediatric neuro-oncology centre.
Design/Methods: Our tumour database was interrogated to identify all cases of cerebellar astrocytoma. Variables included patient age, gender, tumour grade, completeness of resection, duration of follow-up, remission status and adjuvant therapy.
Results: Between 1988 and 2007, 49 patients with cerebellar astrocytoma were reviewed - 43 pilocytic astrocytomas, 4 fibrillary astrocytomas, 1 ganglioglioma and 1 unspecified low-grade tumour. Thirty seven patients underwent complete resection (CR), none of whom relapsed. Of the 12 patients with incomplete resection, six patients progressed at between 4 months and 6 years. We thus changed the duration of MRI surveillance from 5 years to a maximum of 2.5 years (scans at 6, 18 and 30 months post surgery) in those patients who had undergone CR. Since this change in practice, a further 12 patients (all WHO grade 1) have been treated (data until December 2012-to allow > 2 years follow-up). Eleven tumours were completely resected and 1 had a near total resection. None of these 12 patients have relapsed (median follow-up - 4.9 years).
Conclusion: In this service evaluation, none of the 48 patients with completely resected cerebellar astrocytoma relapsed, supporting a change in practice to shorten the duration of post-operative surveillance. This has resulted in a time and cost saving to families and our health service. The data does, however, raise the question as to whether any surveillance imaging is required in completely resected pilocytic cerebellar astrocytoma. For incompletely resected tumours, a standard 5-year post-surgical imaging schema should be maintained.

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SINGLE AGENT VINORELBINE IN PEDIATRIC AND ADOLESCENT PATIENTS WITH PROGRESSIVE UNRESECTABLE LOW-GRADE GLIOMA

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Background/Objectives: The management of progressive unresectable low-grade glioma (PULGG) remains controversial. Treatment options include chemotherapy, usually preceded by a period of observation, to delay or even avoid radiotherapy and extensive surgery in a proportion of children. Within this context an institutional protocol for PULGG with vinorelbine, a semi-synthetic vinca alkaloid, was conducted at IOP/GRAACC/UNIFESP with the aim to evaluate the clinical and radiological response, as well as its toxicity profile.
Design/Methods: From July 2007 to may 2013, 41 patients with recurrent (9) and newly diagnosed (32) PULGG were treated with vinorelbine 30 mg/m^2 on days 0, 8 and 22 for 18 cycles. Response criteria used a combination of magnetic resonance imaging, physical and visual evaluation.
Results: Mean age 6.4 years. Tumor sites: 27 optic pathway (1 disseminated), 1 intramedullary, 3 hemispheric (1 bilateral thalamic), 7 brainstem, 2 cerebellum, 1 gliomatosis cerebri. Twenty-eight patients had neurosurgical intervention, 18 grade I astrocytoma and 10 grade II. Ten of them were evaluated by BRAF status showing 6 BRAF fusions, 2 of them also with BRAF mutation. Four patients had diagnosis of neurofibromatosis type 1 and three diencephalic syndrome. Of the 41 patients enrolled in the study, 40 were assessable for response. The best objective response was observed in 17 patients (1 complete, 10 partial, 6 minor), while 23 had stable disease. The most important toxicity was hematologic, with grade 3/4 neutropenia in 9 patients. None of the patients showed grade 3/4 gastrointestinal toxicity and only 1 grade 3 neurotoxicity (lower extremity pain). With a mean follow-up of 56 months the progression-free and overall survival for the all group in 3 years was 49.3% and 81.8%, and 5 years was 36.8%, and 81.8%, respectively.
Conclusion: The results suggest that vinorelbine may be an option for PULGG, showing some activity with low toxicity and excellent quality of life.

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CHEMOTHERAPY FOR PEDIATRIC LOW-GRADE GLIOMAS

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Background/Objectives: The low-grade gliomas (LGG), WHO grade I-II, corresponding to 50% of tumors of the central nervous system. Surgery remains the mainstay in the treatment, and complete resection the most important prognostic factor.The decision to treat patients with incomplete resection is controversial because of the possibility of sequelae related to a new surgery. Chemotherapy and radiotheraphy should be reserved for symptomatic progression tumors with no possibility of complete resection. PURPOSETo evaluate the efficacy of chemotherapy in pediatric patients (p) with unresectable LGG, symptomatic or progressed after surgery.
Design/Methods: Retrospective descriptive population based study of LGG at a single center from March 2002 to March 2014.
Results: Seventy one children were diagnosed and treated for LLG. Twenty p (28.5%) were performed chemotherapy. All patients had localized disease. In 16 p (80%) partial resection surgery was performed. In the remaining 4 no surgery was performed (3 chiasmatic and 1 in cervical cord tumors). The most common histological subtype was pilomyxoid Astrocytoma (8 p, 40%) followed by pilocytic astrocytoma (3 p, 15%) and diffuse astrocytoma (2 p, 10%). Most frequent location was suprasellar 75% (15p, Optic pathaway 6 p). Fifty percent of p (10) performed treatment with carboplatin plus Vincristine (COG A9952) and 9 p (45%) performed vinblastine weekly. One p received oral Temozolomide. Three p made second-line and 2 p received local radiotherapy for progression after receiving second-line treatment. Fifteen percent had Grade III hematologic toxicity.The mean follow-up was 44 months (range 1-132), 6p(30%) died for progression disease,1p died for postoperative complications and 13 p (65%) are stable or with partial remission to date. The 5 yr. OS was 85%.
Conclusion: Use of chemotherapy in children with unresectable LGG progressed or symptomatic appear to be effective in achieving stable disease with minimal toxicity, delaying the use of local radiotherapy and avoiding progression.

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EXPRESSION OF MRTL AND MYCHEX1 FROM C-MYC LOCUS IN PEDIATRIC BRAIN TUMORS

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Background/Objectives: The *c-myc* protooncogene plays a major role in the regulation of cell growth, proliferation, differentiation, and apoptosis. In addition to the canonical c-Myc p64 and p67 proteins, the human c-*myc* locus also encodes two distinct proteins designated "mrtl" (ORF114) and "MycHex1" (ORF188) within the 5'-"untranslated" region of the c-*myc* P0 mRNA. The aim of this study is to examine simultaneously, for the first time, mrtl, MycHex1, c-Myc p64, and p67 in pediatric brain tumor tissues.
Design/Methods: The mrtl and MycHex1 coding sequences were PCR amplified and analyzed in medullobastoma and malignant glioma tissues. Monoclonal mouse anti-mrtl and polyclonal rabbit anti-MycHex1 antisera were developed. Western analysis was done with whole cell lysates and immunofluorescence (IF) staining and confocal imaging performed following methanol fixation.
Results: Sequence analyses confirmed a known polymorphism at base 1965 (T>G) and revealed new mutations in mrtl sequence associated with non-synonymous amino acid substitutions. MycHex1 sequence revealed no variation from published sequence. Western analyses visualized mrtl, MycHex1, c-Myc (N262) p64 and p67 simultaneously. The relative intensities of mrtl and MycHex1 were positively correlated. IF staining showed mrtl dominantly localized to the nuclear envelope, along with prominent reticular pattern in the cytoplasm consistent with endoplasmic reticulum (ER). MycHex1 was observed as a series of bright foci located mainly within the nucleus and

partially colocalized with fibillarin (a nucleolar protein). MycHex1 also stains other intranuclear structures not recognized by fibrillarin.
Conclusion: This study showed the evidence for expression and stable accumulation of all 4 proteins (mrtl, MycHex1, c-Myc p64, and p67) encoded by three non-overlapping reading frames within the human c-*myc* locus. MycHex1 from the c-*myc* P0 mRNA seemed to be located to a specific domain of the nucleoli, as well as other intranuclear structures. Further work is ongoing to elucidate the functional or regulatory relationships between these molecules.

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CHARACTERISTICS OF METASTATIC OR MULTIFOCAL LOW GRADE GLIOMAS OF THE CENTRAL NERVOUS SYSTEM- A TEN YEAR INSTITUTIONAL REVIEW

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Background/Objectives: Low grade gliomas (LGG) account for 40% of childhood CNS tumours. A minority of these are metastatic or multifocal. *Aim*: To study the occurrence and characteristics of metastatic compared to localised LGG.
Design/Methods: Retrospective review of all children aged ≤17 years with LGG (WHO grade I or II, which meet criteria for LGG2 study) treated in our institution between October 2003-September 2013.
Results: There were 150 patients with LGGs(73 male,77 female). At diagnosis, 45 patients(30%) were aged 0-4 years, 62(41.3%) were >10 years and 43(28.6%) were 5-9 years of age. One hundred and forty two patients(94.67%) had localised tumours: 62(40.7%) posterior fossa, 29(19.3%) hemispheric, 29(19.3%) optic pathway gliomas{18 of these patients had neurofibromatosis type I (NF-1)}, 19(12.7%) deep midline (tectal plate, hypothalamus, corpus callosum) and 4(2.7%) spinal cord. Twenty-four patients had NF-1; 3 patients had tuberous sclerosis with sub-ependymal giant cell astrocytoma(SEGA). Histopathology was confirmed in 74% patients(103 localised and all metastatic patients). Localised diagnoses: Pilocytic astrocytoma(n=82), diffuse astrocytoma(n=5), ganglioglioma(n=8), SEGA(n=2), gemistocytic astrocytoma(n=1), glioneuronal(n=2), astroglial(n=1), ganglioneuroma(n=1) and angiocentric glioma(n=1). First line treatment in localised LGG was as follows: observation only(n=18, 1 biopsy), third ventriculostomy(n=5), surgery(n=102), chemotherapy(n=11) and radiotherapy(n=6). Progression was seen in 36 patients requiring further treatment and there were 6 deaths. Eight patients(5.33%) had metastatic/multifocal disease(3 patients aged 0-4 years, 2 aged 5-9 years and 3 aged >10 years). One patient had disease restricted to the cord with leptomeningeal spread while 7 had disseminated disease. Histopathology included 3 pilocytic astrocytomas, 2 pilomyxoid astrocytomas, 1 oligodendroglioma, 1 diffuse astrocytoma and 1 glioneuronal tumour. First line treatment was surgery(n=4), chemotherapy(n=3) and radiotherapy(n=1). Five patients progressed needing further treatment with one death (infant with extensive pilomyxoid astrocytoma).
Conclusion: Metastatic LGGs have more varied histology than localised tumours(pilocytic vs other pathology(p=0.04)). Most children with LGG are cured. Therefore careful treatment selection to minimise long-term consequences is crucial.

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CHILDHOOD MEDULLOBLASTOMA - EXPERIENCE FROM A TERTIARY CARE CENTER IN NORTH INDIA

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Background/Objectives: Medulloblastoma is the most common posterior fossa tumor of childhood. Outcome depends on risk stratification based on age at diagnosis, extent of surgery, spread of disease and eligibility for radiotherapy.
Design/Methods: This is a retrospective analysis of 21 children diagnosed with Medulloblastoma who were treated during August 2009 to January 2015 in our center.Children has been treated with surgery, concurrent chemotherapy and radiotherapy followed by adjuvant chemotherapy with Packer's regimen or high dose chemotherapy with stem cell rescue. Data was analyzed using SPSS 22.
Results: Age of children ranges from 2 to 25 years (Median 8 years). Out of 21 children 15 were male (71.4%), 6 were female (28.6%). Eight (38 %) were of average risk, 13/21 (62%) were of high risk. Near total resection was done in 14/21 patients and 6/21 had residual disease post resection. All except one (age-2 year) received craniospinal radiotherapy post-surgery. Weekly Vincristine was given to all patients, two patients also received Carboplatin during radiotherapy. Fifteen patients (8 with average risk and 7 with high risk) were treated with Packer's regimen. One patient received baby brain protocol. Four patients with high risk disease were treated with high dose chemotherapy with stem cell rescue (4 cycles). Median survival has not reached. On median follow up of 16 months overall survival (OS) for average risk was 86%, and 62% for high risk. Fifteen out of twenty one (71%) are alive till January 2015, fourteen are disease free, one relapsed but alive. Five out of six died due to disease progression, one died due to HLH. None of the mortality was due to treatment related sepsis.
Conclusion: Outcome of this rare disease is reasonably good with combined modality treatment and it is possible to administer high dose chemotherapy with stem rescue without significant side effects even in developing countries.

P-139

HUMAN CYTOMEGALOVIRUS INFECTION MODIFIES PATTERN OF DNA METHYLTRANSFERASE-1 IN CNS TUMORS AND IN NON TUMOR CELLS

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Background/Objectives: Human cytomegalovirus (HCMV) is a ubiquitous herpesvirus that infects and establishes latency in the majority of the human population and may cause fatal infections in immunocompromised patients. HCMV has been detected in 90-100% of malignant glioblastoma (GBM) and in a majority of primary meduloblastomas (MB), two of the most common type of brain tumors. Epigenetic alterations are believed to be a basic factor behind malignancies and whole genome methylation studies of GBM tumors suggest that GBM recurrence is linked to epigenetic mechanisms and pathways. Previous study from our laboratory has shown that HCMV infection of non-tumor cells affects the host cell DNA methylation machinery (DNA methyltransferases, DNMTs) by preventing its nuclear localization. This may be a strategy for HCMV to abrogate the host cell defense against viral replication.
Design/Methods: The overall aim of our work is to investigate epigenetic alterations caused by HCMV encoded viral proteins in non tumor and CNS tumor cells, and to further investigate if viral alterations of epigenetic mechanisms contributes to tumorigenesis. In order to investigate the mechanism(s) involved in cellular re-localization of DNMTs following HCMV infection, we analysed the expression of DNMT1 in non-tumor (MRC-5 and HUVEC) and tumor cells (GBM and MB) by TaqMan and confocal microscopy.
Results: Re-localization of DNMT1 from the nucleus to the cytoplasm appeared to be associated with cells expressing HCMV-late proteins, and which could be restored in the nucleus by antiviral (Ganciclovir) treatment. Our results suggest that specific viral proteins interact with host cell proteins to modulate the host cell epigenetic response.
Conclusion: We hypothesize that HCMV infection may lead to host cell epigenetic alterations of surviving cells and eventually to neoplastic events.

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PHASE II STUDY OF NIMOTUZUMAB AND RADIOTHERAPY IN CHILDREN AND ADOLESCENTS WITH NEWLY DIAGNOSED DIFFUSE INTRINSIC PONTINE GLIOMAS (DIPG)

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Background/Objectives: DIPG are amongst the most challenging tumors to treat in childhood with no drug proven to be effective. Standard of care remains focal radiotherapy alone however, rapid disease progression usually occurred. Median overall survival is less than 1 year, and the 2-year survival is less than 10%.
Design/Methods: Patients with clinically and radiologically confirmed, centrally reviewed newly diagnosed DIPG were eligible for this multicenter phase II study. The anti-epidermal growth factor receptor antibody, nimotuzumab (150 mg/m2) was administered intravenously once weekly concomitant with focal radiotherapy (54Gy) and every 2 weeks until tumor progression. Response evaluation was based on clinical and radiological assessments. Primary objective was to improve survival with a historic cohort that received radiation therapy alone.
Results: Twenty one patients entered into this study (7/14, male/female; median age, 7.6 years; range 2-16 years). All received radiotherapy. Treatment was well tolerated. 40/502 cycles had adverse effects related to the drug and very mild. The majority of adverse effects were associated with progression of disease. Disease free survival at 7.3 months was 85.7% (CI95% - 70.7-100). Overall survival at 9 months was 71.4% and at one year, 57.1% (CI95% - 33.8-74) which demonstrated better results when compared with historic trials.
Conclusion: This trial demonstrated some activity of nimotuzumab in DIPG. It was well tolerated and improved overall survival. A small subset of patients appeared to benefit from this anti-EGFR antibody and can be considered in future trials with

synergistic drugs. An upfront biopsy can bring the prospect of a better understanding of DIPG biology and selection of better treatment.

P-140A

CHEMOTHERAPY-ONLY STRATEGIES FOR YOUNG CHILDREN NEWLY-DIAGNOSED WITH MALIGNANT BRAIN TUMORS; CAN THEY BE APPLIED SUCCESSFULLY IN DEVELOPING COUNTRIES? THE MALAYSIAN EXPERIENCE

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Background/Objectives: Since the 1980s, treatment strategies for young children with malignant brain tumors have focused on initially delaying and subsequently avoiding irradiation and its profound and irreversible deleterious effects through use of intensive chemotherapy. We report the Malaysian experience with the "Head Start" chemotherapy-only strategy and draw comparisons with the "Head Start" Consortium studies conducted in high-income countries between 1990 and 2009.
Design/Methods: Patients: Since 1997, 17 children under 3 years old at diagnosis of either medulloblastoma (13) or posterior fossa ependymoma (4) were treated with either the "Head Start" HS-I or HS-II regimens. Ten children underwent gross-total, 4 near-total and 3 sub-total resections of primary tumor. Three children had metastases at diagnosis.
Results: Fourteen children (82.5%) completed all 5 cycles of Induction chemotherapy; one died of candidemia following HS-I cycle #4, two developed tumor progression during HS-II Induction. Twelve children (70.5%) proceeded with myelo-ablative consolidation and autologous hematopoietic cell rescue; two children completing induction declined further therapy. All 4 children with ependymoma subsequently relapsed, while 7/8 children with medulloblastoma undergoing transplant continue alive without recurrence between 4 and 7 years from transplant. Overall, 7/13 children with medulloblastoma (54%) all with localized disease at diagnosis, remain alive and irradiation-free following this strategy.
Conclusion: This experience in an upper-middle-income Asian country demonstrates the feasibility of these chemotherapy-only regimens for young children with medulloblastoma, with tolerance and efficacy not significantly different from that encountered in the comparable experience in high-income countries. With expanding and improving infrastructure and supportive care for the management of many childhood cancers, especially given persisting substantial lack of modern radio-therapeutic equipment and expertise, these chemotherapy-only strategies should be evaluated prospectively and more widely throughout middle- income developing countries.

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EFFECT OF CHEMOTHERAPY AND CHEMORADIOTHERAPY FOR MEDULLOBLASTOMA WITHIN PROTOCOL HIT-2000/2008 AMONG CHILDREN UNDER THE AGE OF FOUR YEARS

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Background/Objectives: To estimate the efficiency of chemotherapy and radiotherapy and to determine the prognostic factors.
Design/Methods: From 2009 to 2014, we analyzed 36 cases who got therapy within protocol HIT-2000/2008 after tumor resection. There were 19(53%) girls and 17(47%) boys. Most patients were older than 1 year: 5(14%) patients 3–12 months, 18(50%) - 13–24 months, 13(36%) - 25–48 months. The histological variant of the tumor were: 16/3 (53%) DMB/MBEN, 15 (41.5%) CMB, and 2 (5.5%) LCA. Stage M0 was in 25 (69.5%) patients; M+ in 11 (30.5%). 15 cases (42%) underwent total resection; a residual tumor was in 10 patients (28%). Chemotherapy+radiotherapy used on 19 (53%) patients; 17 (47%) got chemotherapy. Intrathecal/intraventricular Methotrexate used to 22 (61%) patients.
Results: PFS and OS were 0.71±0.08 and 0.86±0.06. The mean time of observation was 36 months, the median time to progression - 17 months. 35 patients completed treatment, 9 were diagnosed with recurrence, and 4 died of PD. PFS/OS was 0.88/1.0 for patients aged 25–48 months, 0.62/0.77 for patients 13–24 months and 0.60/0.80 for patients 3–12 months. There were no differences in PFS/OS depending on the histological variant: 0.61/0.85 for DMB/MBEN, 0.79/0.86 for CMB, and 1.0/1.0 for LCA. Patients with stage M0 had better PFS/OS in contrast for M+: 0.74/0.95 and 0.64/0.65 respectively. PFS/OS among patients with M0R0 were 0.64/0.92; M0R+ 0.89/1.0. PFS was better in patients who received intrathecal/intraventricular MTX (0.79) in comparison to those who didn't (0.63). PFS was 0.67 among patients who got radiotherapy and 0.76 among those who didn't.
Conclusion: Chemotherapy is efficient in MB patients under the age of 4. A low survival rate was observed among patients under 1 year and with metastases. The completeness of the surgical resection and radiotherapy did not affect the results of treatment. The best survival rate was found among patients who got regional MTX.

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RESULTS OF HIGH-DOSE CHEMOTHERAPY WITH AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION IN THE TREATMENT OF MEDULLOBLASTOMA

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Background/Objectives: Medulloblastoma (MB) is one of the most common pediatric malignant brain tumors with less than 30% 5-year overall survival rate in high-risk group. The aim of this study was to assess the effectiveness of single or tandem high-dose chemotherapy (HDCT) with autologous hematopoietic stem-cell transplantation (auto-HSCT) in this patient group.
Design/Methods: From February 2006 to February 2015, 32 pediatric patients with high-risk or relapsed MB received HDCT with auto-HSCT after induction chemotherapy, radiotherapy and surgical treatment. At the moment of HDCT 15 patients were in complete remission (CR), 10 patients were in partial remission (PR) and 7 patients had stable disease (SD). Patients received single or tandem auto-HSCT depending on age. Bone marrow (N=16), peripheral blood stem cells (N=13) or both (N=3) were used for stem cell sources.
Results: The median follow-up is 17 months (range, 2–78). The median time to engraftment was day +15 (range, 11–30) after auto-HSCT. Six patients with SD at the moment of auto-HSCT died of disease progression. Ten of 25 patients with CR or PR relapsed 1-23 months after HDCT, 11 patients are currently in CR and the other 4 children died of toxicity. 2-Year overall survival (OS) was 50% and disease free survival (DFS) was 47%. 2-Year DFS was significantly better among high-risk patients in 1st CR compared to patients in 2nd or following CR: 80% and 38%, accordingly (p=0,05). Patients in CR or PR at the moment of HDCT had better DFS rate than patients in SD: 60%, 40% and 14% (p=0,003), respectively.
Conclusion: HDCT with auto-HSCT in pediatric patients with high-risk MB may be a feasible option for patients in CR or PR after induction chemotherapy. It is ineffective as a salvage therapy in refractory patients.

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MANAGEMENT OF PROGRESSING BRAIN STEM ANAPLASTIC GANGLIOGLIOMA WITH A MOLECULAR BASED THERAPY

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Background/Objectives: To show the changes in the treatment, based in molecular studies, and the clinical evolution in a patient with a CNS tumor.
Design/Methods: A 2yo Caucasian boy diagnosed with a brain stem anaplasic ganglioglioma is presented. Clinical summary revealed a 13 month history of gait disturbances and several cranial nerve paresia, dismetria and left hemiparesia. The tumor was unresectable so only a biopsy could be obtained. He was initially treated with chemotherapy (vincristine, cisplatin, etoposide, and cyclophosphamide) but progressed

after 5 cycles. Treatment was then started with irinotecan and bevacizumab with an improvement over the next 10 months. After 13 cycles irinotecan was stopped because of gastrointestinal toxicity but Bevacizumab was mantained. Three months latter tumor progression was diagnosed. Molecular study of the tumor had been performed at diagnosis, and showed a mutation in BRAF exon 15 (c. 1799> A, pVal600Glu). Treatment with dabrafenib (3,75 mg/kg/day) was initiated after this 3rd tumor progression. 4 weeks later clinical improvement was remarkable and confirmed with a cranial NMR on week 12. Six months later the treatment was stopped 10 days because a VP shunt infection. In this context the patient had a neurological deterioration and tumor progression on NMR. Dabrafenib was resumed and cloroquine was added (3 mg/kg/day) with a clinical improvement that has been confirmed by a cranial NMR. Child is 5yo, attend school and has a residual left hemiparesia and left held tilting.
Results: A personalized treatment in this patient has improved his survival and quality of life.
Conclusion: Molecular analysis of our patient's tumor allowed us, to identify a druggable mutation which gave us the chance to administer Dabrafenib once several considered standard treatments had failed. Our patient that significantly improved since he started Dabrafenib. The rol of adding cloroquine in this context has been previously reported in order to induce autophagy.

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THE WNT/β-CATENIN SIGNALING PATHWAY REGULATES MGMT GENE EXPRESSION IN CHILDHOOD NEURAL TUMORS AND INHIBITION OF WNT SIGNALING PREVENTS CHEMORESISTANCE

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Background/Objectives: High expression of the DNA repair enzyme O6-methylguanine-DNA methyltransferase (MGMT) are frequently detected in cancers and MGMT is an important factor for treatment failure and development of cancer cell resistance against chemotherapeutic drugs. Several drugs inhibiting MGMT have been developed but their systemic uses are limited due to lack of efficiency and hematologic toxicity.
Design/Methods: We searched for cellular regulators of MGMT expression in cancers of different origin as an alternative approach to inhibit MGMT. Pathway-specific gene expression profiling, gene clustering and immunohistochemistry where used to detect correlations between MGMT and other genes and signaling pathways. Pharmacological or genetic inhibition of target genes where used to confirm regulation of MGMT and restoring chemoresistance in vitro and in vivo.
Results: We show that the canonical Wnt signalling pathway regulates the expression of MGMT in childhood neural tumors. A significant correlation between Wnt signaling and MGMT expression in childhood gliomas, medulloblastomas and neuroblastoma that was confirmed by gene expression analysis and immunofluorescence demonstrating co-localization between active β-catenin and MGMT. Small molecule inhibition of key molecules within the canonical Wnt signalling cascade or knock-down of β-catenin downregulates MGMT expression and restore chemosensitivity to DNA alkylating drugs in mouse models of neural tumors.
Conclusion: These findings have potential therapeutic implications for the treatment of chemoresistant cancers, especially in brain tumors where the use of temozolomide frequently is included in the treatment protocols.

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IMPACT OF TUMOR TYPE, LOCATION, AND TREATMENT ON PHYSICAL AND EMOTIONAL OUTCOMES IN PEDIATRIC BRAIN TUMOR

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Background/Objectives: Survivors of pediatric brain tumor suffer reduced quality of life in both physical health and psychological health. There is a paucity of research examining medical factors that may impact physical and psychological health outcomes. It was the aim of this study to identify the impact of brain tumor type, primary location, and treatment modality on parent-reported child pain, physical functioning, and emotions.
Design/Methods: Participants included mothers of 182 children and adolescents (M age = 11.3 years; 47.3% female; $M = 3.8$ years since diagnosis) diagnosed with a brain tumor. Brain tumor types included low grade glioma/astrocytoma (LGA; 48.4%), PNET (23.6%), ependymoma (7.7%), craniopheringioma (7.1%), germ cell (13.2%), and other (7.7%). Primary tumor location included infratentorial (45.6%), supratentorial (33.0%), and midline (18.7%). Parents completed the Child Health Questionnaire and the Child Behavior Checklist. Multivariate regression and post-hoc t-tests were utilized.
Results: Controlling for age at diagnosis, tumor type was associated body pain ($F = 2.5$, $p < .05$), physical functioning ($F = 6.9$, $p < .01$), and withdrawal/depression symptoms ($F = 3.3$, $p = .01$). Specifically, LGA was associated with less body pain, better physical functioning, and less withdrawal/depression compared to PNETs and craniopheringiomas (p's $< .05$). Supratentorial tumor location was associated with less withdrawal/depression compared to infratentorial ($t = -4.3$, $p < .01$) and midline tumors ($t = -3.1$, $p < .01$). Chemotherapy and radiation were associated with decreased physical function (p's $< .01$) and increased withdrawal/depression symptoms (p's $\leq .01$), while radiation was also associated with increased body pain ($F = 6.1$, $p = .02$).
Conclusion: Children with LGA and supratenorial tumors may suffer fewer negative physical and emotional outcomes than children with other brain tumors. Chemotherapy and radiation appears to increase the risk for both physical and emotional concerns. Identifiable risk factors may help guide early monitoring and intervention.

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EMBRYONAL TUMORS WITH ABUNDANT NEUROPIL AND TRUE ROSETTES: CLINICOPATHOLOGICAL REPORT OF THREE CASES

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Background/Objectives: Embryonal tumors with abundant neuropil and true rosettes (ETANTR) are very rare childhood embryonal brain tumors with distinct histopathological features. Standard therapy for other embryonal brain tumors is ineffective and prognosis is dismal.
Design/Methods: Among 42 children with embryonal brain tumors treated at our institution, three patients with ETANTR were identified. We present clinical courses and analyze molecular characteristics including 19q13.42 amplification and LIN28A and DNMT3B expression in three cases.
Results: Case 1: Three-month-old girl presented with increasing head circumference. MRI showed a tumor in the fourth-ventricle, which was sub-totally resected. Complete resolution of the tumor on images was achieved by multi-agent chemotherapy and focal proton therapy. The tumor recurred 17 months after diagnosis. Despite sub-total resection followed by high-dose chemotherapy with hematopoietic stem cell rescue, the tumor progressed and the patient died 2 years after diagnosis. Case 2: One-year-old girl presented with vomiting and CT showed a tumor in right cerebellar hemisphere. The tumor was sub-totally resected. The tumor recurred during multi-agent chemotherapy. Craniospinal irradiation was started, however the tumor progressed rapidly and patients died 5 months after diagnosis. Case 3: One-year-old boy presented with left lower extremity weakness, gait disturbance and left conjugate deviation of eyes. Imaging studies showed a tumor invading midbrain and pons with spinal dissemination. Tumor biopsy revealed the diagnosis. The tumor was resistant to multi-agent chemotherapy and showed partial response to radiotherapy. However the tumor progressed in two months after radiotherapy.
Conclusion: The MRI findings of ETANTR were iso in T1, iso-high in T2, negative for gadolinium contrast and high in diffusion weighted image with ADC value of 0.5-0.7. Microscopic morphology was typical and immunohistochemical staining showed LIN28A expression in all case. DNMT3B was expressed in nuclei in case 1 and 2. Amplification of 19q13.42 was confirmed by fluorescent in situ hybridization in case 2 and 3.

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THE TREATMENT OF HIGH RISK CNS TUMOURS IN PEDIATRICS: A 10 YEAR EXPERIENCE IN A DEVELOPING COUNTRY

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Background/Objectives: Pediatric CNS tumours are a heterogeneous group of malignancies. The prognosis for children with medulloblastoma and high-grade gliomas including anaplastic astrocytoma and glioblastoma multiforme remains poor. The choice of treatment strategy in the realm of a developing country remains controversial.
Design/Methods: A retrospective chart review of children with CNS tumours treated and observed at Lviv institutions from 2005 to 2014 was performed. 74 cases of different histological subtypes were analysed. Diagnosis was confirmed by excision or biopsy of the primary lesion or metastases. Conventional CT and MRI scans were performed according to the site of involvement.
Results: The largest cohorts were patients with LGG (30%), medulloblastoma (23%), HGG (16 %), anaplastic ependymomas (12%) and germ cell tumours (8%). Patients with WHO grade III-IV tumours received multimodal treatment (surgery, distant beam radiotherapy and adjuvant chemotherapy with cyclophosphamide, methotrexate, carboplatin, VP-16, cisplatin, CCNU and vincristine) mainly using recommendations of HIT2000 protocol. All patients with HGG received temozolomide as adjuvant treatment with radiotherapy. At the end of 2014, with a median follow-up of 36 months, the 3-year OS in patients with WHO grade III-IV tumours is 50% including 47% for medulloblastoma. Patients with WHO grade I-II tumours (LGG) received adjuvant distant beam radiotherapy after surgery in the case of residual tumour. The 3-year OS in patients with WHO grade I-II tumours is 82%.
Conclusion: Gross total resection of the primary tumour, no delay in radiotherapy after subtotal resection and appropriate adjuvant chemotherapy were the main factors to influence the survival without considering WHO grade. Temozolomide was a good option as an adjuvant treatmentof HGG alongside radiotherapy. The tumour specimen cytogenetic analysis is the next step in proper implementing of novel agents in the treatment of unfavourable CNS tumours in low income countries.

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PRIMARY INTRACRANIAL GERM CELL TUMORS IN CHILDREN: 35-YEAR EXPERIENCE OF SINGLE CENTRE

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Background/Objectives: Germ cell tumors (GCT) are rare in intracranial region. We aimed to evaluate the characteristics, treatment and outcome in patients with intracranial GCT (IGCT).
Design/Methods: Patients with IGCT diagnosed in Hacettepe University Pediatric Oncology Department, between1980-2014 were evaluated retrospectively. Patients' age and gender, complaints and signs, location and histopathological subtype of tumor, treatment applied and survival time were recorded.
Results: There were 52 patients with a median age of 140(13–210) months. Male/female ratio was 2.25. The most frequent complaints were headache (50%), vomiting (44%), polydipsia/polyuria (34%). Most common signs were lateral gaze palsy (15), parinaud syndrome (13), impairment of vision (10). Endocrinological investigation revealed panhypopituitarism in 18 patients, diabetes insipidus in 4, precocious puberty in 2, diencephalic syndrome in one. Hidrocephalus was diagnosed in 24 patients and half of them required shunt. Tumor was located in sellar/suprasellar region in 40.4%, pineal region in 38.4% and bifocal in 11.5% of patients. Pineal location was more common in boys than girls (p=0.04). Intracranial and/or spinal seeding were observed in 9 patients. Serum α-fetoprotein and/or β-HCG levels were high in 18 patients. Histopathological diagnoses were germinoma in 60.8%, mixed GCT in 19.5%, yolk sac tumor in 4.34%, immature teratoma in 8.7%, malignant teratoma in 6.5% of patients. Gross total or subtotal excision was performed in 34 patients. Forty-three patients received platinum based protocols, 42 received radiotherapy. Mean follow-up time was 47 months. Overall and event free survival rates were 72.6% and 60.4%, respectively. OS and EFS rates for germinoma were better than others subtypes (82.0% vs 68.5%, p:0.03 and 50% vs 34%, p=0.004).
Conclusion: IGCT comprised 4.1% of 1,280 brain tumors and 8.8% of 587 GCT diagnosed in our department in the same period. Endocrine disturbances were an important problem. The survival rates in IGCT were similar to that of GCT in other regions.

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RADIATION SPARING APPROACH FOR PATIENTS WITH ATRT: A MULTI INSTITUTIONAL EXPERIENCE

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Background/Objectives: While radiation has been included in most of the recent multimodality strategies to treat ATRT, the concern of significant neurocognitive deficit in these very young children has led some pediatric neurooncologists to avoid the use of systematic adjuvant radiation. We present here a multi institutional Canadian experience of radiation sparing approach.
Design/Methods: Retrospective review of patients diagnosed between 2001 and 2013 in 3 Canadian centers (Calgary, Vancouver, Toronto) with ATRT and treated with high dose chemotherapy (HDC) with the intent to delay or avoid radiation.
Results: There were 16 females and 10 males. The median age at diagnosis was 21.2 months (4.2-110.2). Fourteen patients had a supratentorial tumor and 8 were metastatic at diagnosis (1M1, 5M2, 1M2/M3, 1 M2/MRT). Fifteen achieved gross total resection (3 underwent second look surgery). Ten patients received additional triple IT chemotherapy. Five of the 16 patients tested had evidence of INI1 germline mutation.Conditioning regimen for consolidation consisted in 1 cycle of (Carbo/VP16/Thiotepa) in 6 patients, 3 cycles of (Carbo/Thiotepa) in 19 and 4 cycles of (CPM/CDDP/VP16) in 1 patient. Ten patient received maintenance therapy with Tamoxifen and Cis retinoic acid following high dose chemotherapy.Only 6/26 (23%) patients received adjuvant radiation. Radiation consisted in focal radiation in 4 and craniospinal irradiation in 2 patients. Median age at time of radiation was 50.4 months (37.3-110.2). Eleven patients relapsed. Ten patients died of disease, one of treatment related toxicity. At a median time of 53.8 months, 15 patients (57.6%) are alive with 11 (73.3%) of them who did not received radiation.
Conclusion: Although there is a lack of clear prognostic factor to identify patients with ATRT who can be spare upfront radiation, our experience describe promising survival rate for patient with ATRT in absence of adjuvant radiation. Upcoming molecular classification in ATRT should help delineating indication of radiation.

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QUALITY OF LIFE IN CHILDREN WITH LOW-GRADE GLIOMA RECEIVING VINBLASTINE AS FIRST-LINE TREATMENT: A CANADIAN MULTICENTER STUDY

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Background/Objectives: The purpose of this prospective study is to describe the quality-of-life (QOL) of children with low-grade glioma (LGG) treated with weekly vinblastine as first-line chemotherapy. To our knowledge, this is the first study that evaluates the QOL during treatment in children with LGG.
Design/Methods: QOL assessments by the PedsQL™ Brain-Tumor-Module (version 1.0) were obtained at baseline, at 26 weeks, and at the end of the 70 weeks vinblastine therapy. Children under 2 years were not eligible. Ages consisted in: 7 patients (2-4 years); 5 (5-7y); 7 (8-12y); and 13 (13-18y). Parents were requested to fill in the questionnaires. Items explored included: cognitive problems, pain and hurt, movement and balance, procedural anxiety, nausea, and worry.
Results: Of the 49 patients eligible for the study, only 24.5% had all questionnaires completed. Sixty-seven percent had at least one completed. Mean change scores at week 26 and week 70 compared to baseline for all QOL subscales showed no significant change. At baseline, scales with lower mean scores (out of 100) were cognitive problems (66.11) and procedural anxiety (58.33). According to age, lower scores were seen in: 2-4 years in procedural anxiety (53.33); 5-7 years in cognitive problems (64.58), movement and balance (62.50), and procedural anxiety (54.16); 8-12 years, in procedural anxiety (55); and teenagers 13-18y in procedural anxiety (42.70) and worry (53.64).
Conclusion: QOL of children with LGG treated with vinblastine as first-line chemotherapy is not altered during treatment. If we take into account that the response rates of the different chemotherapy regimens for LGG in children are relatively similar, the assessment of quality of life should be an element of comparison when deciding chemotherapy for first line therapy. While remaining on vinblastine, LGG patients were able to maintain their QOL in all realms. Vinblastine may be a good choice for first line chemotherapy in this population.

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THE HYPOXIA-ACTIVATED PRODRUG EVOFOSFAMIDE (TH-302) IS EFFECTIVE IN PEDIATRIC HIGH GRADE GLIOMA CELL LINES AS A MONOTHERAPY AND IN COMBINATION WITH CHEMOTHERAPIES

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Background/Objectives: The prognosis of children with pediatric high grade glioma (pHGG) remains poor despite aggressive multidisciplinary therapeutic approaches. Current standard treatment combines surgery, radiation therapy and alkylating agents, such as temozolomide. Evofosfamide (Evo, previously known as TH-302) is a 2-nitroimidazole hypoxia-activated prodrug of the cytotoxic bromo-isophosphoramide mustard. Evo has been shown to exhibit preclinical activity against solid tumors. We present here the first data with Evo in pHGG cell lines.
Design/Methods: Evo was evaluated in 3 well-characterized pHGG cell lines (SF188, UW479, KNS42), cultivated under normoxic or hypoxic conditions (1% O_2). The cytotoxicity of Evo, used as a single drug or in association with SN38, doxorubicin and etoposide, was evaluated *in vitro* using a MTS assay. The synergism was analyzed by the Chou and Talalay method. Radio-sensitizing effects were investigated *in vitro* using clonogenic assays. The antitumor activity of Evo was assessed *in vivo* using animal models.
Results: Growth of all cell lines was inhibited by Evo single agent, and as expected, the cytotoxicity of Evo was higher under hypoxic conditions (IC_{50} were 2-8 fold higher in normoxic *vs* hypoxic conditions). As previously reported, we found a strong synergism between Evo and doxorubicin, and we also demonstrated a significant synergistic effect with SN38 and etoposide, 2 drugs widely used in pediatric oncology (CI≤0.5 in every case). Radio-sensitizing effects and *in vivo* evaluations are currently ongoing.
Conclusion: Hypoxia is a well-known phenomenon leading to glioma cell resistance to cytotoxic drugs. We report here the first preclinical data about a novel hypoxia-activated prodrug Evo in pediatric high grade glioma. Interestingly, Evo appears effective in hypoxic glioma cells and the synergistic effects observed with SN38, doxorubicin and etoposide are of interest for pediatric oncology.

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CONCURRENT ARHI UPREGULATION AND JAK/STAT3 INACTIVATION IN RESVERATROL-TREATED MEDULLOBLASTOMA CELLS

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Background/Objectives: Medulloblastoma (MB) is the commonest pediatric brain malignancyand has extremely poor prognosis because of the difficulty to remove the tumor radically and the lack of effective adjuvant therapeutic approaches. Resveratrol/Res, a natural polyphenol compound, exerts anti-medulloblastoma efficacy and STAT3 signaling is its major molecular target. However, the mechanism underlying resveratrol-suppressed STAT3 activation remains obscure. ARHI has been known as a tumor suppressor gene because of its inhibitory effect on STAT3 activation. So far, the status of ARHI expression in medulloblastomas has not yet been known. The current study is aimed to investigate ARHI expression patterns and its relevance with resveratrol-caused STAT3 inactivation in medulloblastoma cells.
Design/Methods: UW228-2 and UW228-3 human medulloblastoma cell lines were cultured in DMEM culture medium containing 10% fetal bovine serum and DAOY in 10% fetal bovine serum containing RPMI 1640 medium. The three cell lines were treated by 100mM resveratrol for 48 hours and their sensitivities to the treatment were determined by multiple experimental methods. Meanwhile, the cells without and with resveratrol treatment were collected for ARHI- and STAT3-oriented immunocytochemical/ICC, RT-PCR and Western-blotting analyses.
Results: The three medulloblastoma cell lines so far checked are sensitive to resveratrol in terms of suppressed growth, neuronal-like differentiation and distinct apoptosis. The level of ARHI expression is very low and STAT3 signaling is activated in those cell lines; after resveratrol treatment, ARHI is up-regulated in them, accompanied with the decreased frequencies of p-STAT3 nuclear translocation.
Conclusion: The situation of ARHI downregulation and STAT3 activation in three medulloblastoma cell lines can be reversed by resveratrol, suggesting an opposite correlation of ARHI expression and STAT3 activity in medulloblastomas and the potential involvement of ARHI in STAT3 inactivation of resveratrol-treated medulloblastoma cells. *Acknowledgments*: Supported by the grants from National Natural Science Foundation of China (No. 81450016, 81272786, 81071971, 81072063 and 30971038) and PCSIRT Program of China.

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CD57 DEFINES A NOVEL POPULATION OF GLIOMA STEM CELLS THAT ARE POTENTIAL DRIVERS OF GBM INVASTION

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Background/Objectives: Diffuse invasion into normal brain is one of the hallmark features that make GBM difficult to treat. Due to the lack of biologically accurate invasive GBM cells from patients, most of the existing studies on GBM invasion were conducted in surgical samples that were primarily tumor core tissues. Although cancer stem cells are shown to be critical in tumor initiation and therapy-resistance, their role in GBM invasion has not been well understood.
Design/Methods: To identify the cancer stem cell subpopulations that drive GBM invasion, we utilized a panel of 7 (6 pediatric and 1 adult) patient tumor-derived orthotopic xenograft (PDOX) mouse models to isolate matched pairs of invasive GBM cells (from the "normal" mouse brains) and tumor core GBM cells and directly compared their stem cell features.
Results: The invasive cells exhibited stronger neurosphere forming efficiency *in vitro* and displayed higher tumorigenic capacity *in vivo* (particularly at 100 cells/mouse). A systemic screening of putative cancer stem cell markers (CD133, CD15, CD24/CD44, CD57 and CD117) showed that GBM cells in the invasive front were enriched with CD57+ cells (>2 folds than the tumor core), and most of them were CD57+ CD133-. Direct implantation of FACS purified CD57+/CD133- cells (100 – 10,000 per mouse) into the brains of NOD/SCID mice confirmed their tumor forming capacity in vivo. We also showed that CD57+ cells expressed high levels of self-renewal genes and tend to stay in G0/G1 phases. Additionally, we found that CD133+ cells were frequently dual-positive with CD57 (CD33+CD57+) both in the xenograft tumors and in patient GBMs.
Conclusion: We identified CD57 as a novel GBM stem cell marker and showed that CD57+ GBM cells are particular enriched in the invasive front of GBMs. Our findings suggest that new anti-invasion therapies should be developed to target CD57+ cells in addition to CD133+ cells.

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THE IMAGING AND CLINICAL FEATURES OF THE INTRACRANIAL GERMINOMA

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Background/Objectives: To understand the imaging and clinical features of the intracranial germinoma in order to improve the diagnosis.
Design/Methods: Fourty-one cases of intracranial germinoma were reviewed. All of them but one were convinced by pathology and one case had typical image findings and clinical course.They were performed by both CT and MRI before operation.
Results: The age of patients ranged from 8 to 20 years old. In our study, the most common location was suprasellar region(58%),secondly pineal region(15%),basal ganglia region(15%) and involving two regions (10%). The CT appearance of a germinoma was that of an iso- to hyperdense mass and uniform enhancement after IV infusion of contrast.On MRI, the mass showed isointensity on T1W and iso-to mild hyperintensity on T2W, iso-to hyperintensity on DWI. In suprasellar region, patients showed 5:1 female predominance presenting mainly diabetes insipidus or visual disturbance .None of the tumours calcified in CT scan. In pineal region, patients showed 7:1 male predominance presenting hydrocephalus. In CT, calcification was identified in all cases. In basal ganglia region, patients showed 6:1 male predominance presenting hemiparesis and mental status changes.One case no mass was seen. MRI manifested pachy abnormal intensity with ipilateral frontal and temperal lobe atrophy.After chemotherapy and radiotherapy, the lesion disappeared and patient recovered.
Conclusion: Intracranial germinoma usually occur in young teenagers.Tumor in different location appeared different image findings and different clinical presentation.

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CORRELATIVE ANALYSES OF SHH SIGNALING WITH RESVERATROL-INDUCED DIFFERENTIATION AND APOPTOSIS OF HUMAN MEDULLOBLASTOMA CELLS

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Background/Objectives: Medulloblastoma (MB) arises from neuronal progenitors with defects in cerebellum development-related signalings. Sonic hedgehog (Shh) signaling

plays important roles in normal cerebellum development, indicating that altered Shh signaling may leads to dedifferentiation or undifferentiation states of brain cell components such as medulloblastoma formation. Resveratrol/Res suppresses growth and promotes neuronal-like differentiation of medulloblastoma cells via certain unknown manner(s). The aims of current study are 1) the status of Shh singnaling components (Shh, Gli1, N-Myc and cyclinD1) in medulloblastoma cells and 2) the potential influence of resveratrol in Shh signaling when promoting neuronal-oriented differentiation.
Design/Methods: Two human medulloblastoma cell lines, UW228-2 and UW228-3, were treated by 100μM resveratrol and the statused of Shh signaling in the cells without and with the treatment were analyzed by multiple experimental approaches. Selective inhibitors and siRNA interference for Shh signaling were employed to treat UW228-2 and UW228-3 cells to elucidate the significance of Shh signaling for medulloblastoma cell maintenance/survival and resveratrol's anti-medulloblastoma effects.
Results: Shh, Gli1, N-Myc and cyclinD1 were expressed in normally cultured UW228-2 and -3 cells, which were respectively down-regulated in both cell lines after resveratrol treatment along with neuronal-like differentiation and apoptosis of MB cells. Shh selective inhibitor (GANT61; a Gli antagonist) effectively suppressed the growth but without induction of apoptosis of UW228-2 and -3 cells in a time and dose-related fashion. Downregulation of Gli1 expression by siRNA interference inhibited MB cell growth.
Conclusion: The above results demonstrate that 1) activated Shh signaling is neccessary for the growth of medulloblastoma cells; 2) Shh activation occurred in downstream of Smo in UW228-2 and -3 cell lines and 3) the inhibition of Shh signaling is one of the molecular events caused by resveratrol in medulloblastoma cells.

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TREATMENT OF CHILDREN'S CENTRAL NERVOUS SYSTEM (CNS) TUMOURS: A 'MAP' OF THE RESEARCH EVIDENCE AVAILABLE

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Background/Objectives: To determine the evidence available for undertaking systematic reviews for the Research for Patient Benefit (RfPB) programme on the effects of treatments for children's central nervous system (CNS) tumours, a 'map' of the evidence base was produced.
Design/Methods: Seven electronic databases were searched for interventional studies on surgical procedures, radiotherapy (RT), chemotherapy (CT), hormone therapy (HT), immunotherapy, biological therapies and imaging from 1985 to November 2014 across the spectrum of children's CNS tumours. No study design filters were applied. Psycho-social interventions were excluded. All relevant studies were then categorised by tumour histology type, type of intervention and study design on the basis of the available abstract.
Results: A total of 8,448 unique references was identified; with 1,868 included in the 'map'. Eleven systematic reviews, 29 randomised controlled trials (RCTs) including more than 4,992 patients, and 190 single arm phase II trials were identified. Most of the single arm phase II trials were small with less than 40 patients included. The majority of the evidence base was limited to case series studies (1,077) or case reports with less than 5 patients (306). Chemotherapy regimens, used alone or in combination with RT, were the most frequently assessed interventions. Radiotherapy (RT) used alone had also been assessed in both RCTs and single arm phase II trials. Few studies of surgery alone, HT, immunotherapy or biological agents were identified. The highest proportion of studies had been conducted either in patients with medulloblastoma (11 RCTs, 28 single arm phase II trials and 188 case series) or in patients with mixed tumour histologies (29 RCTs, 68 single arm phase II trials and 273 case series).
Conclusion: 'Mapping' the evidence base for children's CNS tumours has highlighted the paucity of well conducted RCTs in this arena, with most patients being entered into uncontrolled studies that provide lower quality evidence.

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LONG TERM FOLLOW-UP OF PATIENTS WITH METASTATIC (M+) AND HIGH-RISK MEDULLOBLASTOMA WITH TAILORED-DOSES HYPERFRACTIONATED ACCELERATED RADIOTHERAPY (HART) CSI PLUS/MINUS HIGH-DOSE THIOTEPA

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Background/Objectives: Since 1998 we launched a mono-institutional, thereafter national strategy, for M+medulloblastoma. We report the results of 54 M+ patients and, from 6/2008, of 6 with large cell/anaplastic (LCA) no M+ and underline outcome/toxicity features.
Design/Methods: An intensive post-surgical treatment applied HDMTX/VCR, HDVP16, HDcyclo, HDcarboplatin followed by HART at total neuraxis dose of 39 Gy (1.3Gy/fraction,2 fractions/day) with posterior fossa boost 60Gy (1.5Gy/fraction,2 fractions/day). If disease persisted before HART, patients received thereafter 2 courses of myeloablative thiotepa, done in all patients with LCA histology. Children aged under 10 years and in complete remission before HART, received reduced 31.2Gy CSI. Results of the first 33 patients were already published.
Results: Ten/54 patients had Chang M1 disease, 9 M2, 34 M3 and one M4; ten also LCA histology; 42(78%) had at least SD pre-HART; 83% with evaluable disease had CR+PR after HART; 11 patients received 31.2Gy CSI; 29 had high-dose thiotepa. No patient progressed after HART. Both responses to CT and RT were prognostic factors; CSI doses and use of HDthiotepa, tailored to response, were not. At 100months median follow-up for the 54 metastatic patients, EFS and OS were 71%/69% and 73%/65% at 5/10yrs, respectively. All the 6 with LCA were alive at median 55 months. Five/60 patients– all receiving HDthiotepa –median 6 months after treatment developed a neuro-functional impairment characterized by worsening/appearance of cerebellar signs, hear/sight loss, seizures, with some deterioration and plateau/improvement after intensive rehabilitation. One/5 suffered from tumor progression and died. No correlation with radiotherapy technique and dosimetry was documented after plan review, moreover, 3/5 had avoided, for clinical reasons, posterior fossa radiation boosts.
Conclusion: Larger patient numbers and longer follow-up confirmed good results with no event after 5-year follow-up. Functional toxicity after HDthiotepa post-HART represents a rare, not fully understood occurrence, probably also correlated to individual susceptibility.

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DISTRIBUTION AND PROGNOSTIC IMPACT OF MOLECULAR SUBGROUPS IN AN HOMOGENEOUSLY TREATED SERIES OF METASTATIC MEDULLOBLASTOMA

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Background/Objectives: Medulloblastoma (MDB) is the most common malignant brain tumor in children. The prognostic system based on clinical parameters and histopathological variants is commonly used in clinical practice. Four different molecular subgroups are recognized, which differ in gene expression, genomic aberrations, histology and survival: WNT and SHH groups, having specific mutations in the homonymous pathway, and groups C and D having several genetic alterations and associated to a worse outcome. Such molecular classification could provide a more consistent approach to the therapeutic stratification of patients. The purpose of this study was to evaluate the distribution and prognostic impact of the four molecular subgroups in a series of 39 MDB metastatic at the onset and homogenously treated in a single institution.
Design/Methods: We investigated the protein expression of different subgroup biomarkers by IHC, RT-PCR, cDNA sequencing and FISH; results were correlated with patient outcomes by Kaplan-Meier statistic analysis.
Results: On the basis of molecular sub-grouping we could identify 5 WNT cases with nuclear translocation of β-catenin and DKK1 positivity, 7 SHH cases with triple positivity of GAB1, YAP1 and Filamin A, 9 group C cases with FSTL5 over-expression and 5 group D cases with negativity for Filamin A, positivity for KCNA1 and negativity for NPR3; 10 cases analyzed were unclassifiable (NC) having heterogeneous biomarkers, for 3 cases the material was not enough to be analyzed. MYC amplification is more frequent (32.5%) compared to the amplification of MYCN (2.7%) and compared to the literature. WNT and NC groups showed superior (but not statistically significant) OS and PFS compared to SHH, C and D.
Conclusion: While we have previously shown that the histological variants maintain prognostic value also in metastatic MDB, especially referring to LC/A histology, sub-grouping into molecular classes via IHC is not efficient to allow a prognostic stratification in our cohort of metastatic MDB.

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PEDIATRIC BRAINSTEM GLIOMAS: RESPONSE AND SURVIVAL FOLLOWING RADIOTHERAPY

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Background/Objectives: Brainstem gliomas accounts for approximately 20% of all central nervous system tumors in children and carries very poor prognosis. A retrospective review was made to analyze the clinical presentation, diagnosis, treatment outcome and survival in pediatric patients with brainstem gliomas treated at Shaukat Khanum Memorial Cancer Hospital and Research Centre Lahore, Pakistan.
Design/Methods: With a median age of 8 years (range 4-13 years), we retrospectively analyzed 76 brainstem gliomas patients (56% males, 44% females), between January 2005 to December 2011. All patients were diagnosed by CT scan or MRI Brain. Median duration from first symptom to appear and diagnosis was 2.3 months. 19% of the patients had focal disease and 81% had diffuse lesions. 32% of the patients presented with long tract involvement, 8% with cranial nerves involvement and 54% with both. 93% of the patients were treated with radiotherapy and 7% of the patients were managed with supportive care only. Median radiotherapy dose was 51 Gy (range 30-60 Gy). Radiotherapy schedules; conventional 1.8 Gy/fraction over a period of 6 weeks in 46% of the patients and hypo fractionated radiotherapy 3 Gy/fraction over a period of 3 weeks in 54% of the patients.
Results: Radiological response was seen in 69% of the patients (partial response 32% and stable disease in 37% of the patients). At the time of review, 20% patients died of tumor progression, 9% were alive with tumor progression and 71% were alive with continuous partial response and clinical improvement. 3 years overall survival was 37% and overall median survival was 7.5 months (range 1-45 months).
Conclusion: Radiotherapy appears to be an effective treatment modality for brainstem gliomas in pediatric patients but with poor outcomes. New treatment strategies including safe surgical resection, alternate radiotherapy schedules and chemotherapy regimens are warranted to improve the outcome in this group of patients.

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GAMMA KNIFE RADIOSURGERY AS SALVAGE THERAPY FOR RECURRENT OR RESIDUAL PEDIATRIC AND YOUNG ADULT BRAIN TUMORS

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Background/Objectives: Gamma Knife radiosurgery (GK) provides high dose radiation to focal brain lesions in a single treatment. We evaluated our institutional experience for GK in pediatric and young adult patients with recurrent or residual brain tumors.
Design/Methods: Between 1998 and 2009, 14 patients with recurrent (n=11) or residual (n=3) brain tumors received 16 GK treatments. Primary brain tumors included high-grade neuroepithelial (GBM=3, anaplastic astrocytoma=1), low-grade neuroepithelial (pilocytic astrocytoma=3, oligodendroglioma=1), embryonal (medulloblastoma=4, embryonal carcinoma=1), and germ cell (germinoma=1) tumors. Most patients had prior fractionated radiotherapy (RT) (n=11) with a median dose of 55.8 Gy in 1.8 Gy per fraction. Toxicity was scored using CTCAE version 4. Local control (LC), distant brain control, and overall survival (OS) were estimated using the Kaplan Meier method.
Results: Median age at time of GK treatment was 11.5 years (range, 2-24) and the median follow-up was 1.9 years (range, 0.4-10 years). Median GK dose was 16 Gy (range, 10-20 Gy) to the 50% isodose line (range, 40-50%). Treated locations include cerebellum (n=2), ventricular system (n=6), cerebrum (n=5), and brainstem (n=3). The median volume treated was 0.6 cm^3 (range, 0.14-12.7 cm^3). One- and 5-year LC was 74% and 56% for all patients, respectively. LC was similar between histologic subtypes. Patients with embryonal tumors had more distant brain failure (80%, n=4) than other histologies (22%, n=2) (p=0.03). The median OS after GK was 6.3 years correlating to a 1- and 5-year OS of 84% and 50%, respectively. Patients with high-grade astrocytoma had worse OS with a median survival of 1.4 years. Treatments were well tolerated and with no radiation necrosis. No significant late toxicity was associated with GK use.
Conclusion: Our results suggest GK is safe and effective therapy for recurrent or residual brain tumors in carefully selected pediatric patients. Further investigation in the efficacy of GK for pediatric patients is warranted.

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PEDIATRIC GLIOBLASTOMA MULTIFORME

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Background/Objectives: Glioblastoma multiforme (GBM) is the most common astrocytoma in adults and has a poor prognosis, with a median survival of about 12 months. But, it is rare in children. We report our experience on the childhood population (20 years or younger) with GBM.
Design/Methods: Twenty-three patients with GBM who were treated at our hospital during 1990–2008 were evaluated.
Results: The mean age was 15.2 years, and the majority of them (14/23) were male. All had received radiotherapy and some had also received chemotherapy. The mean survival was 16.0 months. Two cases survived more than 5 years. Age, extent of surgical resection, radiation dose and performance status were significantly related to survival.
Conclusion: GBM in pediatric patients were not very common in our center, and prognosis was unfavorable.

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THALAMIC GLIAL TUMORS IN CHILDREN AND ADOLESCENTS: A SINGLE INSTITUTION EXPERIENCE

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Background/Objectives: Thalamic glial tumors account for about 5% of central nervous system tumors. Management is often very challenging since these tumors carry a significant risk for neurologic morbidity related to their location and treatment. We reviewed our experience with thalamic glial neoplasms diagnosed and treated at our institution from 1993 to 2014.
Design/Methods: Retrospective chart analysis.
Results: Our study included twenty-three patients (13 male; 10 female). Median age at diagnosis was 11.8 years (range; 1.9-17.8 years). Hydrocephalus was noted in 43.5% of patients at presentation. Eighteen (78.3%) patients had unilateral thalamic tumors. Five patients had bithalamic involvement. Fifteen (65.2%) patients had low-grade histology [pilocytic astrocytoma (n=11), fibrillary astrocytoma (n=2), and other (n=2)]. Seven patients had high-grade histology [anaplastic astrocytoma (n=2), glioblastoma multiforme (n=4), high-grade oligoastrocytoma (n=1)]. Extent of surgical resection included gross total resection (7 low-grade; 2 high-grade), subtotal resection (2 low-grade; 1 high-grade), and biopsy (6 low-grade; 3 high-grade). Ten (66.6 %) patients with low-grade tumors had new and/or worsening post-operative neurologic deficits. All patients with high-grade histology received chemotherapy and/or radiation therapy while 3 patients with low-grade tumors received adjuvant radiation (n=2) or chemotherapy (n=1). No patient with a high-grade tumor was alive beyond 41 months from diagnosis. Median follow-up for patients with low-grade tumors was 3.7 years (range; 0.11-17.9 years). Three year progression-free survival(PFS) was 76.2%. There was 1 patient death unrelated to tumor. Low-grade histology was significantly associated with better PFS and overall survival (OS) outcomes ($p=0.004$ and $p<0.0001$, respectively). Hydrocephalus at presentation, unilateral versus bithalamic involvement, and extent of resection were not associated with PFS for low-grade tumors ($p=0.4$, $p=0.4$, and $p=0.9$, respectively).
Conclusion: Majority of thalamic tumors are of low-grade histology. Though recurrences are observed, low-grade tumors are associated with good OS and risk of long-term morbidity should be an important consideration in the management of these tumors.

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OUTCOME OF PEDIATRIC MEDULLOBLASTOMA IN LIMITED-RESOURCE SETTING – EXPERIENCE FROM A TERTIARY CANCER CENTRE IN INDIA

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Background/Objectives: Advances in surgery and integration of multimodality therapy has translated to improved survival in children with medulloblastoma(MB) over the recent years. But the excellent results are not reproduced in resource-limited countries, due to multiple factors. We sought to find out the characteristics and outcome of pediatric medulloblastoma treated in our department.
Design/Methods: Children 0-14years of age diagnosed with medulloblastoma and treated in Pediatric Oncology Division, RCC, Trivandrum during a 5year period(January2008 to December2012) were identified. Patients >3 years received postoperative craniospinal radiation(36-55Gy for average-risk and 55-60Gy for high-risk) with concurrent Vincristine , followed by 6-8 cycles of chemotherapy. Patients<3years received COG Baby Brain Protocol chemotherapy and delayed radiation.
Results: There were 89 medulloblastoma patients (22%of all brain tumours).19%were 0-3years, 27%were 10-14years and peak age group was 4-9years(53%).Male predominance was observed, male:female ratio being 1.8:1. 61patients(68.5%) were average-risk and 28patients(31.5%) high-risk. Initial metastatic disease was found in only10%. 74patients(83%) had adequate surgery. 19patients did not take any adjuvant

treatment. Combined chemotherapy and radiotherapy was used for 63 patients(70%) and chemotherapy only for 7patients.58 patients completed treatment without much toxicity. There were 6 therapy-related deaths.11patients (12.3%)developed recurrence, of whom 6 had disease progression while on treatment and 5 recurred after treatment completion. No salvage therapy was given for recurrences. At median follow-up of 23 months, 56 patients(63%) are alive,17patients(19%) expired, and 16 are lost-to-follow-up. 5-year disease-free survival(DFS) for the treated cohort was 84.5±5%. DFS was significantly low for children<3years(39%) and for high-risk patients(41%) .There was no significant difference in outcome for patients with initial metastatic status. Age 4-9 years, treatment received (surgery+radiation+chemotherapy) and average-risk disease are favourable prognostic factors for survival.
Conclusion: Survival comparable to published international data is achieved in average-risk pediatric MB patients in our institution with current multimodality therapy.Treatment is refused by a significant minority.Outcome is poor in high-risk patients, especially younger children.

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MEDULLOBLASTOMA IN CHILDREN: THE EXPERIENCE IN THE CENTER OF TUNISIA

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Background/Objectives: Medulloblastoma tumors (MB) are the first brain malignat tumor in the chidhood. MB are classified into high risk and standard risk categories based on age at diagnosis, degree of surgical resection, and disease spread.
Design/Methods: It is a retrospective study of eighteen cases of children with Medulloblastoma histologically proved treated from 1994 to 2013 in the Oncology Department of Farhat Hached University Hospital, Sousse, Tunisia.
Results: The median age was 9.25 years (18 months - 16 years) with 2 patients aged less than 3 year. The sex ratio was 1.25. Cranial hypertension and cerebellar syndrome were the most frequent symptoms respectively in 94.4 % and 83.3% of cases. MB was located in the vermis, 4th ventricle and cerebral hemisphere in respectively 50%, 33.3% and 16.7% of cases. At diagnosis, 4 patients had cerebrospinal metastases. Complete or near complete resection (<1,5cm) was done in 66.7% of cases. Fifty per cent of patients were classified in average risk group and 50 % in standard risk group. Eleven patients received cranial-spinal axis irradiation (25 grey to 30 grey) with a boost to the posterior fossa (54 grey). Fourteen patients received chemotherapy: regimen of "8 drugs a day" for 4 cases and a regimen of etoposide-carboplatin for 9. The overall survival was 60% at 5 years (41.9 months): 40% (27.6 months) for the high risk group and 70% (59.7 months) for the standard risk group.
Conclusion: The results of our study indicate the need of the improvement of treatment of MB especially with the identification of novel molecular prognostic factors.

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GROWTH AND PUBERTAL DEVELOPMENT IN PEDIATRIC BRAIN TUMOR SURVIVORS

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Background/Objectives: To evaluate growth and pubertal development in childhood brain tumor survivors.
Design/Methods: A population-based cross-sectional study; fifty-two (69%) out of 75 invited brain tumor survivors diagnosed below 17 years of age between 1983-1997 and treated in Tampere University Hospital, Finland, were examined at a mean age of 14.2 (range 3.8-28.7) years after a mean follow-up time of 7.5 (1.5-15.1) years.
Results: Thirteen patients (25%) received hormone substitution, nine (17%) more than one; thyroxine (n=10), glucorticoid (n=4), growth hormone (GH) (n=4), sex hormone (n=7) and desmopressin (n=3). Twelve patients (23%) had GH deficiency (GHD). Sixteen were prepubertal, 30 had normal puberty and five had puberty induced with sex hormones and one precocious puberty. The adult height of the 16 patients who were 18 years or older ranged from 140.0 cm to 181.2 cm. In the whole group the height SDS ranged from -4.6 SD to +2.8 SD (mean +0.1 SD). The mean difference between actual height and target height was -0.1 SD (-4.3 SD-+2.8 SD). Shorter stature was statistically significantly associated with tumor malignancy (p=0.005), radiotherapy (p=0.004), chemotherapy (p=0.024), GHD (p<0.001), in pubertal/post pubertal patients sex hormone deficiency (p=0.044) and abnormal sex hormone levels (p=0.008) during the study. The patients who had received craniospinal irradiation or both radiotherapy and chemotherapy were shorter than other patients. Young age at diagnosis, tumor site at sellar region, thyroxin and glucorticoid treatment were not associated with shorter stature. The patients who had residive/residual tumor at evaluation were taller than the others and taller than their target height. Cranial irradiation increased the risk of GHD ($p < 0.001$) and sex hormone deficiency (p=0.003).
Conclusion: Survivors who have had malignant tumor, have received radiotherapy and/or chemotherapy, have GHD and/or sex hormone deficiency are at greater risk for growth problems.

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METRONOMIC CHEMOTHERAPY FOR PEDIATRIC PATIENTS WITH UNTREATABLE MALIGNANCIES

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Background/Objectives: Few therapies prolong the survival and increase the quality of life for pediatric patients with malignancies unresponsive to conventional treatments. Metronomic administration of chemotherapy has lately emerged as an effective and well-tolerated method to fulfill these ambitions.
Design/Methods: Fourteen pediatric patients with various untreatable malignancies received therapy according to the anti-angiogenic Extended Angiocomb protocol consisting of metronomic thalidomide, etoposide and celecoxib. Endpoints of the study were overall survival, quality of life, and radiological response. Adverse effects were monitored. Results were compared to a control group consisting of eight patients in palliative care, with or without other maintenance therapies.
Results: Median survival after start of the study was 6.4 months for study patients and 3.8 months for controls ($p = 0.002$). Four study patients were long-term survivors with overall survival over 24 months. Study patients were able to attend school or daycare and walk without support for a significantly longer time compared to controls (school or daycare attendance: median 4.9 months versus 0.76 months, $p = 0.009$; walking without support: median 4.9 months versus 0.8 months, p<0.001). Radiologically, one patient had a partial response and one patient stable disease during study therapy.
Conclusion: The Extended Angiocomb protocol prolonged survival and increased the quality of life for pediatric patients with untreatable malignancies. Our results suggest that anti-angiogenic therapy should be more thoroughly studied as a treatment option during palliative care for cancer.

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DELAYED DIAGNOSIS OF CHILDHOOD LOW-GRADE GLIOMA: CAUSES, CONSEQUENCES AND POTENTIAL SOLUTIONS

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Background/Objectives: Diagnosis of childhood brain tumors is delayed more than diagnosis of other pediatric cancers. However, the contribution of the most common pediatric brain tumors, low-grade gliomas (LGG), to this delay has never been investigated.
Design/Methods: We retrospectively reviewed cases of childhood LGG diagnosed from January 1995 through December 2005 at our institution. The pre-diagnosis symptom interval (PSI) was conservatively calculated, and its association with race, sex, age, tumor site, tumor grade, and outcome measures (survival, disease progression, shunt use, seizures, extent of resection) was analyzed. Cases of neurofibromatosis type 1 were reported separately.
Results: The 258 children had a median follow-up of 11.1 years, and 226 (88%) remained alive. Greater pre-diagnosis symptom interval (PSI) was significantly associated with grade I (vs. grade II) tumors ($p = 0.03$) and age >10 years at diagnosis ($p = 0.03$). Half of the 16 spinal tumors had a PSI > 6 months. PSI was significantly associated with progression ($p = 0.02$) in grade I tumors ($n = 195$) and in grade I tumors outside the posterior fossa ($n = 134$, $p = 0.03$). Among children with grade I tumors, median PSI was longer in those who had seizures (10.3 months) than in those who did not (2.5 months) ($p = 0.09$).
Conclusion: Delayed diagnosis of childhood LGG allows tumor progression. To reduce time to diagnosis, medical curricula should emphasize inclusion of LGG in the differential diagnosis of CNS neoplasm.

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PEDIATRIC INTRACRANIAL CLEAR CELL MENINGIOMA ASSOCIATED WITH A GERMILINE MUTATION OF SMARCE1

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Background/Objectives: Intracranial clear cell meningioma (CCM) represents a rare and potentially more aggressive subgroup of meningioma that is observed more frequently in children and adolescents. Despite its characterization as a histological entity, there is little evidence identifying tumorigenic etiologies. Recently, a novel mutation in *SMARCE1*, encoding a subunit of the SWI/SNF chromatin remodeling complex, was identified in a cohort of spinal CCMs. To date, no intracranial CCM has been subjected to analysis.
Design/Methods: We report the case of an isolated intracranial CCM in a 14 year old girl. Gross total resection was achieved following a two-stage approach with no evidence of tumor recurrence eight months following presentation. Exon sequencing identified a germline mutation in *SMARCE1*, which was also present in tumor DNA.
Results: Extensive literature review confirmed our study is the first to seek and report a genetic anomaly for childhood intracranial CCMs outside of the *NF2* gene locus, and the first to make an association between a germline *SMARCE1* mutation and childhood intracranial CCMs. Together with the previous description of *SMARCE1* mutations in spinal CCMs, our report suggests that *SMARCE1* aberrations may be implicated in establishing a clear cell histology irrespective of meningioma location.
Conclusion: We would advocate that, where feasible, genetic sequencing is performed on future new cases of childhood neuraxial CCMs and includes interrogation of the *SMARCE1* gene.

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THE IMPACT OF AGE AND RACE ON LONGEVITY IN PEDIATRIC ASTROCYTIC TUMORS: A POPULATION-BASED STUDY

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Background/Objectives: Despite improvements in pediatric brain tumor outcomes, the survivors of childhood brain tumors are burdened by multiple comorbidities. We report on the relative survival ratios and excess mortality rate in children with astrocytic tumors over the past four decades.
Design/Methods: Survival analysis was conducted using flexible parametric model to estimate relative survival and excess mortality rate for non-white and white children (0-19 years old, n=5,956) using the Surveillance, Epidemiology & End Results (SEER) database. We incorporated age group and year of diagnosis into the model to estimate these indices for the period of 1973-2010. We used mortality-to-incidence ratio (MIR) to measure mortality ratio over the study period. The MIR is defined as the crude number of deaths divided by the crude number of cancer incident cases.
Results: The mean age of diagnosis was 9.2±5.3 years (47% female). Caucasian participants were the major group (82.2%). The MIR was highly significant for race (27.4% for non-white children compared to 22.7% for white children (p-value 0.001). Progressive decline in relative survival ratios was noted over time, with non-white children having lower survival rates than white children, and these trends persisted over the duration of the study. Fifty percent of non-white survivors were deceased 30 years post diagnosis, compared to 35 years in white survivors.
Conclusion: Survivors of childhood astrocytic brain tumors have progressively lower survival rates as they get older, and this is higher in non-white when compared to white children. Future research efforts need to focus on understanding the factors mediating the effect of the tumor or its treatment on survival in these patients, and the ethnic variations that drive these survival trends.

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THE EFFECTIVENESS OF LIFESTYLE INTERVENTION, PHARMACOTHERAPY OR BARIATRIC SURGERY ON LOWERING BMI Z-SCORE IN OBESE SURVIVORS OF CHILDHOOD BRAIN TUMORS: A SYSTEMATIC REVIEW

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Background/Objectives: Over the past three decades, high survival rate of childhood brain tumors has been accompanied by long-term cardiometabolic co-morbidities, including obesity, cardiovascular diseases, type 2 diabetes, hypertension and metabolic syndrome. These co-morbidities can have a significant negative impact on the lifespan and quality of life of childhood brain tumor survivors. We conducted this systematic review to determine the effectiveness of lifestyle intervention, pharmacotherapy and bariatric surgery on lowering BMI z-score in survivors of childhood brain tumors.
Design/Methods: This is a systematic review.
The inclusion criteria including obese survivors of childhood brain tumor and comparing randomized controlled trials of lifestyle intervention, bariatric surgery, pharmacotherapy to obese non-cancer controls. The primary outcome measure is BMI z-score.We conducted a three-step search strategy: 1.Initial search conducted in Medline, followed by an analysis of the index terms used to describe articles 2.A second search using all identified keywords and index terms were then conducted in Medline, Embase, PsychINFO, CINAHL, Cochrane Review, DARE, PubMed, and Sport Discus 3.The reference lists of all identified articles were screened.
Results: Using the above search strategy, 474 records were identified. A total of 234 records were found irrelevant and therefore excluded, as they did not discuss treating obesity in the survivors of childhood brain tumors. Instead, a majority of them explored obesity as a late effect after treatment for the brain tumors. Only one randomized controlled trial was identified.
Conclusion: We conclude that there is limited evidence for treatment of obesity in this population. Based on this search strategy, we are widening the inclusion criteria to include non-RCT study designs such as case control, prospective cohort and retrospective cohort. This will allow us to systematically evaluate the interventions studied, so that we can design new intervention strategies to treat and prevent obesity and cardiometabolic disorders in the survivors of childhood brain tumors.

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A REVIEW OF OTOTOXICITY AND NEPHROTOXICITY IN CHILDREN WITH PRIMITIVE NEUROECTODERMAL TUMOURS (PNETS) TREATED WITH PLATINUM BASED CHEMOTHERAPY AND CRANIAL RADIOTHERAPY: WEST OF SCOTLAND EXPERIENCE

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Background/Objectives: Irreversible oto-toxicity and nephrotoxicity are recognised in children with PNETs treated with high dose platinum chemotherapy and cranial radiotherapy. We aimed to determine the number of such patients that developed hearing impairment, identify whether the chemotherapy was changed when deterioration in hearing was detected, to evaluate if there was a difference in audiology outcomes in patients considered standard risk versus high risk and to determine the number of children who had a decline in glomerular filtration rate (GFR).
Design/Methods: It is a retrospective review of patients diagnosed with PNETs since 2000, treated with platinum chemotherapy and cranial radiotherapy. Using electronic records 32 patients were identified. Five patients were excluded (<3 years at diagnosis, <1 year post end of treatment or insufficient information available). A proforma was used to collate information regarding diagnosis, age of diagnosis, treatment regime used (chemotherapy and radiotherapy doses), evidence of ototoxicity and decline in GFR, and where relevant, any subsequent change in chemotherapy.
Results: Twenty-seven patients were included (6 supratentorial PNETs and 21 medulloblastomas). Median age at diagnosis of was 6 years. Seventeen (63%) of patients had changes in their audiograms post treatment (2 supratentorial PNET and 15 medulloblastoma). Chemotherapy was changed accordingly in 70%. Four patients had clinically significant hearing loss resulting in referral and or insertion of hearing aids. There was no significant difference in proportion of children developing hearing loss between standard, high risk medulloblastomas and supratentorial PNETs. 94% of patients had a reduction in their GFRs post platinum chemotherapy. Of these, 44% had a reduction in GFR of >30%.
Conclusion: Oto-toxicity was commonly seen in our cohort of patients with PNETs. This will have a significant effect on learning and educational outcome. A decline in GFR was also demonstrated in this particular group of patients. Future treatment strategies should aim at reducing such toxicity.

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RADIATION NECROSIS IN CHILDREN – AN UNDERREPORTED PROBLEM?!

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Background/Objectives: Radiation necrosis is one of the rare complications of radiation, most likely dose and modality dependent. Multiple reports on radiation necrosis in adults are published, reports on incidence and outcomes in the pediatric age group are rare.
Design/Methods: Patients were identified through the pediatric neurooncology database at McMaster Children's Hospital.
Results: Between June 2008 and June 2013 five patients with a diagnosis of radiation necrosis were identified, age range 1 to 16 years. Underlying diagnosis were atypical teratoid rhabdoid tumor (ATRT) in the posterior fossa, diffuse intrinsic pontine glioma (n = 3) and midline low grade glioma. The majority did receive intensity modulated radiation therapy (IMRT), one patient received cyperknife irradiation. Radiation necrosis was diagnosed by new neurological symptoms (altered level of consciousness, regression of milestones) and subsequent multiple imaging modalities, timeline 1 – 6 months following the radiation treatment. All patients got treated with high dose dexamethasone initially for the malignant cerebral edema. In 2 patients therapy was escalated: one patient received bevacizumab without a bleeding complication and improvement of the neurological symptoms, one patient received a course of hyperbaric oxygen therapy over 1 month. Overall the outcome was poor: all three DIPG patients died due to a combination of worsening radiation necrosis and tumor progression, one within 3 months of their initial diagnosis. The other 2 patients have ongoing severe neurological symptoms with major imaging findings: the patient with the ATRT has a developmental delay (e. g. not walking yet) with a severe speech deficit. The patient with the midline LGG has been hospitalized multiple times for severe somnolence problems.
Conclusion: International cooperation is needed to evaluate the true incidence within the pediatric age group, identify risk factors like the role of extent of surgery or intensive chemotherapy treatment and implement a treatment strategy especially to improve a mainly poor prognosis.

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EARLY POST-OPERATIVE MRI FOLLOWING A RESECTION OF A PEDIATRIC BRAIN TUMOR – WHAT IS THE RIGHT TIMEPOINT?

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Background/Objectives: Early post-operative imaging 24 – 72 hours following a resection of a brain tumor is mandatory to confirm the extent of resection which influences the further treatment in pediatric brain tumors. This time frame has been established to avoid misinterpretation through sclerosis and edema and to recognize immediate post-operative complications like bleeding.
Design/Methods: Over a period of 5 years pediatric brain tumor patients underwent immediate post-operative MRI on the way to the Intensive Care Unit (ICU) following brain tumor resection at McMaster Children's Hospital. Data on imaging, further treatment and outcome were collected and the economic effect calculated.
Results: Between June 2008 and June 2013 65 pediatric brain tumor patients underwent a tumor resection/ biopsy at McMaster Children's Hospital. In 20 patients with posterior fossa tumors an immediate post-operative MRI intubated and still under general anasthesia was performed on the way from the OR to the ICU. In 2 patients residual tumor was detected and a further resection was performed in the same surgery. All other patients showed a gross total tumor resection with no bleeding or massive cerebral edema signs and were therfore extubated and an immediate neurological exam performed. No imaging study needed to be repeated for immediate post-operative complications. On average the patients were between 24 – 48 hours less intubated and sedated and could be transferred to the peripheral ward earlier.
Conclusion: To avoid prolonged intubation and sedation for post-operative imaging and to judge on neurological outcome earlier immediate post-operative seems feasable and safe in our setting. Further multi-center studies are needed to confirm the results.

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DIFFERENTIAL MICRORNAS EXPRESSION PROFILE IN PRIMARY GLIOBLASTOMAS OF CHILDREN AND ADULTS, PILOCYTIC ASTROCYTOMAS AND NON-NEOPLASTIC WHITE MATTER: IDENTIFICATION OF PATHWAYS INVOLVED IN TUMORIGENESIS.

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Background/Objectives: Changes in miRNA expression have been described in several human tumors, including CNS tumors. This study aimed to evaluate miRNA signature in pediatric and adult astrocytic tumors and non-neoplastic white matter.
Design/Methods: We analyzed the global expression of miRNAs in microdissected samples at diagnosis from 29 glioblastomas (GBM) (20 adults and 9 children), 16 pediatric pilocytic astrocytoma (PA) (3 NF1-associated) and 12 non-neoplastic human white matter (WM) using the Human miRNA Microarray Kit (V3 8×15K, Agilent). Ten miRNAs differentially expressed (mir-10, mir-21, mir-34, mir-124, mir-125, mir-136, mir-139, mir-142, mir-144, mir-630) were validated by qRT-PCR using TaqMan probes in 45 samples of GBM (35 adults, 10 children), 39 pediatric PA (4 NF1) and 12 WM. The difference in expression between the groups was analyzed by Mann-Whitney test.
Results: The significant differential modulation of the expression was found in 40 miRNAs in GBM vs. PA, 37 miRNAs in GBM vs. WM and 112 miRNAs differentially modulated in PA vs. WM. Differences were also observed when compared pediatric GBM versus adults (16 miRNAs) and sporadic PA versus NF1 (32 miRNAs). From the 10 miRNA validated by qRT-PCR, significant differential expression was observed in 9 miRNAs when compared GBM vs. WM, 8 between PA vs. WM and 7 between PA vs. GBM. Searching for the validated targets genes to the most differentially expressed miRNAs: miR-10b, miR-34a-5p, miR-139-3p, miR-142-5p, miR-144-3p and miR-630, using of the database miRWalk it was found 84, 226, 12, 44, 60 and 20 targets genes respectively. By using the program Enrichr for evaluation of signaling pathways, it was found focal adhesion, glioma, p53, apoptosis and cell cycle as the main pathways involved.
Conclusion: Our results suggest a potential role of miRNAs in tumorigenesis and progression of astrocytic tumors and may contribute to a better understanding and management of these tumors.

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SILENCIG OF GDF15 GENE AND RESPONSE TO RADIOTHERAPY AND THE TREATMENT WITH TEMOZOLOMIDE IN GLIOBLASTOMA CELL LINES

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Background/Objectives: Glioblastoma (GBM) is one of the most malignant primary brain tumors in adults and children. In a previous study, our group described a significant high expression of the gene GDF15 in primary GBM compared to non-neoplastic white matter. The present study aimed in to investigate the effect of the silencing of GDF15 by shRNA and the response to radiotherapy and temozolamide (TMZ) in pediatric and adult GBM cell lines.
Design/Methods: The GDF15 gene expression was evaluated in 9 GBM cell lines by qRT-PCR. The two lines with the higher expression levels of GDF15 [KNS42 (pediatric) and U343 (adult)] were transduced by the RNA interference (shRNA) using lentiviral vector. After verification of gene (by qRT-PCR) and protein inhibition (by western blot), independent treatments were made with radiotherapy (2, 4, 6 Gy) and TMZ (250 to 1,500 μM) followed by in vitro functional studies: cell proliferation (Resazurin), apoptosis (anexin/propidium iodide) and clonogenic capacity.
Results: After silencing, there was a significant decreased in the clonogenic capacity of KNS42 compared with the control ($p < 0.05$). The gene silencing associated with TMZ had effect in increase the U343 cell proliferation with significant data after 72 hours of treatment with the doses of 500, 1000 and 1500μM of TMZ ($p < 0.05$). The KNS42 showed no change in sensitivity to TMZ after silencing. The silencing with radiotherapy had effect on U343 line, which showed a lower fraction surviving colonies in the silenced line at a dose of 4Gy, compared to the control ($p < 0.05$). No correlation was observed between silencing and sensitivity to radiotherapy in the KNS42 cell line.
Conclusion: This study showed that the silencing of GDF15 promotes different responses in pediatric and adult GBM cell lines, reinforcing their distinct molecular characteristics.

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DNA METHYLATION ANALYSIS OF PAEDIATRIC LOW-GRADE ASTROCYTOMAS IDENTIFIES A TUMOUR-SPECIFIC SIGNATURE AT A SET OF ENHANCERS

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Background/Objectives: Low-grade gliomas (LGGs) are the most common brain tumours in children, and are dominated by pilocytic and diffuse astrocytomas (WHO grades I and II, respectively). Although most of the genetic changes observed in LGGs converge on the MAPK/ERK signalling pathway, there is heterogeneity in clinical behaviour with diffuse astrocytomas having a significantly worse outcome than pilocytic astrocytomas. To improve our understanding of the molecular origins of paediatric LGGs, we have conducted a genome-wide study of DNA methylation in a large, well-characterised group of tumours.
Design/Methods: DNA methylation profiles were determined using the Illumina Infinium HumanMethylation450 BeadChip Kit, and analysed using Illumina Genome Studio and MethLab software. Marmal-Aid was used to compare the findings with publicly available data from other paediatric brain tumours. Gene expression was determined using Affymetrix U133 plus 2.0 arrays and RT-PCR.
Results: We identify a hypomethylated signature at a set of enhancers in pilocytic astrocytomas. This profile is not present in paediatric diffuse astrocytomas, medulloblastomas, adult low- or high-grade gliomas, or control brain tissue. Furthermore, the AP-1 complex, which is regulated by the MAPK/ERK pathway and is comprised of the FOS and JUN family of transcription factors, is predicted to bind to 35% of the differentially methylated regions. In the pilocytic astrocytomas, we find that a subset of AP-1 targets are up-regulated and show positive correlation with both FOS and JUN expression.
Conclusion: This study has revealed a DNA methylation profile in pilocytic astrocytomas that is not present in a broad cohort of other brain tumours, emphasizing the unique molecular biology of pilocytic astrocytomas. When integrated with genomics and gene expression profiles, the findings provide a comprehensive platform for understanding differences in gene regulatory pathways in paediatric low-grade gliomas.

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RESULTS OF PHARMACOKINETIC ANALYSIS OF INTRAVENTRICULAR ETOPOSIDE IN A PHASE II STUDY OF RECURRENT MEDULLOBLASTOMA, CNS-PNET AND EPENDYMOMA

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Background/Objectives: Neoplastic meningitis is a common problem in malignant brain tumor. Especially in recurrence metastatic disease occurs even more often and worsen significantly prognosis. Limited attribution of systemic chemotherapy into CNS is one known problem in therapy of malignant brain tumors. In contrast, intrathecal administrations of anticancer drugs in humans have shown high concentrations in cerebrospinal fluid (CSF) and leptomeninges by using low drug doses. Etoposide has demonstrated in experimental and clinical data significant cytotoxic activity. Penetration of etoposide after systemic administration into CSF is extremely poor (<3%) and did not exceed cytotoxic level, depending on cell line and exposure time, of 0.1-10 μg/ml. In a previous study of intraventricular etoposide administration in 14 patients with leptomeningeal disseminated brain tumors our group demonstrated etoposide concentration in CSF of 9.03, 1.31 and 0.11 μg/ml 0.25 hours, 4 hours and 24 hours after intraventricular administration.
Design/Methods: In this study we present pharmacokinetic data of a phase II trial with intraventricular administration of etoposide according determined schedule (1 mg etoposide on 5 consecutive days, week 1, 3 and 5). Etoposide was measured by using a validated RP-HPLC and PK calculations were performed by TOPFIT 2.0.
Results: The pharmacokinetic of etoposide is well described in a two compartment disposition model. C_{max} was calculated to 11.11 ± 8.22 μg/ml CSF. AUC for etoposide in CSF after 1st dose was calculated to 20.72 ± 6.71 μg/ml*h and clearance was calculated to 0.91 ± 0.36 ml/min. Calculating the ratio of etoposide measured in CSF to the plasma concentrations, a mean ratio (n=23) of 81 ± 64:1, with 212fold higher concentrations as maximum ratio and a 10fold higher concentrations in CSF as a minimum, was detected.
Conclusion: Pharmacokinetic data of this study confirmed results of feasibility study without significant cumulation of etoposide after repetitive administration within five weeks.

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IRRADIATION OF NECROTIC CANCER CELLS, EMPLOYED FOR PULSING DENDRITIC CELLS (DC), POTENTIATES DC VACCINE-INDUCED ANTITUMOR IMMUNITY AGAINST HIGH-GRADE GLIOMA

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Background/Objectives: Despite trimodal standard-of-care therapy, the prognosis of patients diagnosed with high-grade glioma (HGG) remains dismal. Dendritic cell (DC)-based immunotherapy has yielded promising results with objective responses reported in 15 % of HGG patients. The efficacy of DC vaccinations is however abated by the profound HGG-induced immunosuppression and a lack of attention towards immunogenicity of the tumor lysate. Literature analysis of DC vaccination clinical trials for HGG showed that the two most frequently used methods for preparing tumor lysate are: freeze-thaw (FT)-induced necrosis or FT-necrosis followed by high-dose X-ray irradiation. From the available clinical evidence, it is not clear which of the above methodologies have a superior immunogenic potential.
Design/Methods: We made use of the GL261 glioma murine model to directly compare the immunogenicity of FT-necrotic and irradiated FT-necrotic tumor lysates.
Results: Pulsing of DCs with irradiated FT-necrotic (compared to FT-necrotic only) tumor lysate prolonged overall survival and increased tumor rejection in glioma-challenged mice. This was associated with an increase in brain-infiltrating T cells and an increase in the $CD8^+$ T cell to Treg ratio, paralleled by a reduced accumulation of regulatory T cells (Tregs), tumor-associated macrophages (TAMs) and myeloid-derived suppressor cells (MDSCs). Pulsing of DCs with irradiated F/T-necrotic tumor lysate did not influence phenotypic and functional maturation of DCs. Further analysis showed that, the overall content of carbonylated proteins - a surrogate of immunogenic oxidation-associated molecular patterns (OAMPs) - in the FT-necrotic lysate, was increased by the irradiation treatment. Moreover, we found a striking correlation between the amount of protein carbonylation in tumor lysates and the DC vaccine-mediated tumor rejection capacity (such that the latter was partially but not significantly abrogated by addition of *bona fide* anti-oxidants).
Conclusion: Together these data strongly advocate the use of protein oxidation-inducing modalities like irradiation for increasing the immunogenicity of tumor lysate used for pulsing DC vaccines.

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OUTCOME OF BRAIN TUMORS TREATED AT A SINGLE INSTITUTION BETWEEN 1987-2013

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Background/Objectives: To determine the disease free survival (DFS) of all children treated with brain tumors since 1987 till 2013. A secondary objective was to determine DFS between children treated prior to 2000 and thereafter in a single institution.
Design/Methods: All patients 0-15 years of age, diagnosed at Tygerberg Hospital were included and divided into 2 groups: group 1 diagnosed before 2000 and group 2 from 2000 onwards. Data analysis included demographic data (age at diagnosis, sex), tumor type, stage, treatment received and final outcome after 24 months.
Results: There were 168 children included in the study with a mean age of 6.25 years (range: 0-14 years). Group 1 had 54 patient and group 2 114 patients. The overall male to female ratio was 1:0.9; respectively 1:0.6 and 1:0.9 for groups 1 and 2. Astrocytoma (22%) (respectively 31% and 18% for groups 1 and 2) was the most common brain tumor followed by medulloblastoma (16%) (respectively 15% and 16% for groups 1 and 2). DFS improved with time from 36% for group 1 to 46% for group 2 (overall 47%). Patients with medulloblastoma achieved a DFS of 72% for group 2 versus 38% for group 1 (65% overall), and 70% for astrocytoma in group 2 versus 47% for group 1. Treatment prior to 2000 included a combination of surgery-radiotherapy (24%), surgery alone (19%); combined surgery-radiotherapy-chemotherapy (18%); radiotherapy alone 13%, or no treatment (11%), which was similar for group 2 (surgery alone 23%, radiotherapy alone 23%; combined surgery-radiotherapy-chemotherapy 20% or no treatment 22%) except for very few patients receiving combined surgery-radiotherapy (6%).
Conclusion: Medulloblastoma had the best overall DFS of 65%, followed by astrocytoma 60%. The improved survival was mainly noted IN group 2. This was probably due to more standardized treatment protocols used from 2000 onwards.

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QUALITY OF LIFE IN LONG-TERM SURVIVORS TREATED FOR METASTATIC MEDULLOBLASTOMA WITH A HYPERFRACTIONATED ACCELERATED RADIOTHERAPY (HART) STRATEGY

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Background/Objectives: Since 1998 we launched a therapeutic strategy, for metastatic medulloblastoma. An intensive post-surgical treatment applied HDMTX/VCR, HDVP16, HDcyclo, HDcarboplatin followed by HART at total neuraxis dose of 39 Gy (1.3 Gy/fraction, 2 fractions/day) with posterior fossa boost 60 Gy (1.5 Gy/fraction, 2 fractions/day). If disease persisted before HART, patients received thereafter 2 courses of myeloablative thiotepa. Children aged under 10 years and in complete remission before HART, received reduced 31.2 Gy CSI. Studies that evaluate the quality of life (QOL) of patients with metastatic disease are missing especially in a very intensive therapeutic ground. Aim of this study is to evaluate the long-term adjustment of these patients at least three years after the end of treatment.
Design/Methods: Patients and their parents completed standardized self-administered questionnaires on health-related quality of life (PEDSQOL, SDQ, SF-36, EORTC QLQ-C30/QLQ-BN20). The questionnaires were delivered to the patient's home, following a phone call and due consent. Data were analyzed using descriptive statistics.
Results: Data were provided by 16 of 28 eligible survivors (57%), median age years (range 12-35 years), median interval after diagnosis 12 years (range 3,8-15,7). The QOL in general appeared adequate, but the analysis of the single subscales revealed that physical symptoms - principally pain and fatigue - were present only in a small percentage of patients, ranging 25%-37%, while serious problems related to cognitive/emotional/relational functioning occur in a percentage ranging 50%-100%. Small numbers prevents so far correlation with clinical variables.
Conclusion: QOL results are not different from other reported series in non-metastatic medulloblastoma treatment. Apart from disease and treatment effects, personal and social variables mediating disease damages have a strong impact on QOL. A global care of these patient implies therefore specific actions to support the scholastic and relational continuity, from diagnosis to the subsequent follow-up in multi-disciplinary day-hospital dedicated to survivors.

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DELAYED DIAGNOSIS OF PAEDIATRIC CNS TUMOURS – HEADSMART BE BRAIN TUMOUR AWARE

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Background/Objectives: A systematic literature review in 2005 identified that UK total diagnostic interval (TDI) ranked poorly in international comparisons. Consequently, a new NHS Evidence accredited referral guideline was developed and disseminated through a public awareness campaign (HeadSmart be brain tumour aware, www.headsmart.org.uk) to raise awareness of symptoms and the need for timely imaging. The objectives of this project were to: (1) repeat the original systematic literature review from 2005 and conduct an international comparison of TDIs since the launch of HeadSmart in 2011; and (2) identify the tumour subtypes with the greatest proportion of delayed diagnostic intervals to inform the on going awareness campaigns about patient groups at greatest risk of delays.
Design/Methods: TDI data was collected by clinical champions in eighteen regional children's cancer centres. Systematic literature review using PubMed, Embase, The Cochrane Library and ISI Web of Science was undertaken to identify relevant publications between January 2005 and December 2014. Descriptive analysis was used to compare the difference between subgroups.
Results: The UK TDI data showed a reduction in median from 3.3 (2006) to 1.5 months (mean 4.9 months) by May 2013. From 6,482 articles 3 were identified reporting TDI of all brain tumour types. International comparison of published studies showed that the UK data is second only to a 2005 Polish study reporting a median of 1.0 month (mean 4.9 months). Tumour subtypes with the greatest proportion of prolonged TDI were craniopharyngioma, low-grade glioma, germ cell tumours and optic pathway glioma with median TDIs of 3.5, 2.7, 1.3 and 2.4 months respectively.
Conclusion: This strategy to accelerate brain tumour diagnosis in UK using a public and professional awareness campaign is a "world first" in paediatric cancer, producing leading performance in referral intervals. Identifying the subgroups with most skewed TDIs permits this information to be used to appropriately tailor further intervention.

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DEVELOPMENT OF A POTENTIAL PRE-OPERATIVE RISK STRATIFICATION TOOL OF CEREBELLAR MUTISM SYNDROME IN CHILDREN WITH POSTERIOR FOSSA TUMOUR

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Background/Objectives: Cerebellar mutism syndrome (CMS) complicates posterior fossa tumour (PFT) resection in 11-29% of cases. Although the mutism typically improves over 4-8 weeks, motor and cognitive deficits persist. Previous studies have identified potential clinical and radiological predictive factors; however, a unifying pre-operative risk stratification model for use during surgical consent is currently lacking. The project aims to develop a risk stratification tool via: (1) a retrospective analysis of clinical and radiological data included paediatric patients who had undergone PFT resection at an institution to develop a preliminary model; then (2) validate and modify the model further in a larger cohort.
Design/Methods: Post-operative CMS status was ascertained from clinical notes. Pre-operative MRI scans underwent structured evaluation for a 21 tightly-defined candidate imaging risk markers based on prior literature. Logistic regression was used to identify potential CMS predictors, and the strongest predictors were used to test their ability to stratify the patient cohort into low, intermediate and high-risk groups.
Results: The first cohort consists of 51 patients (age: 2-23yrs, gender 14M, 37F, 24 medulloblastoma, 23 pilocytic astrocytoma, 4 ependymoma); thirteen patients (25%) developed CMS. A risk model combining IV ventricular location and brainstem invasion allowed separation of the cohort into low (5%), intermediate (25.5%) and high-risk (71.5%). This model will be further validated by the inclusion of a cohort of 48 patients of which 15 had PFT recruited with similar methodology (age: 0.7-17.6yrs, gender: 19M, 29F) in March 2015.
Conclusion: Retrospectively applying a tightly defined structured evaluation of pre-operative imaging and clinical data has created a risk stratification model for post-operative CMS which will inform risk pre-operatively permitting reconsideration strategies for primary surgical intervention to limit risk of surgical damage to sensitive parts of the brainstem in particular where the areas of post operative damage seem to affect the inferior olivary nucleus and associated brainstem tracts.

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ATYPICAL TERATOID/RHABDOID TUMORS: A CLINICOPATHOLOGICAL STUDY OF 22 CASES AND LITERATURE REVIEW

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Background/Objectives: Atypical teratoid/rhabdoid tumors (AT/RTs) are rare, highly malignant tumors of the central nervous system (CNS) that affect young children and are characterized by a low response to therapy and poor prognosis. It is essential to distinguish AT/RTs from other pediatric embryonal tumors, although prognostic indicators remain controversial.
Design/Methods: we describe the clinical, histological, and immunohistochemical characteristics, along with the treatments and outcomes, of 22 cases of AT/RTs diagnosed in our hospital between 2009 and 2014.
Results: Among the 22 cases, the age at diagnosis ranged from 5 months to 9 years (median, 24 months). Fifteen of the patients were under 3 years old, and 15 patients were male. A supratentorial tumor origin accounted for 45% of all cases. The morphological characteristics were assessed in 19 cases, and rhabdoid cells were seen in more than half of all cases (n=13). Vesicular nuclei were seen in the majority of cases (n=12), although cytoplasmic vacuoles were not evident or scattered in most cases. Immunohistochemical analysis revealed that all 22 cases showed loss of INI1 nuclear expression. Therapy and follow-up data were available in 15 of the 22 cases. Seven patients died from tumor progression within a short time following surgery without any adjuvant treatment, all of whom were under 2 years of age. Five patients were treated with radiation and systemic chemotherapy, four of whom were older than 3 years, and three patients experienced longer term disease-free survival of more than 12 months. Our study showed that rhabdoid cells have histopathological importance but are not

inherent among AT/RTs; rather, the lack of INI1 protein is the most useful marker for differential diagnosis.
Conclusion: Young age and infratentorial location are negative prognostic factors, while gross total surgical resection and adjuvant therapy, such as radiation and chemotherapy, are positive factors.

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QUALITY OF LIFE IN LONG-TERM SURVIVORS OF VERY YOUNG PEDIATRIC LOW-GRADE GLIOMAS

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Background/Objectives: We report quality of life and clinical outcomes in long-term survivors of very young (<5 years at diagnosis) pediatric low-grade glioma (LGG).
Design/Methods: Sixty consecutive patients <5 years old upon diagnosis were reviewed (1970-2009). Fourteen patients completed a mailed questionnaire including the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30 and QLQ-BN20) and a modified St. Jude Long-Term Follow-Up Study. All patient records were retrospectively reviewed for patient, tumor and treatment characteristics.
Results: Median follow-up was 7.7 years overall and 24.9 years for questionnaire responders. Twenty-year overall survival (OS) was 81% and progression-free survival (PFS) was 46% compared to 61% in responders. Overall and in responders, 65% had grade I histology. Gross total resection was achieved in 73% overall, and 86% of responders. Adjuvant radiotherapy was delivered in 17% overall, and 14% of responders. Chemotherapy was given to 10% overall, and 7% of responders. Salvage radiotherapy was given in 7% overall and 7% of responders. A total of 71% reported their health as very good or excellent. Mean (standard deviation) global QOL score was 83 (17) versus 76.4 (22.8) in a reference population of healthy adults. Mean QLQ-BN20 score overall was 6.9. Learning/memory deficits were reported in 4, seizure disorders in 2, migraines in 2, imbalance in 3, transient stroke in 1, transient sensory loss in 1, transient prolonged pain in 1, and chronic abnormal sensation in 1 responder. No patients reported tremors, dysphagia or weakness. One patient had a significant complication related to surgery (stroke). One patient reported a significant complication related to radiotherapy (chronic back pain).
Conclusion: Long-term (>20 year) follow-up of very young pediatric LGG survivors suggests a subgroup of patients have a high quality of life with chronic neurologic symptoms in only a small portion of patients.

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OUTCOME OF INI-1 NEGATIVE CNS TUMOR IN CHILDREN: A SINGLE INSTITUTE EXPERIENCE

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Background/Objectives: Atypical teratoid rhabdoid tumor (AT/RT) and marignant rhabdoid tumor (MRT) have similar histology and similar clinical and demographic features. AT/RT and MRT both have deletions of the INI1 gene. The overall prognosis for AT/RT and MRT is very poor.
Design/Methods: We retrospectively reviewed five children newly diagnosed as INI-1 negative tumor(two AT/RTs, three MRTs) in our institution from 2006 to 2013.
Results: The median age at diagnosis was 44 months (range 7 to 65 months). Three tumors were located in the spinal cord, one in the frontal lobe and the other in the suprasellar region. Two of them had dissemination on MRI at diagnosis. Only one patient achieved gross total resection (GTR), three underwent subtotal resection (STR) and biopsy was performed in the other. All patients received sarcoma-oriented chemotherapy such as ICE (ifosfamide, carbopratine and etoposide), VAC (vincristine, actinomycin and cyclophosphamide) or VDC (vincristine, doxorubicin and cyclophosphamide). One patient underwent high dose chemotherapy (HDCT). Two patients without dissemination received focal radiation and two with dissemination received cranio-spinal irradiation (CSI). The 2-year overall survival was 60% with the median of follow-up of15 months (range 10 to 102 months). Two patients older than 5 years old at diagnosis survived for 62 and 102 months, respectively. One patient with dissemination, who had progression disease with dissemination after HDCT, was alive with disease after re-irradiation and maintenance chemotherapy for six months after relapse.
Conclusion: The prognosis of young children with INI-1 negative tumor is poor but could be improved by intensive chemotherapy and radiotherapy after surgery.

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THE MIR-17-5P EXPRESSION CORRELATES WITH GRADE AND OUTCOME OF CHILDREN WITH EPENDYMOMA

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Background/Objectives: Ependymal tumors are the third most common group of brain tumors in children, accounting for 10-12% of all primary lesions, and concurrently the most common type in children younger than 5 years of age. Approximately 70% of tumors in children develop within the posterior fossa and usually infiltrate surrounding vital brain structures. Lack of recurrently mutated genes observed in ependymomas makes their molecular analyses difficult and suggest plausible epigenetic background of this lesion. Here we focused on one of the epigenetic mechanism with plausible role in solid tumors formation, altered miRNA expression.
Design/Methods: We performed two stage miRNAs expression study in 74 cases of pediatric ependymomas. Primary analysis underwent profiling of miRNAs, afterwards, the expression measurements in validation cohort of patients with complete survival data were performed. Student's t-test with Benjamini-Hochberg procedure was used to compare expression data. Survival analysis was done using the log-rank test and multivariate Cox' proportional hazards regression. $P<0.05$ was considered as statistically significant.
Results: Out of 84 profiled miRNAs, 32 showed differential expression between WHO grade II and III tumors; grade II tumors showed lower expression of those miRNAs. Five miRNAs chosen for validation in the full cohort (miR-200a, miR-19a, miR-17a, miR-106b, miR-9-3p) showed the same tendency of changes. Decrease of miR-17 expression was shown to be associated with increased risk of relapse and shorter overall survival.
Conclusion: Current study provides a better understanding of pediatric ependymomas biology enabling to type epigenetic biomarkers helpful in discrimination between childhood grade II and III ependymomas and in defining factors connected with tendency to relapse and final outcome.Work supported by the Polish National Science Centre grant No 2011/01/B/NZ4/03573.

Posters: CCI (Parent/Survivors)

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PAEDIATRIC ONCOLOGY SOCIAL WORK AND ITS ROLE IN ALLEVIATING POSSIBLE TRAUMA FOR THE CHILD AND FAMILY

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Background/Objectives: The diagnosis of cancer or a life threatening blood disorder in a child is devastating with far-reaching psychosocial and emotional implications for not just the child, but also the family system as a whole.
Design/Methods: The family's psychosocial needs are addressed through the following key aspects of the social worker's role: Counselling at the time of breaking the bad news of the diagnosis; psychosocial assessments; preparation for medical treatment procedures; ongoing individual and/or group counselling and guidance from diagnosis to the end of treatment and palliative- end of life care and support.
Results: With the paediatric oncology social worker rendering the above key services, the impact of the diagnosis and treatment is alleviated. Her presence can break down the medical jargon and procedures can be simply explained in the family's own language. Through the psychosocial assessment, a bigger picture of what is going on in the family is gained and possible problems further down the line can be pre-empted. The patient is prepared for medical procedures, which alleviates fear and anxiety and generates greater cooperation. So the family is supported from the time of diagnosis until the end of treatment, whether it means cure or preparing the family for, and supporting them through, the death of their child.
Conclusion: The path that the social worker walks with the families enables them to access internal and external resources with which to come to terms with and take ownership of their situation.

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THE EFFECT OF THE "HONG KONG – MAINLAND CHINA CHILDHOOD CANCER EXCHANGE CAMP" IN SUPPORTING CHILDHOOD CANCER PATIENTS IN THE TWO PLACES

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Background/Objectives: The Little Life Warrior Society (LLWS) is a childhood cancer mutual support organization in Hong Kong aiming to improve the benefits of childhood cancer patients. Except launching the work in Hong Kong, LLWS has started the work of supporting childhood cancer patients in China in the past 10 years. Till now, 10 LLWSs has already been established in 10 different provinces in China with the help of LLWS in Hong Kong. In order to closely connect the childhood cancer patients in Hong Kong and China, the "Hong Kong – Mainland China Childhood Cancer Exchange Camp" is held every 2 years. The study aims at finding out the effect of the exchange camp in supporting the childhood cancer patients in the two places. Its function as a platform for the communication among patients of the two places will also be explicated.
Design/Methods: Since the establishment of LLWS, 3 exchange camps have been held. Each time after the exchange camp, a questionnaire is designed for participants to complete in order to collect useful data of participants' views on the effect and use of the exchange camp in serving as a platform for patients' communication and mutual support.
Results: Revealed that the exchange camp is very effective in supporting childhood cancer patients in Hong Kong and China in that it can foster the communication among patients from different places. This could help them build up a network of mutual support. Besides, medical and nursing knowledge is shared among patients through their communication and the intensive medical seminars provided during the camp.
Conclusion: The "Hong Kong – Mainland China Childhood Cancer Exchange Camp" help childhood cancer patients in Hong Kong and China to establish a network of mutual support. Ultimately, patients can gain enough support and encouragement in fighting against childhood cancer.

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THE IMPACT OF CHOC SOCIAL WORKERS IN PUBLIC HEALTH SECTOR HOSPITALS IN SOUTH AFRICA

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[1] CHOC Childhood Cancer Foundation, Johannesburg, South Africa

Background/Objectives: CHOC Childhood Cancer Foundation S A (CHOC) was established in 1979 by a group of parents with the aim of supporting children diagnosed with cancer or life threatening blood disorders and their families.
Design/Methods: Through the partnership with public health sector hospitals, CHOC appointed its first social worker in 2004. Over the years this partnership has grown to encompass five social workers and two social auxiliary workers employed in five state funded academically linked hospitals throughout South Africa.
Results: The placement of CHOC employed social workers has made a significant difference not just for the children and their families but also for the medical and nursing teams. These differences encompass: counselling and educating parents from the time of diagnosis until the end of treatment; creating awareness and educating parents about childhood cancer; palliative- end of life care to ensure quality of life and dignity in the dying process; bereavement support; support for the medical and nursing staff, which alleviates the pressure on their already burdened workload; and educating the medical and nursing staff on the psychosocial and emotional needs of the patients and their families.
Conclusion: The medical Heads of the Paediatric Oncology Units have expressed their gratitude to CHOC and acknowledged the significant impact the social workers have made on the lives of the patients and their families. One doctor has been quoted as saying that she cannot understand how a Paediatric Oncology Unit can function without a designated CHOC social worker.

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USE OF BEADS/BUTTONS/SEEDS AS A REWARD FOR THE COURAGE AND BRAVERY DISPLAYED BY CHILDREN UNDERGOING TREATEMENT FOR CANCER

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Background/Objectives: The concept of using beads to "reward" children for their courage while undergoing treatment has been utilised at several hospitals around the world and presented to CHOC as an idea to implement at the Frere Hospital in the Eastern Cape. In Africa the use of beads in various ways represents their culture; the patterns and colours denote different tribes. As the majority of the children who are hospitalised in the Eastern Cape come from rural areas, beads are part of their everyday lives.
Design/Methods: The bead programme was adapted for use in the Frere Hospital. It was decided that each child should be rewarded for their courage and bravery while undergoing the various treatment procedures. Each bead/seed/button represents a procedure. The more painful the procedure, the greater the reward, which is reflected in the beauty of the bead. The children then get to choose the appropriate bead and attach it to their string. These are known as "Memory Beads".
Results: The children enjoy spending time choosing their beads and add them to their string with much pride. Allowing the child to choose their bead is an easy way for Doctors, Staff and CHOC to acknowledge the child for their courage, bravery and heritage. "Memory Beads" create a personal memory for the child and the family of their journey travelled.
Conclusion: The children enjoy spending time choosing their beads and add them to their string with much pride. Allowing the child to choose their bead is an easy way for Doctors, Staff and CHOC to acknowledge the child for their courage, bravery and heritage. "Memory Beads" create a personal memory for the child and the family of their journey travelled.

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THE FIRST SYMPOSIUM FOR SURVIVORS ABOUT MEDICAL LATE EFFECTS IN AUSTRIA

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Background/Objectives: 280 children and young adolescents come down with cancer each year in Austria. Due to a survival rate of over 80% about 235 survive, which leads to an increased number of former childhood cancer survivors in the society.

Design/Methods: Due to the vast range of different activities offered for Austrian survivors, a regular exchange is easily possible between them. Moreover, survivors representatives stay in contact with survivors groups from other countries and maintain close collaborations with medical and psychosocial professionals.
Results: Through this regular exchange the need of a special symposium for survivors about medical late effects got visible, as a lot of survivors are not aware of possible late effects and risks. They have only little information about possible late effects and not enough knowledge about the screenings (what, when and why are they necessary). Cancer and its treatment can lead to chronic or late occurring problems many years after therapy. The communication with former patient about the relevance and challenges of medical and psychosocial follow-up for childhood cancer survivors leads to the first symposium in Austria in 2015. The symposium was scheduled for one day, the survivors got information from paediatric oncologists in lay language, and they had the possibility to ask them directly.
Conclusion: It is very important to give the information to the Survivors, because this helps them to take over the responsibility for their own health, as they are very often lost in follow-up and they don`t know where to go if they have problems or questions (pediatric oncologists, general practitioner or medical specialist). In the future, other tools will be developed in Austria, which will focus on the improvement of the quality of life of childhood cancer survivors.

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MOBILIZING OPPORTUNITIES TO SYSTEMATICALLY ADDRESS ISSUES IMPACTING CAREGIVERS OF CHILDREN: A MULTI-SECTORAL APPROACH TO INFLUENCE SYSTEM CHANGE IN CANADA

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Background/Objectives: As an emerging voice for system change in Canada, caregivers need a scientific approach to influence policy decisions. The Canadian Cancer Action Network adopted the IAP2 Public Participation Spectrum to develop evidence-based recommendations for system change by engaging caregivers, scientific experts and NGOs. Namely: 1) convening a consultative session 'Family Caregivers and childhood cancer: understanding the issues impacting caregivers of children' to address financial burden/gaps in the health-care system. 2) conducting a scan of research publications and resources 3) informing national dialogue (with over 45 stakeholders) to develop/validate recommendations for change 4) collaborating with stakeholders to move from dialogue to action.
Design/Methods: Two parallel processes were used to develop recommendations. An E-Delphi process informed a collaborative caregiver national action plan. E-Delphi participants were recruited through members of the National Steering Committee and other key stakeholders. Simultaneously, 5 regional think tanks were held across Canada to seek multi-jurisdictional input into draft recommendations related to caregivers of children. Think tank participants were recruited through NGOs, support groups and children's hospitals.
Results: This systematic process resulted in practical, feasible recommendations to address the high financial burden on families due to Canada's geographical dispersion and fragmented support systems. Participants validated the need for a unique online portal in Canada, providing timely information concerning financial supports, complete with the ability to personalize based on individual family needs. Further, Government

programs (such as tax deductions and drug coverage) should be aligned with policy goals and families' realities with remaining gaps including a strategy to alleviate the immediate financial burden on Canadian families.
Conclusion: There remains a need for direct financial support for families in Canada, supported by the implementation of a collaborative model of stakeholder and caregiver engagement. A collaborative framework for multi-sectoral/multi-jurisdictional engagement supports efforts to ensure issues impacting caregivers of children remain a key, shared priority.

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THE HOUSE OF THE AVENIR : 20 YEARS HOUSING PARENTS OF CHILDREN WITH CANCER IN MOROCCO

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Background/Objectives: In Morocco, there are about 1000 new cases of kids with cancer each year. About 300 are treated in Rabat at the Pediatric Hematology and Oncology Service, initiated and supported by the Foundation of parents and friends of children with cancer "l'Avenir". To avoid abandonment of treatment, improve the conditions of treatment and help the families living out of Rabat, the foundation built the first house of parents in Morocco in 1995 and runs it up to now.
Design/Methods: It is four floors house, well equipped, with 22 bedrooms (54 beds), showers, play room, living room, kitchen, dining room, and a garden. The main floor is occupied by the Foundation with meeting room, offices for the president, secretaries and treasurer, computer space for the kids, and archives room. It's also a space for sharing, listening, helping each other, meet members of the foundation, volunteers and a psychologist to advise and encourage them. When a new family arrives, the director of the house explains the rules, shows them their room and gives them all they need. They are helped by house keepers, security guards and a driver. The adult pays a symbolic amount (10 MDH about 1 USD).
Results: Besides housing and accommodation, the Avenir provides to families foods, clothes, toys, transport, prosthesis, communication means, drugs, entertainment …as long as their treatment is required. During 2014, the number of families and kids who stayed at the house of the Avenir was 641 with an average of 12 days at a stay, from 1 to 20 times a year depending on the type of the disease and its treatment. The average rate of occupation is 75%.
Conclusion: Since 20 years, the house contributes to soften and improve social, medical and psychological conditions of treatment and somehow makes the disease and its constraints more acceptable.

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A YOUNG SURVIVORS' ROLE: POSITIVELY AFFECTING CHILDREN AND THE YOUTH IN GHANA

J. Owiredu-Okyere[1]

[1] Accra, Ghana

Background/Objectives: I am a survivor of Hodgkin Lymphoma having been diagnosed with the condition at nine years of age. I experienced psychological trauma, some of which was as a result of stigmatization whilst at school. Losing all my hair and having to wear a wig to school made me look odd among my peers and I became a subject of gossip. When I was on admission in Accra, I also noticed the stress and anxiety that my parents and other parents go through. As a youthful survivor and a student, my objective was to bring hope to children and the youth who are going through cancer treatment and to educate my peers in school on cancer as well as show them that children with cancer need love and are just like all other children.
Design/Methods: In 2014, I gave some talks to my classmates in boarding school about childhood cancer, using my experiences. They became really interested and enthusiastic about what they could do to help. We raised money from friends and relations. We obtained permission from the consultant-in-charge of the Paediatric Oncology Unit and the Korle Bu hospital authorities to spend a day with the children on the unit.
Results: In December, 2014, we made our presence felt on the ward in a big way. Activities included a film show, music, dancing with the patients and donation of gifts. We put broad smiles on the faces of the children and their parents. Even the nurses had fun. Everyone, including my classmates would like us to visit again.
Conclusion: Survivors can help change perceptions by educating their peers. They can help relieve some of the psychological distress faced by patients and parents by visiting their former units and interacting with the children.

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IMPACT OF CHILDHOOD CANCER SURVIVORS SUPPORT GROUP-LESSONS LEARNT FROM UGAM

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Background/Objectives: Ugam is a support group formed by Mumbai based young adult survivors of Childhood Cancers attending the After Completion of Therapy (ACT) clinic at Tata Memorial Hospital (TMH). Ugam was formally launched on 7th June 2009, first Sunday of June celebrated as Cancer Survivors Day across the world. UGAM means "To Rise", underscoring the determination of childhood cancer survivors, to rise above all obstacles in life & be VICTORS. UGAM is affiliated to Indian Cancer Society (ICS) under its survivorship programme. UGAM has been set up with an aim to provide a helping hand to the survivors of childhood cancers & become the ambassador of the message "Childhood Cancer is Curable" in society. The present study was done to understand the impact of the support group on the quality of life of childhood cancer survivors.
Design/Methods: Survey was conducted with the help of semi structured interview. Interview guide (questionnaire) was designed to collect basic information & also about psychosocial aspects (self confidence, self esteem, anxiety, coping). Responses rated on 4 point Likert scale before & after joining Ugam to understand impact of Ugam in improving their coping skills.
Results: Of 45/195 (23%) Ugam members who participated in survey,29(64%) are male & 16(36%) females with median age 24yrs (R 18 -50). 87% of the survivors received psychosocial support, 56% benefitted from establishing social contact & sharing with Ugam members.24% encountered new opportunities and 78% received guidance for future. Ugam participants reported improvement in self confidence (59%), self esteem (55%), and handling emotions (46%). Participants reported reduction in anxiety in 40%, fear 44% & loneliness in 79%.
Conclusion: Ugam support group helped its members significantly to bring about a positive change in their perspective and identity as a survivor. Therefore, survivor support group plays important role in psychosocial rehabilitation of young adult survivors.

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SURVIVORSHIP ISSUES AND CARE IN CHILDHOOD CANCER: A HISTORY OF GLOBAL DISPARITIES

R. Rohrer[1]

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Background/Objectives: Children cancer is a rare disease which knows no boundaries of race, gender, class or nationality. In developed countries approximately 1 in 330 children will be diagnosed with cancer before the age of 15 years. The historical rates in many developing nations approximate this number, although many children are undiagnosed in these areas. With often scarce resources for treatment, survivorship issues are minimally addressed due to extremely stretched resources.
Design/Methods: The author will use the archives of the National Cancer Institute and published medical and psycho social students for this work. This study will focus upon the comparative availability and characteristics of survivorship monitoring and care in the United States and India as examples.
Results: One of the major challenges facing the families of childhood cancer patients is financial. It is common in developed nations for one parent to take extended leave or lose employment because of the demands of travel and time for clinic visits and hospital stays for their child. Cost of travel, meals, parking and often lodging are also usual costs. Two issues addressed in this study center on lack of finances and unavailable transportation to clinic or hospital visits. This access for survivors applies to both developed and developing nations. Travel in rural areas existence and general lack of health centers is not only a problem of developing nations.
Conclusion: The author will conclude by examining the efforts of advocacy groups globally to address the unique challenges faced by childhood cancer survivors.

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THE MENTORING PROGRAM IN GERMANY – DEVELOPMENT IN THE LAST YEARS AND STATUS QUO

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Background/Objectives: The presentation will be about the mentoring program in Germany. We present the first steps that happened with this program in Germany, how it went on during the last years and where we stand right now. Our aim is to give information to other survivors how they can establish a mentoring program in their home country, which barriers they may face and where they may find supporters.
Design/Methods: A mentor to a child or teenager with cancer has had cancer in young years as well. But not every survivor is able to become a mentor. The authors are psychologists and survivors, we are two of the trainers that train young adults to become a mentor. We train them in special speaking and empathy skills, but also support them in a better active listening. We present the structure of our training and how our connection between all active survivors in Germany works.
Results: The time fighting against a cancer disease is a hard period of life – especially for children, teenagers and young adults. We always get positive feedback of our mentoring program from the concerned. The mentoring program is supported by the German Childhood Cancer Foundation and well esteemed.
Conclusion: All in all, the mentoring program is a good possibility to help children and young adults to pass their treatment with a psychosocial support got by peers who understand what they feel. Our mentoring program in Germany is growing more and more and we want to help other survivors to have such a program as well.

Posters: Epidemiology

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GEOGRAPHICAL DISTRIBUTION OF THREE AIDS-RELATED CANCERS AMONG CHILDREN IN THE SIX WHO REGIONS

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Background/Objectives: Although cancer is relatively rare in children aged 0-14 years but it remains a significant burden for HIV-infected children. HIV infection has a link with the development of AIDS-related cancers such as Non-Hodgkin lymphoma (NHL), Kaposi's sarcoma (KS), and cervical cancer. This study describes the geographical patterns of the incidence and mortality of the three AIDS-related cancers in the six World Health Organization (WHO) regions.
Design/Methods: Data from International Agency for Cancer Research GLOBOCAN 2012 database was used to examine the incidence and mortality rates for children aged 0-14 years old using age-specific rates and numbers as obtained in the WHO regions.
Results: African region recorded the highest incidence rates for NHL (1.3/100 000 for female and 2.1/100 000 for male). The region also recorded the highest mortality rates for NHL (0.7/100,000 for female) and 1.0/100,000 for male). The situation was the same with KS with the African region having the highest incidence and mortality rates for both gender. African region had the highest number of NHL and KS new cases [38% (6296/16509)] and KS [96% (2081/2162)] respectively while Western Pacific region had 41% (68/165). The regions recorded 18,836 new cases (NHL – 88%, KS -11% and cervical cancer – 0.9%) while the mortality cases followed almost the same pattern. The total number of new cases of NHL for female was 5885, 10624 for the male (P=0.1668), and that of KS was 963 for female and 1199 for male (P=0.8757).
Conclusion: The study shows that distribution of these three AIDS-related cancers followed the pattern of HIV prevalence in the WHO regions. Africa being the most affected region recorded the highest incidence and mortality in children (both HIV-infected and non – infected). KS is majorly an African problem while cervical cancer is rare among children despite the widespread HIV epidemic.

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CONNECTING THE CARIBBEAN: UTILIZING TELEMEDICINE TO FACILITATE CAPACITY BUILDING FOR PAEDIATRIC ONCOLOGY PATIENT CARE

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Background/Objectives: In high-income countries (HIC) childhood cancer survival is over 80%, whereas in low- and middle-income countries (LMIC) this is lagging by 20% or more. To address this gap in patient outcomes, established paediatric cancer treatment centres are well positioned to share clinical expertise. Launched in March 2013 at the Hospital for Sick Children (SickKids), Toronto, Canada, the SickKids-Caribbean Initiative (SCI) aims to enhance care for children with cancer and blood disorders in 6 Caribbean countries: The Bahamas, Barbados, Jamaica, St. Lucia, St. Vincent and the Grenadines and Trinidad and Tobago.
Design/Methods: To increase accessibility to healthcare services, 6 standardized telemedicine facilities have been opened or upgraded, connecting SickKids with participating countries. To commence telemedicine based consultative activities, an indemnity agreement was signed by all sites, SickKids Division of Haematology/Oncology consultant physicians were contracted, and a secure electronic file transfer system was established to adhere with ethical and legislative obligations to protect personal health information.
Results: Using the SCI telemedicine network, monthly Case Consultation Review Rounds provide an educational forum for discussion of diagnostic work-up, management challenges and local treatment plans. Fifty-eight cases have been reviewed. Of the 42 oncological cases submitted, 17 (40.5%) were leukemia/lymphoma, 14 (33.3%) solid tumours and 11 (26.2%) brain tumours. In the event that testing is not available at the referring centres, imaging and pathology samples are reviewed at SickKids.
Conclusion: Telemedicine enhances opportunities for collaboration within the Caribbean region by creating a reliable forum for education, knowledge transfer and the development of consensus management plans. It is a valuable tool to strengthen training by increasing the expertise of sub-specialists locally and promotes academic exchange in paediatric specialties. By building capacity and nurturing expert knowledge through education, SCI hopes to contribute to reducing the gap in childhood cancer survival between Canada and the participating Caribbean countries.

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PATTERN OF CHILDHOOD MALIGNANCY AND TREATMENT REFUSAL IN A TERTIARY CARE HOSPITAL

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Background/Objectives: Refusal and abandonment is the leading cause of treatment failure in children with cancer in the developing world. Malignant neoplasm remains the leading cause of disease-related (non injury) mortality (12.8%) among persons 1-14 yr of age. To our knowledge Bangladesh has few studies about pediatric cancer profile.To evaluate the pattern of pediatric cancer & causes of treatment refusal in Dhaka Medical College Hospital.
Design/Methods: This was a prospective observational study from March' 2014 to February' 2015 in Department of Pediatric Hematology & Oncology, Dhaka Medical College Hospital. Hundred thirty nine cases were included in this study.Detailed information's were obtained in each cases according to protocol. Complete history was taken from accompanying attendants. Through clinical examination was done. Relevant investigations report was collected. All the informations were recorded in the fixed Pediatric Oncology network database (POND). Collected data was classified, edited, coded and entered into the computer for statistical analysis by using SPSS-17.
Results: Out of 139 patients, mean age was 6.11(±3.31) yrs, male female ratio was 1.55 :1. Common clinical features were fever , pallor, Hepatomegaly, Bleeding manifestation, bony tenderness, weight loss, abdominal or mediastinal mass, splenomegaly and lymphadenopathy which were 110(55%), 74(37%), 61(30%), 40(20%), 40(20%), 40(20.10), 37(19%) and 14(7%) respectively. Common pattern of child hood malignancy were ALL, AML, Neuroblastoma, Hodgkin lymphoma, Non-Hodgkin lymphoma, Wilms tumor and Embryonal rhabdomyosarcoma which were 98(49%), 19(9%), 13(6%), 11(5%), and 05(2%) respectively. Refused to treatment was 41(21%). Majority 28(68.29%) were due to financial crisis, followed by lack of family support 25(61%), 13(32%) lack of blood and blood product, 07(17%) had have faith on traditional treatment or homeopathy, 05(12%) had Interested to treat elsewhere.
Conclusion: An structured database provide excellent information about childhood malignancy/ Proper input in database identify the problem magnitude,presentation of diseases, morbidity pattern and cause of refusal of treatment by parents.

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PERCEPTION AND ATTITUDE OF ARAB PEDIATRIC ONCOLOGISTS TOWARD GENETIC TESTING IN CANCER

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Background/Objectives: Genetic predisposition is an increasingly accepted cause of childhood cancers. However, little is known about the perception and attitude of pediatric oncologists in Arab countries toward disclosure of genetic predisposition for cancer (GPC) and genetic testing (GT).
Design/Methods: We designed a questionnaire (29 questions) which evaluates demographics, knowledge and practices toward GPC and was emailed to a list of oncologists. Their emails were acknowledged by one or two local oncologists. We exclusively included replies from Arab pediatric oncologists practicing in Arabic countries; aiming to unify the cultural background and work circumstances.
Results: We had 48 complete responses, 60% from eastern countries. Median participants' age was 46.5 years (range, 35-68 years) with equal male: female ratio .Thirty one (65%) reported >10 years oncology experience and 60% had some oncology training in Europe / North America. GT and genetic counselors are likely available in 60% of countries. Majority of oncologists (83%) believe that confirmation of a genetic cause will change the patient management.67% of oncologists think the community accepts GT while 29% believe cancer is stigmatized and the idea of GPC is culturally and psychologically unbearable. Despite this, most oncologists (92%) feel ethically obligated to tell a parent if GPC is suspected, in order to encourage GT and cancer screening. In fact, half of oncologists had referred patients for GT and almost all oncologists (98%) will offer a specific GT (if available) to their patients. Interestingly, no demographic factor seemed to influence the oncologists' perception or attitudes ($p>0.05$).
Conclusion: Majority of Arab pediatric oncologists are aware of GPC and would encourage such discussions during family encounters. They realize there are some logistic difficulties, cultural and social challenges to such disclosures. When present, oncologists need to utilize the genetic counselors to raise public and governmental awareness and help overcome the challenges in countries with high consanguinity.

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PROFILE AND OUTCOME OF PEDIATRIC CNS TUMORS: EXPERIENCE FROM A CANCER CENTER IN A LOW INCOME COUNTRY

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Background/Objectives: Limited data are available about epidemiology and outcome of pediatric CNS tumors in low income countries (LIC). A multidisciplinary pediatric neurooncology service was established at King Hussein Cancer center (KHCC)/ Jordan in 2004 with a twinning with Sickkids hospital /Toronto. KHCC as well is a referral center for pediatric radiotherapy and has a hospital based cancer registry since 2006. We aimed to utilize the registry data to profile pediatric CNS tumors treated over 7 years.
Design/Methods: We reviewed registry records between 2007 -2013. Patients diagnosed with primary CNS tumors < 18 years at presentation were included. Clinical characteristics, management and survival were documented for patients exclusively treated at KHCC.
Results: CNS tumors ranked second (19%) following leukemia (29%). We identified 476 patients: 349 treated by KHCC team, 91 one-time consultation and 36 solely radiotherapy referrals. Male: female ratio was 1.4 and 73% were Jordanians. Median age was 6.7 years (range,0.2-18 years) with 60 children (17%)≤3 years. Intracranial tumors occurred in 330 tumors (95%); 60% were infratentorial. The main histology was low grade astrocytoma (LGG) 30%, medulloblastoma 24%, high grade astrocytoma (HGG) 20%, ependymoma 8%, craniopharyngioma 3% and germ cell tumors (GCT) 3%. More males were reported in GCT (78%) and medulloblastoma (67%). Ten of seventeen spinal tumors were astrocytoma (2 HGG) and six were ependymoma. Treatment included surgery in 85% and half received radiotherapy and/or chemotherapy. 5yr OS for intracranial LGG was (93.8±3.6%), medulloblastoma (60.2±7%), ependymoma (53.2±12.2%), craniopharyngioma (80±12.7%) while 3yr OS for HGG was 14.1±7.2%.
Conclusion: Being a referral center, malignant CNS tumors requiring radiotherapy are overrepresented. Cancer registries are critical to appreciate incidence and outcome and should be encouraged in LIC. They can be enriched with data about relapse, salvage therapy and morbidities. Multidisciplinary approach and twinning help achieve acceptable survival rates in LIC despite local difficulties.

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DESCRIPTIVE EPIDEMIOLOGY OF CANCER IN ADOLESCENTS AND YOUNG ADULTS IN TWO TERTIARY CANCER CENTRES IN DELHI, INDIA

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Background/Objectives: Although, cancer in adolescents and young adults (AYA) is increasingly an area of focus, there is paucity of clinical and epidemiological data from developing countries. We describe the epidemiology of this group of patients from 2 hospitals in India.
Design/Methods: All patients aged 15 to 29 years with the diagnosis of cancer who were registered with two hospitals in New Delhi during a 12 month period from January 2014 to December 2014 were included. Basic demographic information on age, sex and nationality was available. Using cancer site and morphology codes, the cancers were grouped by the Birch classification of AYA cancers.
Results: There were 287 patients (57.5% male, 85.4% Indian origin) registered with 54 (18.8%), 97 (33.8%) and 136 (47.4%) patients in the 15-19, 20-24 and 25-29 years age groups respectively. The three most common cancer groups were carcinomas (40.8%), lymphomas (12.9%) and leukemias (10.4%) overall. The pattern was similar in females while for males most common cancer groups were carcinomas, bone tumours and lymphomas. For the 15-19 years age group most common cancer groups were carcinomas, lymphomas and leukemias; for the 20-24 years age group carcinomas, leukemias and bone tumours; for the 25-29 years age group carcinomas, lymphomas and germ cell tumours. Among carcinomas, those of the gastrointestinal tract were most common at all ages except 15-19 years were carcinoma of the thyroid was most common.
Conclusion: The occurrence of cancer in AYA in India has been described. The distribution differs from the only previous report from India which may partly be related to referral bias.

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DELAYED CANCER DETECTION ASSOCIATED WITH A LOWER SURVIVAL IN ONCOLOGIC CHILDREN IN QUITO, ECUADOR

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Background/Objectives: Evaluate the mean age at diagnosis of cancer, most frequent sex, distribution and 5-years survival rates in a group of ecuadorian children compared to frequencies and rates in developed countries. According Pan American Health Organization, the higher percentages of childhood cancer cases in the continent were detected in Latin America (65%) in past years. Despite of this, cancer is not the leading cause of disease-related death among children in many undeveloped countries. The underestimation of childhood cancer is a public health problem in undeveloped countries because it reflects the late diagnosis of cases, which increase mortality. While the percentage of cancer survival in developed countries is 75%, in low income countries is 60% due to late diagnostic and abandonment of treatment.
Design/Methods: Open, Retrospective.Medical Data of all patients between 0-14 years old that attend to Oncology Service at BO Hospital in Quito Ecuador from January, 2007 to October, 2012. Data used includes age at diagnosis, sex, Biopsy-based diagnosis and 5-year survival.
Results: A total of 667 (4,6%) from 14635 children were diagnosed with cancer, 56% men and 44% women. The most prevalent age group was 1- 5 years (34%), followed by 8 - 12 years (22%), 5-7 years (19%),0- 11months(14%) and >12 years (11%). Most frequent cancer was leukemia (30%) followed by Central Nervous System (21%), lymphoma (14%), Wilms tumor (9%), Neuroblastoma (5%), Osteosarcoma (4%), Retinoblastoma (4%), Rhabdomyosarcomas (2%) others (11%). The 5-year survival rates were Leukemia 70%, Central Nervous System 60%, Lymphoma 60%, Wilms tumors 95%, Neuroblastoma 60%, Osteosarcoma 40%, Retinoblastoma 70%.
Conclusion: The 5-year survival rates in Ecuador are lower compared to higher income countries. A large number of patients had delayed diagnose (8 - 12 year old), which improve the possibility of advanced stage of cancer and therefore lower survival.

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CAUSE AND PLACE OF DEATH IN A PEDIATRIC ONCOLOGY UNIT

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Background/Objectives: Although pediatric cancer is rare, it is the leading cause of non-accidental death in children. New treatment strategies have significantly improved overall survival, but are associated with significant side effects, including major infections and organ toxicity. The aim of this study was to analyze cause and place of death in children with cancer in a Pediatric Oncology Unit.

Design/Methods: Retrospective analysis of the clinical data of all the children who died between January 2005 and December 2014.
Results: In 10 years 317 children died; 177 were male (56%); median age of death was 9y (IQR 5-14y). Most of the deceased children had solid tumors (N=124, 39%), followed by central nervous system tumors (N=108, 34%) and leukemia/lymphoma (N=85, 27%). Progression of disease was the main cause of death (N=267, 84%). Twenty nine deaths were due to infection (9%), including 19 patients with septic shock, eight with pneumonia, one with varicella and one with a cytomegalovirus infection. Neutropenia was documented in 16 patients with septic shock (16/19; 84%). Eight children died after surgery (3%). Graft-versus-host disease caused three deaths (1%). Two children died due to neurotoxicity, one to cardiotoxicity and another to anaphylaxis. The median time between diagnosis and death was 17m in progressive disease and 7m in toxic deaths. The majority of deaths due to progressive disease occurred in the hospital setting (N=226, 71%), only 33 children (13%) died at home. All toxic deaths (N=48) occurred in the hospital, 48% (N=23) in an intensive care unit.
Conclusion: Disease progression was the main cause of death, followed by infection. Prevention, early diagnosis and aggressive treatment of infection must be, therefore, a main concern of Pediatric Oncology Units. There is the need to develop palliative care services to provide alternatives to hospital death in children with disease progression.

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CHILDHOOD CANCER SURVIVAL IN A SINGLE CENTRE BETWEEN 2006 AND 2010

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Background/Objectives: Survival rates for childhood cancers have greatly improved over the past years. In this study we compared survival data of patients treated in our centre between 2006 and 2010 with those previously published from Southern Portugal, other European countries and the United States.
Design/Methods: We retrospectively reviewed data for 2,193 children (aged between 0 and 14 years) admitted in our department between January 1st, 2006 and December 31st, 2010. We excluded 852 patients that did not have an oncologic disease and also excluded 132 patients coming from Portuguese-speaking African countries. We finally analysed data for 1,209 patients with cancer diagnosis. Neoplasic diseases were grouped according to the International Classification of Childhood Cancer (ICCC3) and in the case of central nervous system (CNS) neoplasms we also used a histological classification. We described age and gender distribution and estimated 5-year overall survival for major cancer groups.
Results: Five-year overall survival was 79.1% (95% CI 75.9–82.5). EUROCARE-5 study (European patients diagnosed between 2000-2007) reported a 77.9% rate while SEER (United States patients diagnosed between 1999-2006) published a 79.9% rate.
According to their survival rate we differentiated a group of diseases with a survival rate above 90% (including renal tumours, lymphomas and hepatic tumours); a group with survival between 75% and 85% rate (including acute leukemias, retinoblastomas, soft tissue sarcomas and epithelial tumours) and a group with a survival rate below 70% (including neuroblastomas, CNS tumours and malignant bone tumours).
Conclusion: Survival rates of our study cohort improved those previously reported by national groups with the exception of malignant bone tumours. Patients with Ewing sarcoma had more relapses than expected and those patients with metastatic disease did not survive. Histological classification for CNS tumours was better than ICCC3 in defining patient groups with a similar outcome. International cooperation is essential to improve outcome of bad prognosis diseases.

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IMPROVING ACCESS TO CANCER CARE FOR CHILDREN AND ADOLESCENT FROM DISTANT AND LOW-INCOME AREA

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Background/Objectives: Brazil is a continental middle-income country but income inequality remains at high levels. It has demographic characteristics areas that does not demand a pediatric cancer center therefore; we demonstrated the value of prompt referral pathways to pediatric patients with suspected malignancy to a cancer center, despite the large geographical distances and economic diversity between them.
Design/Methods: Children and adolescents with signs and symptoms of cancer from Amapa, a northern state of Brazil, are referred to our center in Sao Paulo, a southern state 2.600 km from there. All necessary needs and treatment are supported by public health insurance and NGO. There is no cost for the patient.
Results: The estimated incidence of cancer in the population under 19 years in Amapa is 36 new cases per year. Therefore, between 2010 and 2014, 69 patients were referred and 33 (44%), during the last year, Male/Female 38/31, median age 7 years, (1-16 years). Mean per capita income of these patients is U$ 100/month (Sao Paulo - U$ 700/month). 17% had no basic sanitation at home and their parents had informal employment in 44%. Main diagnosis were acute leukemia (55%), lymphoma (12%), solid tumors (12%) and non-malignant diseases (21%). Median time since they seek medical care to referral to our center was 30 days.
Conclusion: A public health policy to the adequate diagnosis and treatment of childhood cancer needs a comprehensive cancer center with trained staff, necessary equipment and drugs, to improve survival, develop research, and train future workforce. It is a priority to every country to improve access to an affordable, best standard of care. The recognition of the unique demographic and economic characteristics areas are mandatory to create referral routes and care pathways to improve survival. This model can be useful in other countries.

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THE EUROPEAN ROADMAP TO HORIZON 2020 FOR CHILDREN AND ADOLESCENTS WITH CANCER - A LONG TERM SUSTAINABLE STRATEGY

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Background/Objectives: With 35,000 new cases every year, childhood cancer is an urgent public health issue in Europe. Access to standard care is unequally available across the continent. Survivors experience long-term effects, and, in spite of the improvements achieved, cancer remains the leading cause of disease-related death for children beyond one year of age. To define a long term sustainable strategy to increase both the rate and the quality of cure in children and adolescents with cancer over the next decade.
Design/Methods: As part of the FP7 'European Network for Cancer research in Children and Adolescents' (ENCCA) project, a strategy was defined along with the Clinical Research Council (composed of all the European Clinical Trial groups and national societies in paediatric haematology oncology) and with parents and survivors from the Childhood Cancer International European group.
Results: Seven medical and scientific objectives have been set up: i) Introducing safe and effective innovative treatments into multidisciplinary standard care; ii) Driving therapeutic decision by improved risk classification, the use of molecular characteristics and precision medicine; iii) Increasing knowledge of tumour biology and speeding up translation to benefit patients; iv) Increasing equal access across Europe to standard care, expertise and clinical research; v) Addressing the specific needs of teenagers and young adults, jointly with adult oncology; vi) Addressing the quality of survivorship; vii) Understanding the causes of paediatric cancers and addressing prevention where possible. The strategy achieved a broad consensus between all involved stakeholders. The European Society of Paediatric Oncology (SIOPE) is steering the effective implementation through dedicated programmes and cross tumour platforms, and will

facilitate funding through European and national grants as well as from charities and industry.
Conclusion: This European Childhood Cancer Plan is the outcome of a close partnership among all involved stakeholders.
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KNOWLEDGE OF EARLY WARNING SIGNS OF CHILDHOOD CANCER IN FINAL YEAR MEDICAL STUDENTS. ENOUGH IS NOT ENOUGH

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Background/Objectives: The incidence of childhood cancer in South Africa is much lower than in high income countries, partially attributable to under-diagnosis and under-reporting. This study was conducted to determine the level of knowledge of signs of childhood cancer in final year medical students and to explore correlations between knowledge level, participant demographics and previous exposure to a patient with cancer.
Design/Methods: A structured questionnaire based on the St SILUAN mnemonic, testing both recall and recognition of early warning signs of childhood cancer, was administered to final year medical students. Pearson's chi square and Fisher's exact test were employed to determine correlations between demographic data, prior contact with patients with cancer and test scores. An equality ratio compared recall and recognition sections of the questionnaire.
Results: The mean number of signs and symptoms correctly recalled by the 84 participants was 5.7. The mean number of signs correctly recognised was 13.6/20 (68.1%), while 44.1% of respondents could correctly identify more than 75% of the signs. There was no correlation between scores and participants' gender, age and prior contact with a person with cancer. When test scores were combined using an equality ratio, a significant correlation was found between previous clinical experience and a higher score ($p = 0.044$; Pearson's chi square test).
Conclusion: Medical students demonstrated a marked inconsistency between recall and recognition of early warning signs of childhood cancers. However, the majority of students could recognise enough symptoms to meet the university pass standard. Despite acceptable recognition of signs of childhood cancer in final year medical students, the age standardised ratios of children with cancer in South Africa are unacceptably low, indicating that long term recall in medical practitioners is poor. We recommend increased exposure in medical school to paediatric oncology and improved awareness programmes to increase early referrals.

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A 10-YEAR RETROSPECTIVE STUDY OF HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR CANCER AND BENIGN HEMATOLOGIC DISEASES: A SINGLE REPORT FROM A MEXICAN PEDIATRIC HEMATOLOGY-ONCOLOGY CENTER

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Background/Objectives: Hematopoietic stem cell transplantation (HSCT) plays an important role in the treatment of malignant and not malignant diseases. In our hospital, the first HSCT was performed in 2003. The aim of this study was to evaluate the characteristics and the outcome of HSCT in our Center.
Design/Methods: Between January 2003 to December 2013, 95 pediatric patients under the age of 20, with either a malignant or non-malignant diseases were transplanted in our Unit. Clinical records were reviewed and data were retrospectively analyzed.
Results: 95 pediatrics patients were transplanted. Fifty-three (55.8%) were male; average age was 7.6 years (range 1 to 20). Twenty-two were ALL patients (23.2%), AML in 24 (35.3%), hematologic disorder (including immunodeficiencies) in 31 (32.7%), solid tumors in 4 (4.3%) myelodysplastic syndrome in 3 (3.2%), lymphoma in 2 (2.1%), CML in 9 (9.5%). Fourteen patients (14.7%) received an autologous transplant, a full matched related donor (MRD) was used in 49 (51.5%) whereas 32 (33.6%) a full or partially matched unrelated donor (MUD) was used, (4/6 to 6/6 30 cord blood units and 1 haploindentical). Conditioning regimens included myelo- and non-myelobaltive. Total body irradiation was used in all patients with an ALL. Graft was achieved in 21.6 days (range 8 to 71). Some grade of acute GVHD occurred in 33 patients (34.7%) whereas chronic GVHD was seen only in 3 (3.1%). Overall survival rate was 55% with 60 follow up time.
Conclusion: HSCT is feasible in mid-income countries like ours. Both neutrophil and platelet engraftment time were longer compared to other HSCT Centers, this might be explained due to the high number of cord blood units that were transplanted as well as the use of bone marrow instead to peripheral blood. Transplant related mortality has been decreased over the years, due principally to the multidisciplinary team expertise.

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ONCOGENETIC PEDIATRIC CONSULTATIONS: EVALUATION OF INDICATIONS AND PRACTICES IN THE BORDEAUX HEMATOLOGY-ONCOLOGY PEDIATRIC UNIVERSITY HOSPITAL UNIT DURING THE 2011-2012 PERIOD

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Background/Objectives: In literature, cancer genetic predispositions are present in about 10% of children suffering from cancer. Identifying such factors is an "important requirement" to improve children's management. Key points to identify patients with cancer genetic predispositions should be identified.To test first and foremost children at risk of predisposition, a tool allowing the collection of risk factors may be useful in a pediatric oncology service. The description and quantification of these genetic risk situations and their modality of care will help create this tool.
Design/Methods: This study was conducted on all children diagnosed with cancer between 2011 and 2012, in the oncology-hematology pediatric unit of Bordeaux University Hospital. The chosen risk factors included age under one year at diagnosis, multifocal lesions, type of cancer, secondary malignancy, family history of cancer and the call of the clinical examination points.
Results: 223 children with a cancer were treated between 2011 and 2012. There were 76 patients (33.9%) with at least one risk factor for genetic susceptibility to cancer. The two risk factors most frequently encountered were the age under one year at diagnosis (34.2%) and a family history of cancer (48.7%). 65.8% of our cohort presented one risk factor. Finally, only 23 patients (30%) with risk factors were sent in an oncogenetic unit for consultation. They were essentially patients with multifocal disease or multiple risk factors.
Conclusion: A large proportion of children treated for cancer required an oncogenetic consultation. However, a minority of patients with visible criteria for clinicians benefited from it. A systematic data collection file seems useful to improve identification of patients at risk. We proposed one example of data collection form.

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THE AFRICAN SCHOOL OF PEDIATRIC ONCOLOGY INITIATIVE: REPORT FROM THE FRENCH AFRICAN GROUP OF PEDIATRIC ONCOLOGY

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Background/Objectives: To improvethe skills of pediatric oncology (PO) health-care providersin Africa, the French African Group of Pediatric Oncology (GFAOP) set up the African School of Pediatric Oncology.
Design/Methods: This school located in Marrakech, Morocco, develops programs not only for physicians and nurses, but also for pathologists, surgeons, and technicians. This project is supported by Sanofi Espoir foundation (My Child Matters program), Lalla Salma Foundation for Prevention and Treatment of Cancer, the Moroccan Society of Pediatric Hematology and Oncology and the Gustave Roussy Institute's School of Cancer.
Results: From 2011 to 2014, four intensive courses were organized in Morocco: A three-day intensive course for nurses in 2011, afive-day course for pediatric oncologist in 2012, a three-day course for pediatric surgeon in 2013 and afive-day course for nurse educators in 2014.The content was adapted to address topics and issues specific to PO in Africa. Some nurses were selected for training in France (Laurette Fugain association scholarship).A total of 128 health-care providers, from 14 African countries attended the courses: Morocco (62), Algeria (9), Tunisia (6), Mali (6), Burkina Faso (6), Senegal (5), Ivory Coast (5), Togo (5), Madagascar (4), Democratic Republic of Congo (4), Mauritania (3), Cameroun (3), Guinea Conakry (2) and Republic of Congo (1). Among them 72 were nurses, 32 pediatric surgeons, 21 pediatric hemato-oncologists, 2 pathologists and one ophthalmologist.Each course was assessed for its scientific value, applicability to the participants' daily practice, quality of pedagogical material and

interaction with the participants.According to the post course survey 90% of the participants were satisfied or very satisfied.
Conclusion: The GFAOP continuously strives to improve the quality of the training in Africa. Accordingly, a PO diploma was set up in 2014-2015 with the participants of 26 candidates from 9 African countries.

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RISK ASSESSMENT OF ENVIRONEMENTAL CARCINOGENS, EPIDEMIOLOGY AND POLYMORPHISM IN CHILDHOOD LEUKEMIA AND SOLID TUMORS: A STUDY FROM ENVIRONMENTAL HEALTH CENTER, KOREA

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Background/Objectives: This study is aimed to identify environmental factors and genomic variations in the development of childhood leukemia and cancer, and their outcome from a province of Korea with a population of 3.5 million.
Design/Methods: From 2006 to 2014, a total of 472 children were diagnosed to have childhood leukemia and solid tumors from Gwangju-Chonnam area. A questionnaire including parental environmental and occupational exposure, and mother-child life-style was obtained. A total of 371 patients and 378 healthy controls were enrolled in the study. Environmental exposure was assessed by toxicological measurement of house-hold air and water samples. Blood and urine samples were collected from patients and controls and their respective parents. Single nucleotide polymorphisms (SNP) were evaluated for enzymes involved in metabolism, cell cycle regulation, differentiation, and signal transduction.
Results: The 6-yr Kaplan-Meier estimated overall survival (OS) for all 472 patients was 76.7±3.0%. The 6-yr OS for 235 leukemia patients was 73.4±3.5%, while that for 237 children with solid tumors was 79.7±4.5%. Maternal smoking history was the most significant factor associated with leukemia in children [Odds ratio (OR), 4.76 (95% CI, 1.23-18.46)]. Carcinogenic exposures in house-hold air and water were not significantly different from controls. Urinary 1-hydroxypyrene concentration was higher in patients ($P<0.001$), and blood cadmium concentration tended to be higher in patients and their parents. SNP analysis showed that genomic variations of *ARID5B* and *CDKN2A*, but not *IKZF1*, might play an important role in the risk of childhood acute lymphoblastic leukemia in Korea.
Conclusion: Considering the heterogeneity of childhood cancers and complex pathogenesis of each disease category, a large number of patients are required to elucidate precise association with environmental carcinogens. However, parental smoking was associated with the risk of leukemia. Moreover, ethnic difference in genotypic polymorphism and the susceptibility to malignancies should be contemplated.

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AN OVERVIEW OF YOUTH CANCER ISSUES IN MBINGO BAPTIST HOSPITAL

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Background/Objectives: Cancer in young adults has received significant world-wide attention over the last decade. In Mbingo Baptist Hospital the care of children (0 to 15 years) with cancer has improved since 2003, to attain a cure rate of 60%. Little attention, poor coordination of care and limited resources have been devoted to the young adults (15-22 years) with cancer, thus accounting for a significant poorer survival rate. This study looks at the pattern of cancer, the duration of symptoms prior to treatment, the ability to complete treatment and survival rate.
Design/Methods: All patients' information were collected from the hospital records. The diagnosis was based on clinical presentation, imaging, fine needle aspirates, Cerebrospinal fluid, bone marrow and abdominal fluid analyses. The study involves young adults from 15 to 22 year diagnosed of cancer in Mbingo Baptist Hospital in the Northwest region, Cameroon from 2009 to 2014.
Results: A total of 120 adolescents were recorded, from 5 patients in 2009 to 43 patients in 2014. The majority of patients (39%) had lymphoma, followed by osteosarcoma (11%) and hepatocellular carcinoma (10 %). Late presentation continues to be a big problem. The duration since onset of symptoms was found to be 0,5 months to 24 months. 31 patients had recorded disease stage, with 54% being stage 3, and 32% stage 4. Chemotherapy was given only to 41(34%) patients. 53% of these completed their treatment and 47% could not complete their treatment due to financial reasons, progressive disease, side effects and unknown reasons. Few patients were followed up and the survival rate less than 10 %.
Conclusion: The number of adolescents with malignancies is growing. A comprehensive care model is needed to optimize care for this population. Resources for free treatment, appropriate protocol for this age group have to be made available. Active follow up has to be implemented.

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CHILDHOOD CANCER REGISTRY OF CHELYABINSK REGION

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Background/Objectives: The Chelyabinsk region child population resides mainly in major industrial cities and is, therefore, exposed to a variety of anthropogenic and natural adverse factors. Active development of regional pediatric cancer calls for extra attention in patients' follow up and epidemiological indicators monitoring as it is necessary for adequate care planning and therapy results improvement. The Regional Childhood Cancer Registry was set up to address these challenges.
Design/Methods: The institutional registry was developed in 1992-1996. It provides a retrospective pediatric cancer data collection for that period. Since 1996 prospective data collection was initiated and starting from 2008 all cases of childhood cancer (patients of 18 years or less) were prospectively registered.
Results: As at 1 January 2014 a total of 1545 pediatric cancer patients cases were registered. A median patients' age was 6.1 years, 1443 patients were younger, than 15 years. Male/female ratio was 1.26. The most common pediatric cancer type was leukemia (32%). Central nervous system tumors accounted for about 25% of all pediatric cancer cases, lymphoma for about 15% of cases. Age-standartized rate (ASR, world standard) for the period of 2008-2012 was 15.72 per 100,000 child population. We examined the geographic distribution of childhood cancer and demonstrated one high risk cluster with statistically significant increasing of incidence in two adjacent cities (ASR in Miass city - 20,27 per 100,000, in Zlatoust city — 22 per 100,000).
Conclusion: Our results on the regional incidence, age-sex distribution and cancer morbidity structure correspond to previous published data. The cancer incidence increase described by this study requires further epidemiological research and greater observation span.

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SYMPTOMATIC VENOUS THROMBOTIC EVENTS ARE ASSOCIATED WITH SIGNIFICANTLY INCREASED REQUIREMENT OF CENTRAL VENOUS CATHETERS IN PEDIATRIC CANCER PATIENTS: A POPULATION-BASED STUDY FROM MARITIMES, CANADA

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Background/Objectives: Central venous catheters (CVCs) have revolutionized the care of pediatric cancer patients (PCPs). CVC associated symptomatic venous thrombotic events (sVTE) are known to occur during childhood cancer therapy and may lead to CVC loss. Loss of a CVC typically mandates immediate replacement requiring general anesthesia, surgical intervention and is a significant cost to health care system. The frequency of CVC replacement post sVTE is not well described. This study was designed to assess the requirement of CVC replacement in PCPs with and without sVTE.
Design/Methods: All PCPs in 3 Maritime Provinces (Nova Scotia, New Brunswick and Prince Edward Island) are treated at IWK Health Center in Halifax in a shared care model with regional provincial hospitals. After ethics approval, case records of all cancer patients (<20 years of age) managed from January 2000 to December 2014 were retrieved. Data were integrated from: (i) pediatric oncology hospital database, (ii) Provincial Cancer in Young People database, (iii) Electronic medical records, (iv) Pharmacy database (v) IWK central line database and (vi) Hospital Health records. Patients with signs or symptoms attributable to VTE and radiologically documented VTE treated with anticoagulants were identified. Information of all CVCs required in all PCPs was extracted.
Results: Forty (5.4%) of 731 PCPs had sVTE. Central venous system (81.6%) was the most common location of sVTE.Among the patients with and without sVTE, 72.5% and 27.5% respectively ($p=0.001$) required >1 CVC. The mean numbers of CVCs/individual in patients with and without sVTE were 2.5±1.3 and 1.6±1.1 respectively ($p=0.021$). Presence of sVTE increased the odds of requiring >1 CVC to 3.6 (95% confidence interval: 1.76-7.3).
Conclusion: This population-based study demonstrates that increased CVC requirement is an adverse clinical outcome of sVTE. Given the clinico-economic implications of

CVC loss, future trials should focus on identification of "at-risk" patients and prevention of sVTE.

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PILOT PROGRAM OF NEWBORN SCREENING FOR SICKLE CELL DISEASE (SCD) IN ANGOLA - ANGOLA SICKLE CELL INITIATIVE (ASCI)

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Background/Objectives: An estimated 12,000 babies are born with SCD annually in Angola alone. Without treatment, most of these babies die before five years of age. Early diagnosis through newborn screening followed by treatment including daily penicillin reduces mortality. In March 2011, the Republic of Angola entered into a public-private partnership with Chevron and Texas Children's Hospital/Baylor College of Medicine to pilot a comprehensive newborn screening and treatment program in order to reduce morbidity and mortality of children with SCD in Angola.
Design/Methods: This unique program provides screening, diagnosis, care, treatment, health professional training, research, and community mobilization to improve care of children with SCD in Angola. The Ministry of Health provides governmental institutional support for execution of the project throughout the Angolan healthcare system, including access to babies and support of maternity staff for blood spot collection; staff, supplies and medications for the care and treatment provided in government health facilities; and space for laboratory operationsChevron provides funding for the projectBaylor College of Medicine and Texas Children's Hospital contribute expertise, personnel, training including pediatric hematology-oncology subspecialists based in Angola and manage program funds and operations by providing organizational capability, technical support for data management and procurement of drugs and supplies, and leadership guidance.
Results: As of February 2015, the program has screened more than 100,000 newborns. Of these, 2,000 were diagnosed with SCD 19 birth and health centers in Cabinda and Luanda provinces collect samples from newborns for testingMore than 1,000 healthcare professionals have been trained in SCD screening and treatment.
Conclusion: While the program has achieved remarkable screening results, challenges include locating and enrolling affected babies in treatment. Moreover, competing health priorities impede full integration of sickle cell program into the Angolan government healthcare system. Finally, the program needs to diversify its funding source to expand nationally.

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WHAT INFLUENCE CARE PATHWAYS BEFORE DIAGNOSIS IN CHILDREN AND ADOLESCENTS WITH MALIGNANCIES?

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Background/Objectives: To describe the care pathways in children and adolescents with solid cancers, in order to analyze its determinants and impact of a potential delay before diagnosis.
Design/Methods: Retrospective study on patients aged less than 25 years at first consultation in the oncology department of pediatric, adolescent and young adult in Institut Curie during one year was performed and analyzed relationships between cancer characteristics, components of care pathways, and socio-demographic characteristics. Analyze of a relationship between delayed diagnosis and its potential consequences was performed.
Results: A total of 106 patients were selected, diagnosed at a median age of 6 years. Most frequent tumors were low grade cerebral tumors and sarcomas. Pain was the most frequent initial disorder observed (34.3%). Only 27.6% of first signs were unspecific (concerning 18.6% of patients) of cases. Median value of the time before the first consultation was 3 days [0-1727]. Median total time to diagnosis was one month [range: 0-64] and median number of consultations before diagnosis 2 [range: 1-7]. Time to diagnosis was shorter if father was of foreigner nationality vs. French (34 vs. 72 days, $P < 0.03$), and longer if parents were separated (74.5 vs. 42.5 days, $P < 0.03$). Retrospective analysis found that a shorter diagnosis may have been possible earlier in 44.3% of patients. Overall, potential vital risk due to a possible delayed diagnosis has been estimated at 14.1 %, and functional risk at 20.7%.
Conclusion: Overall time to diagnosis is quite fast, even if first signs of pediatric cancers are very polymorphic and seem associated to social but also age and economic status, in a slightest measure.

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A REVIEW OF 15 YEARS OF PRIMARY CHILDHOOD CANCER DATA AT A TEACHING HOSPITAL IN GHANA

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Background/Objectives: Since 1998, the Paediatric Cancer Clinic of the Komfo Anokye Teaching Hospital (KATH) had collected patient demographic and clinical data. This primary data is relevant for internal restructuring and development of protocols for the advancement of clinical care and research. We reviewed the data derived from patient visits from January, 1998 to October, 2013.
Design/Methods: Data that had been collected and kept in a registry using Microsoft Excel® program from January, 1998 to October, 2013 was analyzed with STATA IC 12.0 statistical software.
Results: Overall, data on 1,197 patients were entered into the register; 63% males and 37% females. The age range was from 1 month to 192 months (16 years) with a mean of 84 months (7 years). On the average 75 patients were enrolled per year. Burkitt lymphoma was the commonest cancer making up 34% of the total with; 22% being abdominal, 8% jaw and 4% from other sites. Nephroblastoma was diagnosed in 23% of the children, Leukaemia 16%, Non-Hodgkin non-Burkitt lymphoma 7%, and Hodgkin lymphoma 6%. Neuroblastoma, Rhabdomyosarcoma and Retinoblastoma made up 14% of the total number of cases seen. While 33% of the patients completed their treatments, 34% abandoned treatment and 31% died. Of those that abandoned treatment, 81% completed half or less of their therapy and 10% completed their treatment courses but have been lost to follow up. The rest, 9% did not start treatment at all.
Conclusion: Burkitt lymphoma was the commonest cancer seen in our hospital between 1998 and 2013. Only a minority of the children completed their prescribed treatments leading to high treatment abandonment rater and cancer related mortality in the clinic.

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CHILDREN ENROLLED INTO THE PEDIATRIC CANCER CLINIC OF A TEACHING HOSPITAL IN GHANA IN 2014

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Background/Objectives: The Komfo Anokye Teaching Hospital (KATH), Kumasi, Ghana, enrolls an average of 75 children per year into its Paediatric Cancer Clinic. In 2005, the highest enrollment of 125 children was recorded. We reviewed the clinical data of all new enrollments to the Paediatric Cancer Clinic from 1st January, 2014 to 31st December, 2014.
Design/Methods: The clinical data of newly enrolled children was extracted retrospectively, from their clinical records for the period under review using Microsoft Excel®. The data was analyzed with STATA IC 12.0® statistical software.
Results: A total of 135 children were enrolled into the clinic. There were 78 males (58%) and 57 females (42%). The highest enrollment of 18 occurred in May and the least was 5 recorded in September. The average enrollment per month was 11. The mean age was 80 months. Overall, 43% of the children enrolled were diagnosed with Burkitt Lymphoma, followed by 14% with Leukaemias. Ten, 10% were diagnosed with Retinoblastoma whereas 7.5% had Wilms Tumour. By the end of 2014, 20% of the children had died. The final causes of death were advanced disease 55%, cardiopulmonary failure 35% and Tumour Lysis Syndrome 10%. Currently, 41% continue to access clinical care in the clinic while 39% have abandoned treatment.
Conclusion: The average patient enrollment to the Paediatric Cancer Clinic of KATH in 2014 is almost double the known average of 75 new patients per year. Treatment abandonment rate however, has increased while the mortality rate has decreased. There was an increase in the number of children diagnosed with leukemia and retinoblastoma in 2014.

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CANCER IN SYRIAN REFUGEE CHILDREN

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Background/Objectives: We aimed to determine the features of Syrian refugee children treated due to cancer who have been followed by us.
Design/Methods: The records of Syrian refugee chidren in some regions of Turkey treated with a diagnosis of cancer were evaluated between March 2013 and January 2015 retrospectively.
Results: The total of 36 patients (M/F: 1.6) with median age of 5(1.2-18.0) years were analyzed. The types of *cancer diagnosed* in the patients were leukemia (n=27), lymphoma (n=3), langerhans cell histiocytosis (LCH)(n=2), rhabdomyosarcoma (n=2), neuroblastoma (n=1) and Ewing's sarcoma (n=1). Fifteen of 27 leukemia patients admitted with relapse. Seven of 15 relapsed leukemia patients couldn't receive chemotherapy because of the war. Two of the patients with lymphoma had multiorgan metastasis. One of these patients deceased with tifilitis during induction chemotherapy. Although all the patients with LCH and rhabdomyosarcoma were diagnosed in Turkey, they couldn't receive chemotherapy immediately due to problems related with migration. The patient with Ewing's sarcoma died with progression. The patients with stage 4 neuroblastoma was sustaining the chemoterapy during this study.
Conclusion: Shelter, health, education and food aid for Syrian refugees in Turkey is provided, and health services is given in the standard of Turkish citizens.Socio-economic and accommodation problems of family is tried to be solved by extending stay in the hospital. Althgough the translator has been supplied by Turkish goverment, language difference has caused communication difficulties during the treatment. However treatment of Syrian refugee children with cancer couldn't be apllied in time because of the war and migration. So relapses are inevitable for them. In this study we want to call attention to Syrian children with cancer who were obligated to migration.

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RELATIONSHIP BETWEEN MULTIDRUG RESISTANCE ORGANISMS (MDROS) AND DEMOGRAPHIC VARIABLES OF CHILDHOOD CANCER IN TERTIARY CANCER CENTRE

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Background/Objectives: There has been a rising prevalence MDROs bugs in the general population. The alarming high prevalence of community acquired MDRO colonization especially carbapenem resistant organisms was raised from 20% to 40% during the course of the therapy. Aim: To assess the rate of MDRO carrier status at presentation and rate of conversion to MDRO during the treatment. To find the association between the prevalence of MDROs and demographic variables.
Design/Methods: Prospective study. Rectal swab of patients presenting to pediatric hematolymphoid were sent within 7 days from date of registration for 2015. Also stool cultures/rectal swabs of all patients who got admitted at presentation to the pediatric ward were sent. Repeat rectal swabs were sent for the patients from this cohort when they got readmitted at least 15 days from past discharge or when clinically indicated.
Results: Total of 618 baseline surveillance rectal swabs were sent the baseline no growth was seen in 7.3% and MDROs grown in 18.7%. Follow up swabs were sent of 570 patients of which 0.5% showed no growth and 20.5% showed MDROs showing a doubling up of MDROs from baseline culture. Of the 618 patients 46.9% were from west, 37.5% (232) from BIMARU states (Bihar, Madhya Pradesh, Rajasthan and Uttar Pradesh). Total MDROs 45.7% (53) were seen in patients from BIMARU. There were 27 deaths and 13 ICU admissions respectively out of these 618 patients. Of the 27 deaths, 22.2% patients had MDRO whereas only 3.7% had pan sensitivity. Of the ICU admissions 22.5% had grown MDROs whereas only 7.3% had pansensitivity (P 0.08).
Conclusion: This illustrates the baseline MDRO colonization showing its association with the BIMARU state which contributes MDRO buds colonization in waters of Ganga and Yamuna flowing alongside these states and also due to poor sanitation conditions thereby showing a significant trend in the morbidity and mortality rate being affected.

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CHILDHOOD CANCER IN REUNION ISLAND AND MAYOTTE

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Background/Objectives: Little is known about childhood cancer epidemiology in Reunion Island (RI) and the archipelago of Mayotte, two French overseas territories located in the Indian Ocean on either side of Madagascar, characterized by mixed populations. This study aimed to describe the incidence and overall survival (OS) of childhood cancers in these two areas.
Design/Methods: Data was extracted from the population-based Cancer Registry of Reunion Island. All incident cases of cancer in children younger than 15, diagnosed from 2005 to 2011 and living in Reunion Island or Mayotte were included. Cancers were classified according to the International Classification of Childhood Cancer, Third version. Incidence rates were standardized (world standard) and survival rates estimated by the Kaplan Meier method.
Results: From 2005 to 2011, 236 cases of childhood cancers were registered in these two populations (176 in RI, 60 in Mayotte). For RI, the age-standardized incidence rate (ASR) for all cancers was 125.0 per million [106.3-143.7]. Leukemias, central nervous system (CNS) tumors and soft tissues sarcomas were the most frequent malignancies with respectively 30%, 22.7% and 8.5%. For Mayotte, ASR for all cancers was 101.8 per million [76.0-127.6]; the most frequent cancers were CNS tumors (20%), leukemias (15%) and both neuroblastoma (11.7%) and malignant melanomas (11.7%). For the two regions, ASR for the main cancer groups seems lower than in mainland France (155.8 per million), excepted for germ cell tumors and malignant melanomas for which higher incidence was observed in Mayotte. The 5 years OS rate for all patients was 78.8% [72.2; 84.0].
Conclusion: Incidence of all childhood cancers in RI and Mayotte is lower than in mainland France although few disparities exist in the distributions between cancer groups, notably for Mahori patients. OS for these two territories is comparable to the results described in mainland France.

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CHILDHOOD CANCERS IN DUBAI: PRIORITIZING ONCOLOGY SERVICES

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Background/Objectives: An estimated 250,000 new children are diagnosed with cancer every year worldwide. When diagnosed early and treated with appropriate protocols, 70% of children will be cured of their cancer. Children living in Dubai and the Northern Emirates are fortunate to have an advanced medical care center located in Dubai Hospital where such treatment is available. We looked at our hospital based registry to see our pattern of cancers compared to the rest of the world. There are an estimated one and a half million children under the age of fourteen years in Dubai and the Northern Emirates.
Design/Methods: A database was setup in October 2012 to record details of all children presenting to the Pediatric Oncology department of Dubai Hospital for treatment. The dataset for the years of 2013 and 2014 were analyzed.
Results: We saw sixty-three new children with cancers in two years. The number almost doubled in 2014 as compared to the previous year. The increase in numbers was seen in the non-Emirati group of children. Leukemia composed 62% (thirty two) of all the cancers followed by renal tumors and then lymphomas. We fortunately had no treatment related death during chemotherapy. Twenty three children (37%) travelled abroad either for further therapy not available in the United Arab Emirates, back home or as a personal choice.
Conclusion: Although the spectrum of cancers seen in childhood in Dubai is comparable to the rest of the world, the figure is rising dramatically either due to more awareness or net immigration. We need to prioritize and allocate more resources to pediatric oncology services to cope with the increasing numbers.

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EPIDEMIOLOGY OF CHILDHOOD CANCER IN RUSSIA

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Background/Objectives: To determine current rates of childhood cancer incidence and mortality at a national level for Russia and to evaluate recent trends.
Design/Methods: Using the Annual reports of Ministry of health and Federal State Statistics Service we calculated childhood cancer incidence and mortality rates for the 5-year period 2008–2012 and trends between 1989 and 2012 by sex, age and site. Rates were directly age-standardised to the 2000 World Standard Population, and linear regression was used to determine the magnitude and significance of trends.
Results: The age-adjusted incidence rate in children aged 0-17 years was 125 per 1000000 individuals per year for 2008-2012. The highest age-specific incidence (159 per 1000000 children/year) was observed in0-4 years. Between 1989 and 2012 a significant increase in the cancer incidence was observed in children aged 0-14 years: average annual percent change was 1.6%. The greatest increase for this period was observed for soft tissue sarcomas (3.7%), hepatic tumors (3.6%), thyroid carcinomas (3.7%), CNS neoplasms (2.9%), renal tumors (2.1%) и leukaemias (1.9%). The decrease of incidence

was observed for Hodgkin (- 1.6%) and non-Hodgkin (-1.4) lymphomas. Childhood cancer mortality for 2008-2012 was 40 cases per 1000000 children/year. The highest age-specific mortality rate (52,3 per 1000000) was observed in infants. The significant decrease of mortality were found from 1989 (70 per million) to 2012 (37 per million). The greatest average annual decrease for this period was observed for leukaemias (-3.8%) and lymphomas (-6,8%). The significant decrease of mortality in 1999-2012 was found for malignant bone tumors(-5.9), renal tumors (-2.9%) and CNS neoplasms (-1,1%) with the only exeption for soft tissue sarcomas (average annual increase was 3.2%).
Conclusion: The rates of cancer mortality are generally decreasing in Russia there are still very high levels for common childhood cancer types.

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TECHNOLOGY DECIPHERED FOR PEDIATRIC ONCOLOGISTS

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Background/Objectives: Pediatric oncologists maintain busy schedules practicing their speciality. This leaves them little time to understand the nuances of radiology which has rapidly evolved during the last three decades. The objective of this presentation is to provide a radiology primer to the pediatric oncologists.
Design/Methods: The presentation enumerates the different imaging modalities available to the pediatric oncoligsts. The strength and weaknesses of these modalities are elaborated. Radiation hazards for the children are also discussed.
Results: Ultrasound and chest X ray are frequently the initial modality of investigation for a child with suspected abdominal or thoracic malignancy respectively. Computed tomography and/or Magnetic Resonance Imaging are used for complete mapping of the disease load. Newer modalities like Positron Emission Tomography and Whole body Diffusion Weighted MRI are evolving promising tools.
Conclusion: A number of radiological modalities are available to the pediatric oncologists. Local availability of equipment and expertise are important in making a choice. All efforts should be made to keep the radiation dose to minimum.

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PEDIATRIC ONCOLOGY IN THE LAKE REGION OF TANZANIA: EVALUATION OF CLINICAL DIAGNOSIS, TREATMENT AND OUTCOMES

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Background/Objectives: The majority of new pediatric cancer diagnoses are made in resource poor countries where survival rates range from 5-25%, compared with 80% in high-resource countries. This study provides a snapshot of the pediatric oncology burden at Bugando Medical Centre (BMC), a tertiary referral center in the Lake Zone of Tanzania, one of two cancer treatment centers in Tanzania. Results will provide pilot data to highlight areas of need and direct future interventions to improve pediatric oncology outcomes.
Design/Methods: Study design is a retrospective review of recorded hospital admissions and clinic visits to the oncology ward at BMC from January 2013-December 2013. Fifty charts were randomly selected for preliminary analyses, with 46 available for review.
Results: 32% of the patients were female (n=15), and the average age was 5.7 years old. The most common recorded diagnoses were retinoblastoma (n=8) and Burkitt lymphoma (n=8), followed by Wilms tumor (n=7), lymphoma (n= 5) and Acute Lymphoblastic Leukemia (n= 5). Of these, 78% (n=36) were diagnosed clinically, and only 22% (n=10) had available histopathologic confirmation. All patients received at least one chemotherapy treatment. However, 78%% (n=10) did not complete prescribed course of therapy due to progressive disease (n=13), therapy toxicity (n=4), medication unavailability (n=1) or abandonment of care (n=28). Treatment outcomes included 9% overall survival with documented response to treatment (n=4), 22% lost to follow up (n=10), and 69% died (n=32). Of recorded deaths, 13% (n=4) occurred during treatment, 41% (n=13) resulted from disease progression, and 47% (n=15) took place following treatment abandonment.
Conclusion: Abandonment of therapy and death from progressive disease were the two most common outcomes for this study. Future interventions to improve outcomes should target methods to reduce factors contributing to treatment abandonment including access to medications, transportation, reducing cost of therapy and educational interventions.

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EPIDEMIOLOGY OF MEXICAN CHILDREN WITH CANCER: GEOGRAPHIC VIARIABILITY AND OUTCOMES FOR 15,702 PATIENTS

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Background/Objectives: Cancer is the leading cause of death in Mexican children between five and 14 years of age, causing over 2,000 annual demises. The Federal Government financially supports cancer treatment for all children. Patients are treated within a network of 65 public hospitals, following national treatment protocols. To present epidemiologic data and variability among thousands of patients treated for cancer under the National Childhood Cancer Program.
Design/Methods: Patients registered in the Childhood and Adolescence National Cancer Registry between 2008 and 2013 were analyzed. Prevalence, incidence, tumor type, geographic variability, mortality, and abandonment rate were recorded.
Results: Total number of cases significantly increased annually over the study period ($p<0.05$).Diagnosis was documented in 15,702 children, with a relative risk of 1.2 for males (56%).The highest incidence was in children less than four years, with higher mortality in adolescents. Incidence was 7.5 / 100,000 Mexicans under 18, varying by state of residence (3.30 - 16.04). Median age was 4.9. Most common neoplasia was leukemia (51%), followed by lymphoma (12%), CNS tumors (10%), sarcomas (10%), and germ cell tumors (5%). Overall 5-year survival was 50.8%, varying among region, age, gender, and diagnosis (18.7% - 64%). Overall mortality was 5.3 per 100,000, being higher for males (5.9) than females (4.6), and also for adolescents (8.8) vs other age groups (4.4).Abandonment was 5.0% at one-year, and 13.16% at five-year follow up, also with great variability regarding gender, state, and type of tumor. Extensive variability was found when disaggregating groups by tumor type, age, sex, and geographic location.
Conclusion: There is a high incidence of childhood cancer in Mexico. Extensive variability is seen among different groups, regarding age, gender, tumor type, geography, survival, and mortality. Understanding such differences is paramount to optimize care delivery and improve outcomes.

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ESTABLISHMENT OF A NATIONAL PAEDIATRIC HAEMATOLOGY-ONCOLOGY PROGRAM IN BOTSWANA

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Background/Objectives: Worldwide, approximately 160,000 children are diagnosed with cancer annually. The overall cure rate is approaching 80% for children with cancer in high income countries. In contrast, in low and middle income countries (LMICs), where children are often diagnosed too late or remain undiagnosed, the majority die from these curable cancers, particularly in sub-Saharan Africa.
Design/Methods: A novel partnership between the Botswana Ministry of Health, Texas Children's Cancer and Hematology Centers (TXCH) and the Baylor International Pediatric AIDS Initiative (BIPAI) led to establishing Botswana's only pediatric hematology-oncology program in 2007 at Princess Marina Hospital (PMH), the main government hospital in Gaborone. Since its inception, the program has been led by a full time in-country pediatric hematologist-oncologist (PHO) from TXCH. In 2013, a Care Coordinator position was added and a second PHO joined in 2014. In addition to clinical services, the program provides training and education locally and nationally and is establishing a comprehensive oncology database to research the presentation and treatment of paediatric malignancies in Botswana.
Results: Since 2007, over 450 new haematology-oncology patients have enrolled in the program with 94 presenting in 2014. Prior to 2007, 22 cases of paediatric cancer had been diagnosed at PMH according to available hospital records. An average of 40 children were diagnosed with cancer per year at PMH in 2013-2014 (leukaemia [19.8%], sarcoma [16.0%], Wilms tumor [12.3%], lymphoma [11.1%], brain tumors [9.9%], retinoblastoma [6.2%], Kaposi sarcoma [3.7%] and others [21%]).
Conclusion: The TXCH-Botswana program demonstrates that a long-term sustainable twinning partnership between a center in a high-income country and a resource-limited setting in sub-Saharan Africa is achievable with resultant exponential program growth. By focusing on high-quality clinical care in an academic environment with an emphasis on training and education, local capacity is being created to establish a regional model of excellence in paediatric haematology-oncology care.

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EPIDEMIOLOGY OF CHILDHOOD CANCER PRESENTING TO A TERTIARY CARE PEDIATRIC CENTER IN INDIA

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Background/Objectives: Cancer incidence world over is showing an increasing trend. Data regarding incidence, distribution of cancer with regard to age, sex, region and death are limited in developing countries owing to lack of countrywide cancer registries.
Design/Methods: Data pertaining to age, sex, symptom diagnosis interval, type of cancer, treatment taken, final outcome and trend of disease was retrieved from the case records of 3568 patients who presented to our unit from January 2004 to June 2014.
Results: The common cancers seen are acute lymphoblastic leukemia (35.8%)(ALL), retinoblastoma (9.4%), acute myeloid leukemia (7.8%), followed by neuroblastoma (6.3%), Wilms tumour (6%)(WT), non-Hodgkin lymphoma (6.4%)(NHL), Hodgkin lymphoma (5.2%)(HL). Brain tumours, Ewing sarcoma, hepatoblastoma & chronic myeloid leukemia constituted 1 to 2% malignancies.The male to female ratio was 2.2:1, being 6:1 in HL. Peak age was between 36 to 72 months. The median age of patients with ALL was 5.2 years, 7.5 years for lymphomas whilst WT, neuroblastoma, germ cell tumours presented below 3 years. A 25% increase was observed over 10 years. This was consistent in all malignancies.The symptom diagnosis interval (SDI) differed. The mean SDI for leukemia's was 7 weeks and 11 weeks for NHL. HL had a median SDI of 24 weeks. One fourth (26.2 %) patients refused therapy. One fourth of the patients treated defaulted. Refusal of therapy, default, death and relapse were taken as events and the event free survival (EFS) was 35%. The EFS amongst treated patients is 47%. Sixteen percent patients expired.
Conclusion: The demographics of malignancies are consistent with worldwide data. The number of patients reporting has escalated by 25% over 10 years. Increased awareness and better diagnostics may account for increase. We need to establish a countrywide population based registry to provide good epidemiological data. To treat all and prevent default remains a challenge.

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INFECTIOUS DISEASE AGENTS IN FEBRILE NEUTROPENIA IN PATIENTS WITH CHILDHOOD CANCER AT A NATIONAL REFRENCE HOSPITAL

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Background/Objectives: Approximately 80% of patients with childhood cancer and chemotherapy treatment will have an episode of febrile neutropenia (FN). The percentage of positive blood cultures is correlated with the risk of overall infection. The purpose of the present study is to describe the precentage of positive blood cultures and the infectious disease agent.
Design/Methods: We reviewed all blood cultures of patients with childhood cancer from August 2012 to December 2013 at our institution. We described percentages of negative or positive blood cultures and identified the disease agent in case of positive testing. The demographic and clinical characteristics are described as means or proportions according to variable type.
Results: We included 171 blood cultures. The patient average age was 10.4 years. In 52% of the cultures the result was negative, and 48% were positive. Fifty-one percent of our patients were female and 49% were male. According to the type of cancer, high-risk acute lymphoblastic leukemia representes 42.1% of our population, osteosarcoma 22.8%, 9.9% germ cell tumors and the rest were patients with Hodgkin disease and rhabdomyosarcoma. Gram positive bacteria were isolated in 53.9% of positive cultures, and Gram negative bacteria in 46.1% of positive cultures. The most frequent Gram positive bacteria was *Staphylococcus epidermidis* folowed by *Staphylococus aureus* and *Staphylococcus hominis*. The most frequent Gram negative bacteria was *Escherichia coli* followed by *Klebsiella pneumoniae*, and *Acinetobacter baumanii*. Gram positive bacteria were more frequently isolated in female patients, whereas Gram negative bacteria were most frequently isolated in male patients.
Conclusion: The percentage of positive blood cultures in our practice is relatively high compared to other series. The most frequent infectious disease was a Gram positive agent. Although not statistically significant, we found a difference of disease agent according to the gender.

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METHODOLOGY AND PROCESS FOR ASSESSING FEASIBILITY OF INTRODUCING PEDIATRIC HEMATOLOGY/ONCOLOGY SERVICES IN A RESOURCE-LIMITED SETTING: EXPERIENCE IN SUB-SAHARAN AFRICA

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Background/Objectives: As mentioned in recent articles, there has been a significant increase in the incidence of cancer in Sub-Saharan Africa, (SSA), however there is poor access to pediatric hematology-oncology (PHO) care. Consequently, a great need exists to build capacity in the local healthcare infrastructure and workforce to meet this evolving need. Since 2008, Texas Children's Global HOPE has aimed to increase overall survival and quality of life for children with cancer and blood disorders and to build sustainable health professional capacity in PHO care.
Design/Methods: Our program recognized the importance of partnering with local stakeholders to conduct a thorough assessment of the current capacity to better inform a jointly developed vision and strategies to achieve the aims. We developed a systematic methodology and detailed electronic database for conducting site assessments and performing strategic planning. This assessment approach has been successfully utilized in both international and domestic sites to determine the unique needs of PHO programs and their environments. This process identifies and assesses country level and institution specific clinical, education, research and administrative operations and resources, identifies gaps and needs for improvement and proposes solutions to advance PHO care at a level of excellence the partners jointly agreed to attain. A detailed implementation plan is developed for program improvement including timelines and budgets.
Results: This methodology has been utilized in 3 SSA countries. Outcomes include completed country-wide assessments with sustainable intervention plans built into agreements with LMIC governments.
Conclusion: While partnership is essential to making significant progress in the advancement of PHO services in LMICs, we recommend utilizing helpful tools such a systematic methodology and approach to assessment and planning, to facilitate effective and efficient programmatic plans and outcomes.

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INDIAN PEDIATRIC HEMATOLOGY ONCOLOGY GROUP: A COOPERATIVE EFFORT TO IMPROVE CHILDHOOD CANCER CARE IN INDIA

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Background/Objectives: There is an urgent need to improve survival of children with blood and a cancer disorder in India. Indian Pediatric Hematology Oncology Group (IPHOG) was formed in March 2013 with goals to a) improve survival of childhood cancer, b) improve survival of children with blood disorders, c) make hematopoietic stem cell transplant (HSCT) available to children who need it, d) train more physicians in pediatric haemato-oncology and e) form a cooperative study group for research in childhood blood and cancer disorders.
Design/Methods: The members met online every fortnight through the Cure4kids website hosted by St. Jude Hospital, USA. Group identified barriers to improve cure and developed strategies to overcome them. Educational Seminars and Tumor Boards were also conducted.
Results: IPHOG has 104 members now across 17-States (Maharasthra-21,Delhi-22,Haryana-8,Karnataka-6&Tamilnadu-4) and across 7-countries (India-85,USA-9,Canada-5,Australia-2,UK-1,Singapore-1&UAE-1). They are oncologists-88, surgeons-3, pathologists-2, radaition-oncologist-1, nuclear medicine-1, molecular genetics-1 and fellows- 8. A total of 42 meetings were held over 2-years. It published a paper in Pediatric Hematology Oncology journal in 2104 (Barriers to cure for children in India and strategies to improve outcomes). It identified delayed diagnosis, abandonment, sepsis, lack of uniform treatment protocols and relapse as five major barriers. IPHOG applied for a grant to establish a LCH treatment network in India to Histiocytosis Society in July 2013 which was unsuccessful however a positive feedback was received from Histiocytosis Society. National Neuroblastoma Network has been established by IPHOG to know about epidemiology and outcome of neuroblastoma in India. So far 37 centres across 13 states have reported 120 new cases. IPHOG has started a one-year fellowship in Pediatric Hemato-oncology (2 students) and a one-year fellowship in Pediatric HSCT(1 student).
Conclusion: IPHOG has identified local causes of treatment failure for children with cancer in India and has put strategies in place to improve care and outcomes in the participating centres.

Posters: Germ Cell Tumours

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CLINICAL FEATURES AND TREATMENT RESULTS İN GERM - CELL TUMORS OF CHILDHOOD: 24 YEARS EXPERİENCE OF A SINGLE CENTER

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Background/Objectives: Germ cell tumors (GCTs) are formed an important group of gonadal neoplasms and are also found in a number of extragonadal sites like mediastinum, sacrococcygeal regions and retroperitoneum which represents approximately 1-3 % of all childhood malignancies. The aim of this study was to evaluate the demographic data of the children with GCTs in our center retrospectively and treatment results are compare the results of the literature.
Design/Methods: Seventy two children (29 male, 43 female) from September 1991 to September 2014, new diagnosed with GCT were enrolled to the study. Cases to the changing surgery to radical surgical excision, biopsy approached with the multimodal treatment approach, as well as combination chemotherapy (cisplatin, bleomycin, etoposide) was performed. Serum alpha-fetoprotien (sAFP) on admission was studied.
Results: The study included 72 pediatric cases of histological confirmed GCTs of the gonadal, extragonadal. Mean age of the cases was 44 month (range:1-80 month).Abdominal pain and enlargement or mass was the commonest presentation(41% of cases).Most of the cases, the tumor site was gonadal(43 cases gonadal, 24sacrococcygeal, 3 mediastinal, 1 labium major, 1 orbital).Histopathologic subtypes were:19 mature teratoma, 13 immature teratoma, 29 yolk sac tumor, 5 dysgerminoma, 6 mixed GCT. POG/CCG surgical staging of the studied cases were applied. Mature teratoma cases were not taken to be evaluated staging and survivals. Twelve cases(23%) were in stage I, 11(21%) in stage II, 16(30%) in stage III, and 14(26%) in stage IV. The median sAFP level at diagnosis was 7900ng/L(22-123000).The mean follow up time was 83 month (range10-287 months).Local recurrence was observed in 8 cases, 6 patients died of recurrent.4 patients out of the follow-up after completion of therapy while in remission.
Conclusion: Five-year overall survival rate is 87%, event-free survival rate was found to be 84%. Survival rates in the whole group are in parallel with advances attained in the World.

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KLINEFELTER SYNDROME AND GERM CELL TUMORS

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Background/Objectives: Klinefelter syndrome (KS) is the most common sex chromosome disorder, occurring in about one out of 600 males. Various malignancies have been associated with KS. Breast cancer has been most highly associated with the 47,XXY mosaics, suggesting up to 20-30 times greater incidence in patients with KS compared to patients with normal karyotype. A large number of extragonadal germ cell tumors (EGGCT) have been described in association with KS, most often located in the mediastinum with a relative risk of at least 50.
Design/Methods: Our centre, seven year old boy was diagnosed with testicular mature teratoma and a malignant mediastinal mixed germ cell tumor. Since KS is the only known risk factor for mediastinal GCTs, karyotype was done, showing 47,XXY compatible with KS. To review the literature on GCT associated with Klinefelter's syndrome, a PubMed search was conducted in the English-language literature using the keywords 'Klinefelter's syndrome' and 'Germ Cell Tumors'. Every paper was reviewed, and all the patients with KS and a GTS were documented by first author of the paper, year of publication, location of primary tumor, age of the patient and histology of the tumor.
Results: A total of 102 papers were reviewed and 124 patients with KS and GCT were found. The median age group is 15-19 year old. The localisation is in 70% the mediastinum, followed by the brain, testis and abdomen. Histology is principally mixed GCT, followed by teratoma and germinoma.
Conclusion: In contrast to the GCT in adults, which are mostly gonadal, in childhood they are more often extragonadal. In KS the principal localization of a GCT is the mediastinum except for children under the age of 5 year in which the abdominal location is more frequent. Mixed GCT are much more frequent in KS, while teratoma is the most common GCT in children without KS.

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PEDIATRIC GERM CELL TUMORS IN DENMARK 1984-2013

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Background/Objectives: Germ cell tumors (GCTs) are a heterogeneous group of tumors derived from primordial germ cells. GCTs are benign or malignant tumors localized either gonadal or extragonadal. Only few reports on national population-based cohort of GCT's are available. We have mapped the pediatric cohort of GCTs in Denmark (5,6 mill. residents) over 30 years.
Design/Methods: All Danish pediatric GCTs diagnosed from 1984 to 2013 were collected from the Danish Children Cancer Registry. Case records were reviewed by two data extractors. We extracted data on localization, gender, histology, tumor markers, treatment and clinical outcome. Updated results will be presented at SIOP 2015.
Results: We have identified 223 GCTs (45% gonadal, 20% sacrococcygeal, 13% central nervous system and 22% other sites) in patients aged 0-15 years (crude incidence:1.2/100.000, 64% girls). Extragonadal GCTs were mainly observed in early childhood with sacrococcygeal localization as the most common. Gonadal GCTs were in contrast observed in late childhood with ovaries as the most frequent site of origin. Mature teratomas were the most frequent observed histological classification (55%) and usually localized in the ovaries. Alfafetoprotein was elevated in 15% and 4% had elevated beta-human chorionic gonadotropin. One third of all GCTs were malignant. Of these, 50% were treated with chemotherapy. Almost all cases had surgery. Only intracraniel GCT were irradiated. Relapse rate was 10%. Mortality rate was 4%. Very few children had adverse events (oto- and nephrotoxicity) related to chemotherapy.
Conclusion: In Denmark pediatric GCTs are rare and are mainly benign with mature teratoma being the most frequent. We identified a peak of extragonadal GCTs in early childhood and a peak of gonadal GCTs in late childhood. In malignant GCTs morbidity is very low but chemotherapy is administered for about 50%. The incidence of GCTs in Denmark seems similar to other studies.

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BILATERAL JUGULAR VEIN (JV)OBSTRUCTION IN GERM CELL TUMOR (GCT): CASE REPORT

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Background/Objectives: This is a report of GCT with bilateral internal jugular vein thrombosis without catheter related nor prior coagulation abnormalities.
Design/Methods: Treatment details and treatment responses of the patient were summarized.
Results: Case: A 10-year-old-girl, initially present with fever, abdominal distension for 1 month with 1 week history of painful left supraclavicular fossa. Ultrasound Chest and CT abdomen revealed thrombus in the both side of jugular vein (left: 5.1 × 1.3 × 1.6cm), (Right: 3.6 x0.8 x0.6 cm) and mass (18×12×8 cm) occupying lower abdomen respectively. Alpha feto protein raised upto 20000U/L. Coagulation profile; PT, PTT, D-dimer, Protein C, Protein S, Factor V leiden, Antithrombin III, Antiphospholipid Ab were in normal range. Treated with VCR, Bleo, CDDP(PEB) together with SC Enoxaparin (1 mg/kg) 12 hourly. After 2 cycles with PEB, defaulted 2 weeks and back with persistence mass, so continued enoxaparin for 21 days followed by oral wafarin overlapping with UFH for 5 days, continuing aspirin and warfarin for 10 weeks together with VCR, Bleo, CBDCA(JEB), four cycles and evaluation found both JV were patent and tumor mass also reduced to 7×4.6×4.8cm with calcification is noted in right lower abdomen. Tumor removal and right salpingoophrectomy was done, omental seedling was also found and JEB 3 cycles was given. The patient remains well for three months.
Conclusion: Complete resolution of the thrombus can be achieved by chemotherapy together with anticoagulants in GCT (abdomen) with thromboembolism in distant sites like JV in a resource limited country.

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TREATMENT RESULTS OF PEDIATRIC GERM CELL TUMORS FROM A SINGLE INSTITUTION

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Background/Objectives: Herein we reported our treatment results of children with GCT, between 1988 and 2015.
Design/Methods: Medical records of patients were analyzed retrospectively.

Results: Forty-nine patients with GCT were included in analysis, GCTs constitute 5,7% of all our patients. The median age of diagnosis was 12years (0–18), M:F ratio was 0.5. Primary tumor was gonadal in 63%, extragonadal in 25% and intracranial in 12% of patients. Histopathology revealed mature teratoma (25%), immature teratoma (14%), germinoma (8%), embryonal carcinoma (8%), yolk sac tumor (8%), mixed germ cell tumors (21%), disgerminoma (% 8), endodermal sinus tumor (4%), sex-cord stromal tumor (2%). Stage distribution of gonadal GCTs was stage-I (45%), stage-II (15%,) stage-III (20%), stage-IV (20%); and extragonadal GCTs was stage-I (42%), stage-II (8%), stage-III (25%), stage-IV (25%). On average four courses (2-10) of cisplatinum based chemotherapy were given. Radiotherapy was performed in 7 patients. Gonadal GCTs : Primary surgery and delayed surgery were performed in 29 and two cases, respectively. Twenty-one patients received CT, two patients received radiotherapy. Three of them died with progression. Ekstragonadal GCTs: Primary surgery was performed in 7 (complete resection:5, macroscopic residue:2), with only biopsy in two patients with sacrococcygeal GCTs (n:9). One of them had metastatic disease, four received chemotherapy, and two died with progression. CR achieved by primary surgery in one retroperitoneal GCT. Two metastatic patients (anterior mediastinal:1, intra-abdominal midline:1) treated by incomplete surgical resection, chemotherapy and radiotherapy. CR achieved in one. Median follow-up-time was 3years (1mos-20yrs); 10 and 15-years-EFS were 77% and 64%; 10 and 15-years-OS were 79%.
Conclusion: The survival rates were acceptable. High number of teratomas may have a positive effect on these results. Due to the limited number of patients, no conclusion can be made about the treatment success according to clinical and histopathological subgroups. Colloborative studies are needed to define risk-based treatment strategies.

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TREATMENT OF CHILDHOOD GERM CELL TUMORS IN BELARUS-SINGLE CENTER EXPERIENCE

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Background/Objectives: Malignant germ cell tumors (GCTs) are a heterogeneous group of neoplasms, putatively originating from the primordial germ cell. Since 2002 we have been used German MAKEI-96 and MAMO-98 treatment protocols in Pediatric extracranial GCTs in Belarus.
Design/Methods: Totally 85 malignant extra cranial GCTs registered in 2002-2012 in children or adolescents aged 0-18 years, were included in this study. Testicular GCTs in 18 pts were registered, ovarian - 43 and extra gonad sites in 24 cases. MAMO-98 was implemented in all testicular GCTs and the rest extra cranial GCTs according to MAKEI-96. Data on tumor location, histology, stage, and detail of follow up were collected from cancer register.
Results: All children tolerated the protocol therapy well without complications. From 18 pts with testicular GCTs only 1 relapsed and 5-years EFS was 94%. There were 2 relapses in ovarian group of pts and 95% EFS was achieved. The results of extra gonad sites were less optimistic, and EFS was equal 77% with 6 relapsed pts. In general these results are considerably better than we got before initiating MAMO-98 and MAKEI-96 protocols.
Conclusion: Therapeutic approaches included in MAMO-98 and MAKEI-96 showed good outcome in all types of GCTs in Belorussian children and merit further continuation.

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SACROCOCCYGEAL TERATOMA: 33 CASES AT A SINGLE INSTITUTION

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Background/Objectives: Sacrococcygeal Teratoma (SCT) is the most common congenital neoplasm. Derive from embryonal germ cells, often containing elements from the three germ layers. They can be prenatally detected by ultrasound. Most common presentation is sacral mass, but they can elicit urinary, fecal, or neurologic symptoms. They tend to become malignant as children grow older. Surgical resection is the treatment of choice.We aim to describe our experience with surgical management of SCT at a single institution.
Design/Methods: Retrospective review of children treated for SCT at the Surgical Oncology Department of the National Institute of Pediatrics in Mexico City, between 1981 and 2015.
Results: There were 24 girls and nine boys, with ages between one day and 14 years, most of them neonates.Only six patients (18%) were prenatally diagnosed with ultrasound.Most common presentation was sacral mass. Urinary incontinence and chronic constipation were seen in one patient each.Altman classification: type I (52%), II (30%), III (12%), and IV (6%).Mature teratoma was histologically confirmed in 91% of patients. Three cases had endodermal sinus elements.Surgical complications included wound infection and dehiscence (4 patients), urologic and fecal complications in four and two patients respectively.Blood loss was 20 ml. Average length of stay was 7 days.Two patients died, one from congestive heart failure before surgery, one due to disease progression with lung metastases. Most (94%) are alive and free of disease.
Conclusion: Eerly surgical resection offers the best chance of cure for SCT. Most neonates have benign tumors. Complete tumor resection excising the tip of the coccyx is paramount to prevent recurrence. Prognosis is excellent if patients are treated at referral centers with experience in pediatric oncology.

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PARAVERTEBRAL GERM CELL TUMOR WITH INTRASPINAL EXTENSION AND CORD COMPESSION: A RARE PRESENTATION

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Background/Objectives: Primary malignant germ cell tumors of mediastinum account for only 10-15% of all mediastinal tumors. The commonest site in mediastinum is anterior mediastinum. In posterior mediastinum, neurogenic tumor and bronchogenic tumor predominates. Posterior mediastinum germ cell tumor is rare and posterior mediastinal germ cell tumor arising in paravertebral region with intraspinal extension and causing cord compression is extremely rare and in our knowledge such presentation has never been described before.
Design/Methods: To describe a case of 3 years old male child with paravertebral germ cell tumor with intraspinal extension and cord compression in view of its rarity.
Results: A 3 years old male child presented with complaints of progressive weakness of both lower limbs and loss of bowel and bladder control after an accidental fall from height 15 days back. Child developed weakness of both lower limbs two days after fall. It was followed up by loss of bladder and bowel control. MRI dorsolumbar spine revealed a paraspinal mass from D8 to L2 level with intraspinal extension through foramina of D10-11 and D11-12 causing cord compression and encasement with features suggestive of Neuroblastoma. FNAC was inconclusive but possibility of germ cell tumor could not be ruled out. Since the child had features of cord compression child was given first course of PEB. AFP came out to be raised (146600ng/ml). Urinary VMA/HVA were within normal limits and there were no skeletal metastasis. Child improved following 2 courses of PEB with significant improvement in lower limb movement and bladder and bowel control.
Conclusion: An unusual case of posterior mediastinal germ cell tumor with paraplegia is described.

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RECURRENCE SACROCOCCYGEAL TERATOMA IN CHILDREN: 11 CASES ANALYSIS

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Background/Objectives: To discuss the effects of risk factors on recurrence of sacrococcygeal teratoma (SCT) in children.
Design/Methods: A retrospective review was made in 11 cases (8%) of recurrent tumor in 136 children with sacrococcygeal teratoma between Jan. 2006 and Nov. 2014 in Shanghai Xinhua Hospital. Clinic factors and pathologic analysis were identified.
Results: Eleven children had recurrence of SCT, 3 were male, 8 were female. The age was 4 days to 11 years old, median age was 12 months while they were underwent primary surgery. Second operation was performed in a median interval of 23 months (5 months —10 years) after first operation .The recurrence of mature teratoma was observed in 4 patients, yolk sac tumor in 7.Third recurrence yolk sac tumor was presented in 3 patients after second operation. Third time procedure was performed to removed the tumor in these kids.
Conclusion: Cause of recurrence of sacrococcygeal teratoma is include incomplete resectioni and malignant histology. Regular follow-up after surgery is important to find tumor relapse earlier and to improve the outcome.

Posters: Histiocytosis

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LANGERHANS CELL HISTIOCYTOSIS (LCH) IN CHILDREN AND ADULTS: A COMPARATIVE STUDY OF 40 CASES

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Background/Objectives: Langerhans Cell Histiocytosis (LCH) can develop at any age. Clinical presentation, severity and therapeutic approach vary in children and adults, but few studies have analyzed the differences Aim: Review of epidemiological and clinical LCH cases collected from 1995 to 2014 in 3 hospitals from the Basque Country (Spain) to compare data between adults and pediatric patients.
Design/Methods: The analysis of epidemiological and clinical data was performed by using SPSS software.
Results: Forty patients were included (22 males and 18 females). Range of age: 0-84 years-old. Pediatric cases (until 18 years-old): 18 cases, 9 females and 9 males. Median age at diagnosis: 6.6 years-old. Initial organ involvement: 17-bones (8 unifocal), 1-skin, 1-lung, 1-gastrointestinal with multisystem disease in 8 but no risk organ. Chemotherapy was administered in 10. Evolution: No deaths, relapses in 4. Nowadays, 16 were in complete remission. Adult cases: 22 cases, 9 females and 13 males. Median age at diagnosis: 32.5 years-old. Clinical features: 9-bones (7-unifocal), 9-lung, 6-lymph nodes, 3-skin, 2-spleen, 2 CNS, 1-genital, 1-liver, 1-hematopoietic-system. Multisystem disease was found in 8. Treatment: 4-chemotherapy and 4-radiotherapy. Relapse in 2 patients. Missing data in follow-up but 2 deaths and 5 malignancies associated (2-Hodking, 2 lung, 1 leukemia).
Conclusion: LCH was most frequent in children and in the first 40 years of life (median of 18 and 75% cases were less than 35 years old). Bone lesions were the most common in both groups. Multisystem involvement was detected in 40%. Pulmonary, lymph nodes and risk organ involvement were most frequent in adults. Only children were included in national or international studies. Chemotherapy was more used in children and radiotherapy in adults. Prognosis was better in children and associated malignancies and deaths were observed only in adults. A better follow up is needed to know the long term sequelae and monitoring programs should be implemented.

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INVESTIGATION OF CENTRAL NERVOUS SYSTEM DISEASE IN PATIENTS WITH LANGERHANS CELL HISTIOCYTOSIS. EXPERIENCE OF EGE UNIVERSITY FROM TURKEY

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Background/Objectives: Langerhans cell histiocytosis (LCH) is a rare disease in childhood involving clonal proliferation of CD1a positive Langerhans cells. Clinically, its manifestations range from isolated bone lesions to multiple system disease (MSD) and failure. CNS-LCH is a rare significant form of LCH due to its high morbidity rate. In CNS-LCH diesase early age, craniofacial bone involvement and MSD constitute a risk. The aim of our study was to determine via a multidisciplinary approach, the frequency of CNS-LCH cases.
Design/Methods: This is a retrospective and cross-sectional study of 30 patients with LCH followed in Ege University, Department of Pediatric Oncology. Neuropsychological examination, EEG and cranial MRI was done by the departmants of pediatric neurology and radiology.
Results: In this study, the mean age at diagnosis of patients was 81.3 months (8-192 months). Eleven (36%) patients under 36 months old were considered as early age. Seven (63%) of them had MSD. Skeletal system was the most commonly affected system (97%). Twenty (66%) of all cases showed single-system involvement, MSD was seen in 10 (34%) patients. Clinical and radiological findings of CNS disease were detected in 10 (33,3%) cases. Six of them had clinical and radiological disease findings approved as "certain CNS disease". Since 4 patients had developmental delays and/or the risk of organ involvement in addition to the radiological findings, they were approved as "highly probable CNS disease". There were 7 cases with MRI lesions that were compatible with LCH, but did not have a risk for CNS diease. These cases were approved as "suspected CNS disease" and follow-ups were scheduled.
Conclusion: In patients with LCH, especially MSD and early age there is a risk in terms of CNS disease. A multidisciplinary perspective (neuropsychiatric exams and cranial MRI) is crucial in the diagnosis of CNS disease and management.

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EXOSOME-TRANSFERRED APOC3-NCRNA COMPLEX MEDIATES IRON REGULATION IN β-THALASSEMIA MAJOR

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Background/Objectives: Exosomes are small membrane vesicles (50–90 mm in diameter) containing bioactive proteins and genetic materials that may be transferred to accept cells, resulting in potent biological effects in the circulatory system. Exosome-transferred APOC3-ncRNA may be a crucial function in iron regulation. However, the role in β-thalassemia major is remains unclear. The aim of this study was to investigate how Exosome-transferred APOC3-ncRNA adapts to iron regulation in β-thalassemia major.
Design/Methods: Using Proteomics, RNA-sequencing and lncRNA Q-PCR array, we demonstrated expression of exosomes-transferred APOC3-ncRNAs in plasma of β-thalassemia major patients (n = 40). Identification of exosome by Dynamic light scattering (DLS), Flow cytometry and western blots. Lentiviral infection, ncRNAs transfection and in vitro studies revealed that knockdown or overexpression obviously increased or ameliorated exosomes-induced iron regulation. Bioinformatics analysis, luciferase assay and in vitro studies revealed that ncRNAs functioned as a repressing mediator and formed a feedback loop with ncRNAs and target gene to mediate iron regulation.
Results: We observed that ncRNA is differential expressed in the exosomes of β-thalassemia major. We analyzed the effects of ex vivo-derived exosomes for iron regulation by monocytes/hepatocytes model. In vitro model showed that exosomes were internalized by THP-1/HuH-7 cells, and regulates the IRP1/FPN/HAMP. In turn, Exosome-transferred APOC3-ncRNA mediates inflammatory cytokine expression and iron regulation via p38/pAKT/TRAF6/NF-kB pathway. Knockdown of APOC3-ncRNA reversed IRP1/FPN/HAMP expression.
Conclusion: This is the first example of extracellular APOC3/ncRNA regulating gene expression via circulatory exosomes-transferred to accept cells. Increased Exosome-transferred APOC3-ncRNA expression is one of the key factors that might have contributed to abnormal iron regulation in β-thalassemia major patients.

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ROSAI DORFMAN DISEASE: ANALYSIS OF CLINICAL AND PATHOLOGICAL CASES IN PEDIATRICS IN A SINGLE CENTER

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Background/Objectives: Sinus histiocytosis with massive lymphadenopathy or Rosai Dorfman disease (RDD) is considered a benign pathology of unknown cause. Presents with unilateral or bilateral cervical lymph node involvement, painless, fever and various hematological disorders. The diagnosis is pathological. Usually treatment is not necessary.Therapy is required, however, for patients with extranodal RDD having vital organ involvement or those with nodal disease causing life-threatening complications. The purpose is review the pathological and diagnostic clinical features of patients (p) with RDD.
Design/Methods: Report of seven cases of patients treated at Hospital de Niños Ricardo Gutierrez, analyzing the clinical, immuno histochemical and pathological features between October 1992 and october 2013.
Results: Seven cases are reported, mostly male (5), aged between 1 and 18 years. All of them had single or multiple cervical lymphadenopathies, with concomitant symptoms like fever (2 p), and lymphadenopathy in different locations (4 p). Histologically, lymph nodes show dilated sinuses, heavily infiltrated with large histiocytes, lymphocytes and plasma cells. The presence of the engulfment of lymphocytes and erythrocytes by histiocytes that express CD68 (6/6p) and S-100 (5/6p), was considered diagnostic of RDD. CD1a was typically negative (1/6p). In 4 cases, treatment was not necessary. Three patients were treated with corticosteroids for one month and 1 with vinblastine for bad response.
Conclusion: Rosei Dorfman disease is a histiocytic proliferative benign idiopathicdisorder characterized by sinus histiocytosis with massive lymphadenopathy. It is a clinicaland specific pathology. Cervical location is the most common. The definitive diagnosis is histological. Currently there is no standardized treatment. The evolution is usually favorable.

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PRIMARY HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS: THE EXPERIENCE OF A TERTIARY CARE CENTRE IN SOUTH INDIA

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Background/Objectives: Hemophagocytic lymphohistiocytosis (HLH) is a rare, often life threatening syndrome characterized by reactive, systemic proliferation of benign histiocytes throughout the reticuloendothelial system. In a tropical developing country, the diagnosis may be missed as there are other more common causes for the triad of

high fever, splenomegaly and cytopenia. We describe the profile and outcome of children with primary HLH in a pediatric unit of a developing country.
Design/Methods: Retrospective review of all cases of Primary HLH diagnosed over a 3 year period in the Pediatric hematology oncology unit.
Results: Eleven cases of primary HLH were diagnosed as per the HLH 2004 diagnostic criteria. All the cases were referred as cases of pyrexia of unknown origin (PUO). A syndromic diagnosis was made in 8 patients; 7 had Griscelli syndrome and 1 had Chediak Higashi. All were treated as per HLH 2004 protocol. Two children had neurological involvement of HLH. Seven children responded to induction therapy. One expired before treatment could be initiated and two expired due to refractory HLH while on induction chemotherapy. Stem cell transplant was advised to all patients once HLH was under control but the only child who underwent SCT at another centre, succumbed to sepsis. Four cases are on continuation therapy and on follow up. Three were lost to follow up while on continuation therapy.
Conclusion: HLH should be considered as a diagnostic possibility in a child who presents with PUO, especially if there are dysmorphic features suggestive of Griscelli or Chediak Higashi syndromes. While therapy with HLH 2004 protocol is successful in the majority of cases, access to stem cell transplant is still a challenge in the developing world.

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LANGERHANS CELL HISTIOCYTOSIS: PERSPECTIVE FROM THE DEVELOPING WORLD

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Background/Objectives: Langerhans cell histiocytosis (LCH) is a rare disorder. Outcome data is lacking from developing countries like India. We present our experience of diagnosing and managing LCH.
Design/Methods: Cases of LCH diagnosed at two Pediatric Hematology-Oncology Units in India over a period of 4 years were retrospectively reviewed. Demographic details, clinical features, histopathology radiological findings, details of therapy and outcomes were analyzed.
Results: Nineteen cases of LCH were diagnosed. Mean age of presentation was 29 months. Male to female ratio was 2.8:1. All cases were confirmed by biopsy and CD1a stain. Ten presented with multisystem disease and 9 had single system disease. Risk organ involvement was seen in 9 cases (liver 37%, spleen 21%, bone marrow 16%). Eight cases had single system involvement (bone) with 4 cases of multifocal disease and 4 with single lesions. Both axial and appendicular skeletal involvement was seen. Lung involvement was seen in 42%. Isolated mediastinal mass and nail involvement were seen in one case each. Multiple hypoechoic lesions in the liver mimicking abscess and lung lesions mimicking tuberculosis were seen. Radiological findings assisted in diagnosis in all the cases.Therapy was given as per LCH-III protocol. Eight cases required two induction cycles and two children required salvage chemotherapy. Curettage was done for single site bone lesion in four cases and one child required spine stabilization. Fourteen children have completed treatment and are on follow up (Median 20 months ; range 3 -84 months). Progressive sclerosing cholangitis requiring liver biopsy was seen in two children of which one opted for liver transplant. One child developed staphylococcus aureus meningitis while on continuation treatment and abandoned treatment.
Conclusion: A high index of suspicion and familiarity with the clinical and radiological findings of LCH will ensure prompt diagnosis and therapy. Good treatment outcomes are possible in developing world also.

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FAMILIAL HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS IN CHILDREN: SINGLE CENTRE RESULTS

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Background/Objectives: Familial hemophagocytic lymphohistiocytosis (FHL) is an autosomal recessive disorder characterized with uncontrolled activation of T-helper lymphocytes and macrophages and over-release of inflammatory cytokines. The only curative treatment is hematopoetic stem cell transplantation (HSCT). This study evaluates the clinical and laboratory data of children with FHL.
Design/Methods: Twenty five FHL cases followed and treated at our clinic between 2005 and 2015 were retrospectively evaluated in our study.
Results: Fourteen of the cases were boys and eleven were girls. The age at presentation for patients was two week-36 months (mean 4.2 months). There was a history of consanguineous marriage in 20 of the families (80%). Fever, anemia, and hypertriglyceridemia were present in all patients. Hepatomegaly was detected in 72%. Splenomegaly was more frequent in patients (88%). Hypofibrinogenemia was detected in all patients. All patients had neutropenia and thrombocytopenia. Hyperferritinemia was present in 92%% of patients. Only seven patient found to have hemophagocytosis in the cytological evaluation of the cerebrospinal fluid (29.2%). Mutation analysis were performed in 17 patients and of these, 3 had UNC13D, 6 had PRF1 and 2 had STX11 gene mutation. All patients vere treated with HLH-2004 protocol. HSCT was performed in 8 patients (%32). The overall mortality rate was 56 % (14 cases) in our series. Fourteen children died due to opportunistic infection (n = 8) or disease progression (n = 6).
Conclusion: In conclusion, FHL is a disease with high mortalite rates and the only curative treatment is HSCT. Donor search for HSCT must be started and HSCT should be performed after the remission.

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OUTCOME AND DISABILITIES IN CHILDHOOD LANGERHANS CELL HISTIOCYTOSIS

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Background/Objectives: Langerhans cell histiocytosis (LCH) is characterized by abnormal proliferation and accumulation of bone marrow–derived Langerhans cells (histiocytosis) juxtaposed against a backdrop of hematopoietic cells, including T-cells, macrophages, and eosinophils. Data on sequelae /disabilities on children having completed treatment for LCH is scarce. This study describes the varied clinical profile, outcome and disabilities in children treated for LCH followed at a tertiary center in India. The role of PET CT in evaluation of LCH is also highlighted.
Design/Methods: Case records of children diagnosed and treated for LCH at our center were evaluated. Symptom profile, lag period between onset of symptoms and diagnosis were ascertained. Extent of disease was ascertained according to LCH 2009 guidelines after relevant investigations including PET CT. Details of treatment response and reactivation were recorded. Follow up details and sequelae described.
Results: 45 children were diagnosed with LCH in last three years. Most children had multisystem involvement.23 completed treatment and are under follow up. Mean period of follow up 23 months. LCH was often a missed diagnosis. Sequelae was seen in 14 patients (60%).Reactivation was seen in 5 patients (4 had multisystem involvement: risk organ involvement was seen in 3) All children with disease reactivation had onset of symptomatology at less than two years of age. Sequalae included short stature, Diabetes insipidus, Chronic liver and lung disease, sclerosing cholangitis, bony defects, ear discharge/hearing defect and proptosis. Pulmonary artery hypertension and nail changes were also seen.
Conclusion: LCH, often a missed diagnosis, has varied clinical presentation and treatment outcomes. Reactivation of disease does occur and is seen more often in children with disease onset at less than 2 years of age. Sequalae are common.PET CT emerged a useful modality to assess treatment response in both newly diagnosed and refractory cases of LCH.

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HYPERFERRITINEMIA IN SEVERELY ILL PATIENTS: ASSOCIATIONS WITH CLINICAL AND LABORATORY FINDINGS

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Background/Objectives: Hyperferritinemia has been identified as an important biomarker of the genetic (primary) form of hemophagocytic lymphohistiocytosis (HLH), a disease associated with excessive inflammation and characterized by defect lymphocyte cytotoxicity function. HLH may also develop in a secondary (acquired) form in severely ill patients, a potentially treatable hyperinflammatory condition. In children, the extent of hyperferritinemia can help identify and distinguish HLH from other conditions. Furthermore, increasing levels of ferritin has been correlated to increased risk of intensive care unit (ICU) admission and death. We analyzed ferritin levels in patients admitted to ICU in order to correlate hyperferritinemia to clinical and other laboratory parameters in this group of severely ill patients.
Design/Methods: Thirty-two adult patients with ferritin levels $>500\ \mu g/L$ were prospectively studied at an ICU with regard to clinical and laboratory features on

admission, including soluble CD25 (sCD25) and detailed lymphocyte cytotoxicity analyses and genetic studies in some.
Results: Hyperferritinemia and elevated sCD25, both markers of inflammation, were positively associated to each other in patients with septicemia, a state of known excessive inflammation. Here, hyperferritinemia was also associated with elevated CRP. Ferritin and sCD25 levels were inversely correlated to platelet counts in the total cohort and in patients with septicemia. Notably, thrombocytopenia is a sign of severe illness that affects outcome and mortality of ICU patients. Similarly, elevated sCD25 was inversely correlated to hypoalbuminemia. Interestingly, hyperferritinemia (>5,000 μg/L) was also associated with decreased cytotoxic function. Notably, of four patients with abnormally low cytotoxic function, three had <5% circulating NK cells and one had a heterozygous variant in an HLH-causing gene (*STXBP2*).
Conclusion: Our study suggests a correlation between hyperferritinemia and other laboratory values indicative of inflammation and of poor outcome in severely ill patients at intensive care units.

Posters: Late Effects

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CARDIAC PROBLEMS IN PATIENTS WHO UNDERWENT TO HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background/Objectives: Cardiac complications may be observed after hematopoietic stem cell transplantation (HSCT). Despite significant improvement in supportive care, HSCT may be associated with significant morbidity and mortality. In this study, we aimed to evaluate the frequency of serious cardiac complications with clinical characteristics after HSCT in our patients.
Design/Methods: This is a single instutional study. The demoraphic and clinical characteristics of patients with cardiac complication were recorded among 69 subjects who underwent to HSCT, retrospectively.
Results: The frequency of subjects with cardiac events among 69 subjects who underwent to HSCT was 5.8%. In addition, 5 events were detected after HSCT in 69 subjects who underwent to HSCT (7.25%). Autologous HSCT in 3, and allogeneic in a case were performed. The median age was 12.5 years (range 12-15) and M/F ratio was 1/3=0.33. The disease distributions were the following: Hodgkin lymphoma (HL) nodular sclerosis (NS) variant: 2 (50%), PNET: 1 (25%), T cell lymphoblastic lymphoma: 1 (25%). Primary localizations of disease were cervical lymph node in 2 subjects, pelvic mass in 1 subject and pelvic bone in 1 subject. All of the subjects had Stage IV disease.Pericardial effusion in 3 subjects, and sinus bradycardia and ventricular tachycardia in 1 patient were detected. The mortality rate was 50%, and both of them were with pericardial effusion. Poor risk factors, myocarditis, pericarditis and heart failure owing to cumulative doses of anthracycline, cyclophosphamide, CMV infection or other infections, mediastinal irradiation, and cryopreserved stem cell product with DMSO were the main reasons in this study.
Conclusion: Cardiac complications after HSCT are very important side effects. Early intervention can prevent death related to this complication. They should be followed-up closely for this complication.

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SURVIVORS OF ALL ARE AT INCREASED RISK OF BEING OBESE/OVER-WEIGHT, BUT NOT FOR METABOLIC SYNDROME AT A MEAN DURATION OF 3.8-YEARS FROM END OF TREATMENT

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Background/Objectives: Metabolic syndrome (MS) has been commonly reported in survivors of childhood ALL from developed countries. Data from developing countries is lacking.
Design/Methods: Survivors of childhood ALL at a referral hospital in North India were evaluated for MS. Anthropometric measurement (weight, height, waist-circumference, triceps/sub-scapular skin fold thickness), biochemistry (fasting glucose/insulin, lipid-profile, thyroid function, CRP), measurement of blood pressure and SMR staging were performed. MS was defined by the IDF, as well as NCEP ATP-III criteria modified by Cook et al, and ford et al.
Results: The median age of 76 survivors was 11.9 years (range 7.4-19). The mean time from completion of chemotherapy was 3.8±1.9 years (range: 2-11). Cranial irradiation was administered to 15 (20%) patients. The mean BMI at diagnosis, completion of treatment and at study enrolment was 14.2±1.7, 16.2±2.8 and 18.3±3.7, respectively ($p<0.0001$). Twenty-four (32%) survivors were obese or overweight. The fasting blood sugar and insulin level were within range in all the survivors. CRP was elevated (>3 mg/L) in 19 (25%) survivors; a marker of subclinical inflammation and risk factor for cardio-vascular disease. Subclinical hypothyroidism was observed in 14 (18%) survivors. The prevalence of insulin resistance (17%), hypertension (7%), hypertriglyceridemia (20%) and a low HDL (37%) was comparable to the prevalence in children/adolescents in earlier cross-sectional population based studies from India.The prevalence of MS ranged from 1.3% to 5.2%, as per different defining criteria. Cranial radiotherapy, age at diagnosis, sex, socio-economic status or dose of anthracycline were not observed to be a risk factors for MS.
Conclusion: The prevalence of MS in survivors of childhood ALL, at a mean duration of 3.8 years from completion of chemotherapy, was 1.3% - 5.2%. It was similar to the prevalence in children/adolescents in earlier cross-sectional population based studies from India. Twenty-four (32%) survivors were obese or overweight, a prevalence higher than population based data.

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MARKERS OF TUBULAR RENAL INJURY IN CHILDREN WITH CANCER RECEIVING CISPLATIN AND/OR IFOSFAMIDE

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Background/Objectives: Children with cancer receiving nephrotoxic chemotherapeutic agents such as cisplatin and ifosfamide are at risk of both acute and chronic, and reversible and irreversible, kidney injury. Monitoring for changes in glomerular function is now routine, with biochemical markers of glomerular function such as serum creatinine (sCr), and the use of chromium 51-labelled ethylenediaminetetraacetate (51 Cr-EDTA) to measure glomerular filtration rate (GFR). Markers of tubular injury are however less well defined.
Design/Methods: A two-step systematic review was undertaken to determine which markers, if any, have been described in studies relating to children with cancer, and then specifically those receiving cisplatin and/ or ifosfamide. EMBASE, MEDLINE and CINAHL were searched. Search terms were independently matched to the thesaurus of each database. An initial search was conducted to generate a list of markers of renal tubular injury that had been identified or explored in either *in vitro* and or *in vivo* biological or clinical studies. Only biochemical, genetic, peptide, and microRNA markers were included. A second literature search was conducted to identify articles relating to renal injury in paediatric patients receiving cisplatin or ifosfamide. The two searches were cross-referenced.
Results: A total of 97 markers of tubular injury were identified from the defined search terms. Of these, 14 were cross-referenced to the defined population, including fractional excretion of phosphate, cystatin C, interleukin-18 and variance in amino acid and metabolite profiles.
Conclusion: The clinical utility of potential biomarkers is currently limited by considerations such as small sample size in studies conducted, the requirement for specialist modalities (e.g. nuclear magnetic resonance spectroscopy), complexity of analysis (e.g. urine amino acid profiles) and cost of assays (e.g. ELISA). Further work is needed to identify new biomarkers of tubular kidney injury arising from nephrotoxic chemotherapy, with studies in larger cohorts of patients to validate their utility, sensitivity and specificity.

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ACUTE KIDNEY INJURY IN PAEDIATRIC ONCOLOGY PATIENTS RECEIVING CISPLATIN

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Background/Objectives: Paediatric cancer patients receiving cisplatin are at risk of developing acute kidney injury (AKI). Routine markers for monitoring transient and permanent changes in glomerular function (GF) include serum creatinine (sCr) and glomerular filtration rate (GFR) measurement. Markers of tubular injury are however less well defined. Using routine clinical data, the current study aimed to identify the incidence of the AKI in patients being treated within a tertiary paediatric oncology, and potential markers for future studies.
Design/Methods: Core data including sCr levels, gentamicin levels and magnesium supplementation were collated from the electronic and pharmacy records of 68 children who had received cisplatin. AKIN scores were given based on biochemical data alone.
Results: Complete data was available on 63 patients; 35/63 (56%) of patients had an AKIN score of 0, 21/63(33%) had an AKIN score of I, and 7/63 (11%) had an AKIN score of II. A total of 71% of patients with AKIN II had received gentamicin (number of courses: range 1–12, mean 5.8) between commencing chemotherapy and data

collection, compared with 33% of patients with AKIN 1 (range 1–8,mean 3.14). 86% of those patients with AKIN II required magnesium supplementation on treatment (vs 24% of AKIN I patients), with 71% of those patients with AKIN II requiring magnesium supplementation after treatment(vs 19% of AKIN 1 patients).
Conclusion: 44% of patients had an AKIN score of I or II. Those patients withan AKIN score of II received a higher mean number of courses of aminoglycosides than other groups (AKIN Ior 0), and were more likely to require magnesium supplementation, both on and off treatment. This suggests that cumulative aminoglycoside doses may have a role in the stratification of patients at risk of AKI for researchand follow-up purposes, and that the utility of magnesium supplementation as a marker of AKI merits further investigation.

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DISCUSSIONS ABOUT REPRODUCTIVE AND SEXUAL HEALTH AMONG YOUNG SURVIVORS OF CANCER

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Background/Objectives: Infertility and sexual dysfunction can result from many cancer treatments and may become a source of significant distress for young cancer survivors. Our aims were to 1) characterize the frequency in which reproductive and sexual health discussions occur in a population-based cohort of young cancer patients and 2) identify clinical factors associated with such discussions.
Design/Methods: All patients aged 18 to 39 years who were diagnosed with solid tumors from 2008 to 2010, evaluated at any 1 of 5 regional cancer centers in British Columbia, Canada and alive at 2 or more years after their original diagnosis were included. Demographics, tumor and treatment characteristics, and information on patient-physician conversations regarding reproductive and sexual health were analyzed. Using regression models, we explored the relationships between clinical factors and whether or not discussions had occurred.
Results: We identified 453 patients: median age 35 years (IQR 31-38), 28% men, 88% ECOG 0, and 73% reported being in a relationship. Tumor sites included breast (50%), testicular (27%), gynecological (17%), and colorectal (6%). A significant proportion of patients received chemotherapy and radiation that posed the potential risk of infertility or sexual dysfunction. However, only 224 (56%) and 24 (6%) of individuals had a discussion about reproductive and sexual health, respectively, within the first month of their diagnosis. At 6 months, an additional 25 (6%) and 16 (4%) patients had discussed these concerns with their physicians. Age, gender, ECOG, relationship status, and type of chemotherapy and radiation were not correlated with whether or not discussions had occurred (all $p>0.05$). In regression models, tumor site was associated with differences in reproductive and sexual health discussions where individuals with gynecological cancers were most likely to engage in such conversations.
Conclusion: Among young survivors of cancer, fertility and particularly sexual function are inadequately addressed near the time of initial cancer diagnosis.

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COGNITIVE FUNCTIONING OF CHILDHOOD ALL OR NHL SURVIVORS AND LINKS WITH BIOMARKERS DURING TREATMENT

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Background/Objectives: Contemporary treatment can cure children with NHL or ALL. However, chemotherapy-induced neurotoxicity causes long-lasting functional deficits in some survivors. Besides primary cure, early identification and subsequent care for these individuals must therefore be focus of research in child oncology. Individuals with polymorphisms causing lower activity of the methyltetrahydrofolate reductase (MTHFR) enzyme have a higher risk for methotrexate-induced neurotoxicity, since this enzyme plays a key role in the folate metabolism. Previously, we reported increased levels of biomarkers of neurotoxicity in the cerebrospinal fluid (CSF) of patients during and information processing difficulties in survivors after treatment. We aim to link 1/ MTHFR genotype, 2/ biomarkers during treatment and 3/ long-term neurocognitive function in survivors of ALL and NHL.
Design/Methods: CSF-Tau and phospho-Tau were consecutively measured during treatment in respectively 28 and 7 patients with ALL and NHL. After a median time since treatment of 13.03 years, the outcome of neurocognitive tests and questionnaires was compared with sex- and age-matched controls, and the genotype on position 677 and 1298 of the MTHFR-gene was analyzed in survivors.
Results: Survivors performed significantly slower as compared to controls on tasks assessing memory, focused attention, cognitive flexibility and inhibition. These observations were reflected in higher scores on self-reported cognitive dysfunctions. The MTHFR1298 CC genotype displayed the highest levels of biomarkers. Combined with age below five at diagnosis, biomarkers helped us to detect patients with more severe neurocognitive problems.
Conclusion: To our knowledge, this is the first study to link genetic susceptibility with biomarkers and final neurocognitive outcome. We developed tools to identify early during chemotherapy children at risk for more severe late neurocognitive difficulties. These patients can be supported at an early stage with appropriate learning plans. The results of this study can also be applied to assess neurotoxicity in future treatment protocols.

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PAEDIATRIC CANCER SURVIVORS IN JOHANNESBURG DEMONSTRATE A HIGH RATE OF SUBCLINICAL RENAL DYSFUNCTION

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Background/Objectives: Clinical manifestations of renal dysfunction in children who have completed treatment for cancer include hypertension, proteinuria and renal insufficiency. This cross sectional study aimed to determine the prevalence, extent and factors associated with residual effects of cancer therapy on the renal system.
Design/Methods: A descriptive cross sectional study was performed to assess 130 children between the age of 1 and 18 years who completed treatment at a single institution and who were followed up at the paediatric oncology unit of the hospital. Physical examination, blood pressure and screening urine dipstick were performed on all patients by a single researcher. Blood results of samples routinely drawn, as part of the current standard follow up protocol of the unit (full blood count, calcium, magnesium and phosphate, and urea, electrolytes and creatinine), were analysed. Patients with abnormal results were referred to the paediatric renal clinic for further evaluation.
Results: After a median follow-up post treatment of 2 years, the various manifestations of renal dysfunction included decreased glomerular filtration rate (GFR), hypomagnesaemia, hypophosphataemia, proteinuria, haematuria and hypertension. In total, 34 survivors (26.15%) had at least one manifestation of renal dysfunction after completing treatment, of which none were clinically significant. The most prevalent manifestation of renal dysfunction detected was decreased GFR (17.69%). Hypomagnesaemia and hypophosphataemia were present in 8 (6.15%) and 6 (4.62%) of the survivors respectively. Patients who had pre-existing renal dysfunction were three times more likely to have renal dysfunction post-treatment ($p=0.02$). Ifosfamide, carboplatinum, and nephrectomy were significantly associated with a reduction in GFR ($p = 0.03, 0.02, <0.01$).
Conclusion: Although the rate of renal dysfunction was relatively high, it was not clinically significant. Patients with pre-existing renal dysfunction should be assessed by a nephrologist prior to initiation of cancer therapy, and nephro-protective measures should be employed stringently in all children with cancer.

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HEALTH-RELATED FITNESS IN LONG-TERM SURVIVORS OF CHILDHOOD CANCER

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Background/Objectives: In long-term childhood cancer survivors (CCS) adverse effects of treatment may result in impaired health-related fitness. Most studies in CCS assessed level of physical functioning subjectively with questionnaires. Only one study assessed survivors of acute lymphoblastic leukemia (ALL) objectively, using tests. The current study investigated health-related fitness in CCS in survivors other than of ALL.
Design/Methods: Cardiopulmonary endurance, mobility and muscle strength of survivors of acute non lymphocytic leukemia (ANLL), neuroblastoma or Wilms tumor (WT), aged ≥18 years, were investigated using 9 standardized validated tests. The Short Questionnaire to Asses Health-enhancing physical activity (SQUASH) was also used. Results were compared to healthy controls using multivariate analysis of covariance (ANCOVA), adjusted for age, sex and educational level.
Results: CCS had poorer cardiopulmonary endurance (mean (standard error; se) of standardised difference score (SDS) on six minute walking test: CCS: -0.53 (0.12) vs controls: -0.05 (0.12), $p=0.008$), less mobility (side flexion trunk; CCS: 20.1 cm (0.4) vs controls: 22.4 cm (0.4), $p<0.001$), and less muscle strength (vertical jump: CCS: 39.7 cm (0.8) vs 43.8 cm (0.8), $p<0.001$) than healthy controls. Survivors of ANLL had poorer cardiopulmonary endurance (-1.06 (0.3) SDS) than survivors of neuroblastoma: -0.59

(0.2) SDS and WT: -0.21 (0.2) SDS) (p=0.04). CCS with a scoliosis (25%) performed poorer on side flexion of the trunk (p=0.02), performing push ups (p=0.006) and sit-ups (p=0.01) compared to CCS without a scoliosis. Being a survivor (p=00.1), higher body mass index (BMI) (p<0.001) and lower levels of physical activity (p=0.03) were the most important predictors of physical functioning.
Conclusion: CCS seem to have impaired health-related fitness, in particular cardiopulmonary endurance. Survivors of ANLL and those with a scoliosis appear to have the highest risk of impaired health related fitness. Life style interventions may help to improve health-related health related fitness in CCS.

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NEUROCOGNITIVE AND NEUROIMAGING OUTCOMES FOLLOWING CHEMOTHERAPY-ONLY TREATMENT FOR PAEDIATRIC LEUKAEMIA: A SELECTIVE REVIEW

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Background/Objectives: Neurocognitive late-effects are reported in up to 50% of acute lymphoblastic leukaemia (ALL) survivors. Exploring the neurological underpinnings of such deficits would provide important information on the mechanism by which chemotherapy affects brain maturation. Few studies have successfully explored the relationship between functional cognitive outcomes and neuroimaging findings. This paper will review this literature for children treated with chemotherapy-only for ALL.
Design/Methods: Keyword searches were performed on electronic databases (Scopus and PubMed) for peer-reviewed journal articles. Papers were retained if: (i) participants were aged 0-18 years at time of chemotherapy-only treatment, (ii) they included original research on the association between cognitive and neuroimaging outcomes, and (iii) were published in the year 2000 or later.
Results: Ten papers meet all 3 inclusion criteria. A significant relationship was found between cognitive and neuroimaging measures in 6 studies. Significant correlations were found between hippocampal size and visual memory, hippocampal structural integrity and IQ, amygdala size, verbal memory and sustained attention, and structural integrity of the frontal lobes and processing speed. Significant relationships were found between abnormal white matter connectivity, IQ and response inhibition and greater activation in the dorsolateral prefrontal cortex and working memory. Imaging findings include gross volumes, structural integrity and functional activation.
Conclusion: Despite heterogeneity in study methodologies, the current literature suggests that brain regions in the limbic system that are responsible for new learning may be particularly sensitive to chemotherapy treatment, as well as white matter tracts that deliver information between cortical regions. These findings have significant implications for intervention and treatment planning for future ALL treatment protocols. In particular, the inclusion of sensitive imaging techniques, the exploration of imaging biomarkers that may predict functional risk, and the use of neuroprotective agents and/or the decreased use of neurotoxic agents in vulnerable ALL subgroups need to be further explored.

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IS CISPLATIN OTOTOXICITY RELATED WITH GENOTYPE OF DNA REPAIR GENES ERCC1, ERCC2, XRCC1?

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Background/Objectives: We aimed to investigate the relationship between hearing loss during cisplatin treatment and DNA repair genes, namely ERCC1/XPD, ERCC2 and XRCC1.
Design/Methods: Fifty patients treated with cisplatin were included in the study. The healthy control group consisted of 59 patients. The polymorphism in DNA repair genes was studied by Light Cycler after DNA isolation by PCR.
Results: Among the patients, 22 had hearing loss (HL) documented in their charts. For ERCC1 gene, the patients with HL had 50% (11) of GG (wild type), 32% (7) of AG (heterozygous), and 18% (4) of AA genotypes (homozygous), while the patients without HL had 30% (8) of GG, 59% (16) of AG, and 11% (3) of AA genotypes. In control group, there were 49% (29) of GG, 42% (25) of AG, and 8.4% (5) of AA genotypes. For ERCC2 gene, the patients with HL had 18% (4) of GG (wild type), 45% (10) of TG (heterozygous), and 36% (8) of TT genotypes (homozygous), while the patients without HL had 11% (3) of GG 37% (10) of TG, and 52% (14) of TT genotypes. In control group, there were 17% (10) of GG, 44% (26) of TG, and 39% (23) of TT genotypes.For XRCC1 gene, the patients with HL had 14%(3) of CC (wild type), 64%(14) of CT (heterozygous), and 23% (5) of TT genotypes (homozygous), while the patients without HL had 37% (10) of CC, 48% (13) of CT, and 15% (4) of TT genotypes. In control group, there were 31% (18) of CC, 54% (32) of CT, and 15% (9) of TT genotypes.No difference was found among the groups in the distribution of each 3 genes evaluated according to the result of Chi square test.
Conclusion: Genotype of DNA repair genes is not related with hearing toxicity due to cisplatin.

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"THE TIME OF YOUR LIFE" LIFESTYLE OF ADOLESCENTS AFTER CHILDHOOD CANCER TREATMENT

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Background/Objectives: Adolescents after childhood cancer treatment can, just as their peers, come into contact with an unhealthy lifestyle including smoking, drinking alcohol, using cannabis, lack of exercise and unhealthy nutrition. Due to the possible (late) effects of their treatment, they might be more vulnerable to the consequences of an unhealthy lifestyle than their peers without a cancer treatment history. The purpose of this study was to explore the lifestyles of adolescents after childhood cancer treatment and to compare them with lifestyles of adolescents without a history of cancer treatment.
Design/Methods: We included 37 adolescents (aged 12-17 years) within a five year period after their cancer treatment in our study. Data was collected using a written standardized questionnaire on obesity, physical activity, smoking, drinking alcohol and cannabis use. Results were compared with national figures of the general population in the same age group.
Results: Adolescents after childhood cancer treatment reported to spend significantly less time on physical activity per week (cycling in leisure time P= 0.00, sports P= 0.00) compared to the reference data and were three times more often underweight (11.4% vs. 3.6%, respectively). Adolescents after childhood cancer treatment stated to know significantly less cannabis users than the reference group (P= 0.00). The percentage of adolescents who reported to have smoked in the past was significantly higher compared with the reference group (P = 0.01). Both groups were similar with regard to alcohol use.
Conclusion: Adolescents after childhood cancer treatment generally show comparable lifestyles as their peers from the general population. However, they have a lower physical activity rate than healthy adolescents. Given the fact that adolescents treated for childhood cancer are probably more vulnerable for the consequences of an unhealthy lifestyle, monitoring and advise regarding lifestyle is essential.

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SYSTEMIC INFLAMMATION, OXIDATIVE STRESS AND NEUROCOGNITIVE FUNCTION IN LONG-TERM SURVIVORS OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA (ALL)

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Background/Objectives: Limited data are available on associations among chronic inflammation, oxidative stress and neurocognitive function in long-term survivors of childhood ALL. This study evaluated these associations in children treated on an institutional protocol without cranial irradiation.
Design/Methods: Long-term survivors of ALL (n=71; 50.7% male; mean[SD] age 14.3[4.7] years; 7.4[1.9] years post-diagnosis), completed neurocognitive testing at >5 years post-diagnosis. Serum collected on the day of testing was assayed for markers of inflammation (interleukin-6, tumor necrosis factor-alpha [TNF-α], C-reactive protein [CRP]) and oxidative stress (oxidized low-density lipoprotein [OxLDL], myeloperoxidase, and malondialdehyde). Pharmacological and physiological treatment-related factors were collected during therapy, including serum concentrations of high-dose IV methotrexate (HD-MTX), plasma homocysteine following HD-MTX, and dexamethasone, all quantified as area under the curve (AUC). Serum cortisol was measured once following oral dexamethasone. Spearman's correlation and Mann-Whitney U tests were used to assess associations among treatment-related factors, inflammatory and oxidative stress biomarkers, and neurocognitive function.

Results: Survivors demonstrated excess impairment (defined as an age-adjusted score $<10^{th}$ percentile) on two measures of executive function: cognitive flexibility (37.1%) and verbal fluency (42.9%). Homocysteine AUC was positively correlated with CRP ($r = 0.31$; $p = 0.012$), OxLDL ($r = 0.27$; $p = 0.026$) and interleukin-6 ($r = 0.27$; $p = 0.035$). Elevated CRP was found in survivors who had impaired cognitive flexibility (median[IQR] 3759.75 ng/ml [435.84–10309.36] vs. 638.43 [157.25–2198.55]; $p = 0.025$) and verbal fluency (2832.80 [253.85 – 9681.45] vs. 584.03 [149.59–1621.56]; $p = 0.028$), as compared to survivors without impairment. MTX AUC was negatively correlated with TNF-α ($r = -0.305$; $p = 0.012$) and myeloperoxidase ($r = -0.282$; $p = 0.019$). No association was identified between biomarkers and dexamethasone AUC or cortisol level.
Conclusion: These findings suggest that homocysteine levels following HD-MTX may be related to chronic inflammation, which is associated with executive dysfunction in long-term survivors of childhood ALL. Future research will assess whether the effects of treatment factors on neurocognitive function are mediated by chronic systemic inflammation.

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OSTEOPOROSIS IN OSTEOSARCOMA SURVIVORS AND ITS RELATIONSHIP WITH VITAMIN D GENE POLYMORPHISM

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Background/Objectives: Osteoporosis is an important late side effect seen in cancer survivors. Polymorphisms in Vitamin D receptor (VDR) gene increase the risk of osteoporosis. Here we analyzed the relationship between VDR gene polymorphisms and osteoporosis in osteosarcoma survivors.
Design/Methods: Forty osteosarcoma patients treated in Ankara Oncology Training and Research Hospital were included the study. Bone mineral density (BMD) of proximal femur of the non-operated side was measured by dual energy x-ray absorptiometry (DEXA). Patients were defined as osteoporotic and osteopenic when BMD z-score was less than -2 and between -1 and -2, respectively. Single nucleotide change polymorphism in Cdx2, FokI, BsmI, ApaI, TaqI regions of VDR gene were examined with SNAPshot mini-sequencing technique. The relationship between VDR genotypes and BMD was evaluated.
Results: There were 24 boys and 16 girls with a mean age of 12.75±3.1 years. In 50% of patients, the tumor was located in the femur. Patients received CCG94-7921 protocol (methotrexate+cisplatinium+doxorubicin). Extremity sparing surgery was performed in 27 patients and amputation in 13. A median 23 months after the end of treatment, the mean BMD score was -0.93±1.35. Reduction in BMD was present in 45 % of patients (27.5% osteoporotic, 17.5% osteopenic). Frequency of osteoporosis was higher in patients having Fok I polymorphic allele than patients with wild FokI genotype (50% vs. 7.7%, p:0.004). Fifty-five percent of patients having heterozygous or homozygous ApaI polymorphic allele were osteopenic, while osteopenia was observed only 18% of patients with wild type ApaI (p=0.038). There were no relationships between the BMD score and other VDR gene polymorphisms.
Conclusion: Vitamin D and its receptor have an important role in regulation of bone metabolism. An association between variation in VDR gene and decreased BMD has been reported. We showed that Fok I and Apa I region polymorphisms in VDR gene are related with osteoporosis in osteosarcoma survivors.

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A PHYSICAL ACTIVITY INTERVENTION IN SURVIVORS OF CHILDHOOD CANCER: A PILOT STUDY

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Background/Objectives: About 70% of childhood cancer survivors develop medical late effects of previous therapy, many of which can be prevented or mitigated by physical activity. However, survivors exercise at similar or lower levels than their already sedentary healthy peers. We studied the 1) feasibility, and 2) effectiveness of a novel home-based six-month exercise intervention with a motivational activity tracker.
Design/Methods: Pediatric oncology survivors currently ≥15 years and exercising less than the U.S. Department of Health and Human Services physical activity guidelines were enrolled and instructed to wear the Fitbit One (a 4.8 × 1.8 cm motivational activity tracker) daily for 6 months. Baseline and follow-up evaluations included a VO_2 maximum test by cardiac stress test, an Actigraph accelerometer for 7 days, and self-report surveys.
Results: Of 145 eligible participants, 19 enrolled (13.1% participation rate) with a mean age of 24.3 ± 5.8 years (range 15-35); 74% were female. Three participants withdrew with an 84% retention rate. Patients wore the Fitbit an average 19.0±4.7 days/month for months 1-3, and 15.0±7.9 days/month for months 4-6. Post-intervention, all (100%) participants "believed that regular exercise will help with long term effects of therapy" and 92% were inclined to exercise at home. All participants would recommend the Fitbit to other survivors: 25% suggested patients receive it during therapy and 75% suggested it off therapy. Overall, cardiorespiratory fitness as measured by VO_2 maximum test increased from 25.7±7.3 ml/kg/min to 27.2±7.0 ml/kg/min, and total weekly moderate vigorous physical activity increased from 250.6±63.4 minutes to 295.6±133.5 minutes, but the changes were not statistically significant (p=0.69 and 0.35, respectively).
Conclusion: This pilot study of a motivational activity device demonstrated feasibility as measured by retention, receptivity, and belief of utility. There was some improvement in cardiorespiratory fitness and weekly physical activity, though the results were not statistically significant with this small sample.

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EVALUATION OF IMMUNE RESPONSE AFTER VACCINATIONS POST-CHEMOTHERAPY IN CHILDHOOD CANCER SURVIVORS

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Background/Objectives: Survivors of childhood cancers are recommended to receive revaccinations post-chemotherapy, although the universally recommended vaccination schedule for such children has not been established. We evaluated immune response following post-chemotherapy vaccinations in childhood cancer survivors.
Design/Methods: The study included 59 patients who had survived at least 5 years off-chemotherapy without evidence of recurrence. The study patients received hepatitis B and MMR vaccines since 1 year after finishing chemotherapy according to our institutional protocol. Immune response to hepatitis B and MMR vaccines was measured and seropositivity rate and factors hindering immune response to hepatitis B and MMR vaccines were analyzed.
Results: Among 59 childhood cancer survivors, 41 children received hepatitis B and MMR vaccines post-completion chemotherapy. Their age was 63±52 (range, 1-206) months at diagnosis and 90±54 (range, 12-221) months at off-chemotherapy. Fifty eight percent of patients had hematologic malignancies and 42% non-hematologic malignancies. The seropositivity for hepatitis B virus was 88%; with higher rate in non-hematologic malignancies (100%, 18/18) than in hematologic malignancies (78.3%, 18/23) ($p = 0.05$) and reciprocally associated with the duration of chemotherapy ($p = 0.0043$). The seropositivity for measles, mumps, and rubella viruses was 61%, 37% and 83% respectively, showing significantly lower response to mumps virus and was not differ between patients with hematologic malignancies and those with non-hematologic malignancies. Unlike hepatitis B virus, the duration of chemotherapy did not affect seropositivity for measles, mumps, and rubella viruses. Ten children who failed to be immune to any of measles, mumps, and rubella viruses received booster MMR vaccination which resulted seropositive rates of 77.8%, 60%, 100% respectively.
Conclusion: Longer duration of chemotherapy and hematologic malignancies were adversely associated with achieving immune response to hepatitis B vaccine, but not to MMR vaccine. Our results also underline the need for booster vaccinations in no responders to vaccinations post-chemotherapy in childhood cancer survivors.

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SECOND MALIGNANT NEOPLASMS IN CHILDHOOD CANCER SURVIVORS IN A PAEDIATRIC ONCOLOGY CENTRE IN SINGAPORE

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Background/Objectives: One of the most feared complications of childhood cancer treatment is second malignant neoplasms (SMNs). This study aims to evaluate the incidence, risk factors and outcomes of SMNs in a tertiary paediatric oncology centre in Singapore.
Design/Methods: A retrospective review was conducted on patients diagnosed with childhood cancer under age 21 and treated or consulted for a second opinion at the National University Hospital, Singapore, between Jan 1990 and Nov 2013. Case records of patients who developed SMNs were reviewed.
Results: A total of 1,227 cases of childhood cancers were identified in this 23-year study period with a median follow-up period of 2.98 years (range: 0-24.06 years). The most common primary malignancies were leukaemia (46.4%), central nervous system tumours (11.3%) and lymphoma (11.1%). Fifteen cases developed SMNs and the most

frequent SMNs encountered was acute myeloid leukaemia/ myelodysplastic syndrome (n=7). Overall 20-year cumulative incidence was 5.3% (95% *CI*: 0.2-10.4%). The median interval period between diagnosis of primary and secondary malignancy was 3.41 years (range: 0.24-18.30 years). Overall 5-year survival rate for SMNs was lower than that of primary malignancies.
Conclusion: Reduced exposure to radiotherapy may have contributed to a smaller proportion of secondary solid tumours as compared to Western cohorts. Significant risks of SMNs were found especially in survivors of childhood ALL and osteosarcoma, and are likely to be therapy-related. This suggests a need to review our current treatment protocols in relation to potential pharmacogenetics and genetic predispositions.

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COMMUNICATION ABOUT LATE EFFECTS DURING ROUTINE FOLLOW-UP CONSULTATIONS BETWEEN PEDIATRIC ONCOLOGISTS AND ADOLESCENTS: A VIDEO-BASED OBSERVATIONAL STUDY

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Background/Objectives: Survivors of childhood cancers benefit from information about late effects for optimal health self-management, yet many lack such knowledge. We investigated 1) to what extent potential late effects were discussed at routine follow-up consultations with adolescent survivors; 2) to what extent the paediatric oncologists (P.O.s) informed about late effects.
Design/Methods: We video-recorded consultations with 10 P.O.s and 66 adolescents, aged 12-20 years, who had been treated for leukaemia (72.7%), lymphoma (21.2%) or received hematopoietic stem-cell transplantation for a benign disease (7.6%). We identified and coded discussions of potential late effects during the consultations and then categorised the amount of information about late effects provided into three levels: none, basic and extended information.
Results: Potential late effects were discussed in 85% of the consultations. Of these, 71% were P.O. initiated, and 60% concerned existing health problems. The P.O.s provided none, basic and extended information about late effects in 41%, 30% and 29% of these discussions. Consultation length, type of potential late effect (physical vs. patient-reported and current vs future risk), and P.O. were associated with amount of information provided, whilst patient's age, time since treatment and late effect risk-stratification were not.
Conclusion: We identified a clear bio-medical focus of information practices, and many missed opportunities to provide information about late effects. The results suggest that a standardization of information provision practices regarding late effects is needed to ensure adequate patient education.

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INEQUALTIES IN CHILDHOOD CANCER SURVIVORSHIP

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Background/Objectives: Inequalities in patient-reported outcomes of survivors of childhood cancers and their supportive care needs are not often investigated and not well understood. The aims of this study are to identify inequalities in childhood cancer survivors based on individual-level data, and to investigate inequalities in late effects among adult childhood cancer survivors.
Design/Methods: Data will be extracted from the National Cancer Registry Ireland on people under the age of 18 when diagnosed from 1994 through 2012 with invasive cancer (ICD10 00-C96), excluding non-melanoma skin cancer. This data will be linked to family socio-economic status (SES) using information on parental occupation at the child's birth. Data will be analysed to estimate discrepancies in mortality based on SES. Additional data will be collected from survivors currently over 18 years of age (anticipate n=800). Data will be collected on supportive care needs, health-related quality of life, functional status and cancer symptoms, and Depression Anxiety and Stress Scale. These survey data will be linked to registry data to provide rich information on social inequality in childhood cancer survivors.
Results: In 2012 there were 2,356 childhood cancer survivors in Ireland, of which 1,102 are female and 1,254 are male. Of these, 1,186 were 18 or older. The most cancer among childhood cancer survivors of all ages is lymphoid leukaemia (n=534) followed by Hodgkin disease (n=259) and brain tumour (n=232). Further data on types of cancer, discrepancies in survivorship and inequalities in late effects will also be presented.
Conclusion: This study will collect data directly from a large number of childhood cancer survivors in Ireland. Findings from this study will highlight inequalities in late effects, providing critical information on the health needs and inequalities among long-term childhood cancer survivors.

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MOROCCAN CHILDHOOD CANCER SURVIVORS : A MEDICAL AND DEMOGRAPHIC SURVEY

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Background/Objectives: Childhood cancer is curable but survivors are at risk of numerous late effects. Among children treated from cancer between 1978 and 2004 at the Children hospital of Rabat, 1000 were considered cured by their last news. The present survey aims to establish a database of Moroccan childhood cancer survivors and to lay-out a strategy of long-term monitoring in order to improve their outcome.
Design/Methods: The survey type is transversal, exhaustive and descriptive. The data collected include initial and current medical and demographic status. To reach the survivors, we have used several means including phone, email, social networks, and postal mail. The questionnaire was completed by the survivors themselves, their parents or their physician.
Results: Two hundred and eight survivors' questionnaires had been gathered until February 2015; In average, 16 years had passed since the diagnosis. Initial demographic data are as follows: 77% were under 10 years of age, sex ratio 1.7; 75% have been diagnosed from 1995 to 2004 and were from urban areas. Initial medical data show that the majority of patients had acute lymphoblastic leukemia, lymphoma, and nephroblastoma; almost all patients received chemotherapy, 1/3 was operated and 1/3 irradiated; the great majority has never relapsed. Currently, the survivors are aged from 10 to 44 years, with a good level of education (50 % are more than high school), are living with their parents (77%), student (36%) or employed (39%), single (78%) and have physical activity (60%). Medical findings show that 68% of survivors have medical issues, mostly physical, aesthetic and psychological issues. Six second cancers and five deaths are found.
Conclusion: This first study on the Moroccan childhood cancer survivors, establishing a database, is the first step of a long-term follow up strategy, including side effects prevention, early diagnosis, and adequate treatment in order to improve survivors outcome.

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ELECTROCARDIOGRAPHY AND ECHOCARDIOGRAPHY ARE BOTH IMPORTANT IN THE FOLLOW-UP OF LONG-TERM SURVIVORS OF CHILDHOOD CANCER

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Background/Objectives: Non-invasive screening plays an important role in early detection of subclinical heart failure after anthracycline treatment for childhood cancer. Our aims were to describe ECG abnormalities in a group of asymptomatic long-term survivors of childhood cancer and to determine the agreement between ECG and echocardiography abnormalities in follow-up.
Design/Methods: ECG and echocardiography were routinely performed in 414 survivors visiting our center during a period of 4 years. Inclusion criteria were past exposure to anthracyclines and both an echocardiography and a 12- lead ECG at follow-up. Exclusion criteria were clinical heart failure, congenital heart disease and use of cardiac medication. The level of agreement between ECG and echocardiography was calculated by Cohen's kappa.
Results: Seventy-four survivors were excluded. The mean follow-up period was 14.5 years (range 5-32 years), while mean age was 21.4 years (range 6-43 years). ECG was abnormal in 52 patients (15.3%). The most common abnormalities were conduction disorders and high left ventricle voltages. A prolonged QTc (>0.45 milliseconds) was found in only 2 survivors, both with a cumulative anthracycline dose above 300 mg/m^2. Echocardiography was abnormal in 44 patients (12.9%), mostly because of mild valvular abnormalities with normal FS and EF. The level of agreement between ECG and echocardiography abnormalities was low (kappa=0.10). In the group with normal ECG and echocardiography compared to the group with abnormalities detected by one or both methods, the LVIDs/BSA was lower (p=0.03). End systolic wall stress was higher in the group with one or more abnormalities compared to the group without abnormalities (62.6 versus 57.6 g/m2, p=0.04). The number of abnormalities was not related to anthracycline dosage.
Conclusion: ECG and echocardiography abnormalities are quite common in survivors of childhood cancer. Their level of agreement corrected for chance is low indicating the

importance of both tests in the long-term follow-up of asymptomatic survivors treated with anthracyclines.

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AUDIT OF PLATINUM INDUCED OTOTOXICITY IN SURVIVORS OF CHILDHOOD CANCERS IN LATE EFFECT CLINIC AT TERTIARY CANCER CENTRE

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Background/Objectives: Ototoxicty is a frequent and dose limiting side effect of platinum compounds, and is often compounded by other risk factors such as concurrent cranial radiotherapy (CRT), coexistent ear pathologies, renal impairment and use of other ototoxic drugs. Aim: To find out the incidence of sensorineural hearing loss (SNHL) among the survivors (≥ 2 years after cessation of therapy and disease free) of childhood malignancies who had received platinum agents and are followed up in *A*fter *C*ompletion of *T*herapy (*ACT*) clinic at Tata Memorial Hospital, Mumbai.
Design/Methods: ACT clinic database from February 1991 to December 2014 was analysed for ototoxicity among survivors who had received platinum agents.
Results: Of 1714 survivors enrolled during the period, 269 (15.6%) had received platinum compounds with or Without CRT. Median age at diagnosis was 4 years (Range 1 to 30 yrs). Median age at follow up was 14 years (Range 3 to 45 yrs). Male to female ratio was 1.5:1. 217 survivors received cisplatin, 29 carboplatin and 23 received both. Twenty one survivors received CRT along with platinum agents. Mean dose of cisplatin was 348 mg/m^2 and carboplatin was 1461 mg/m^2. Audiometry data was available only in 67 survivors as pure tone audiometry (PTA) could not be done in large cohort of younger (<5 yrs) survivors. Among survivors who received only cisplatin (n=40) incidence of SNHL was 35%, only carboplatin (n=13) 23% and who received both (n=14) incidence was 28.5%. With concomitant use of CRT incidence of ototoxicity was 50%, 33% and 60% respectively in the above group.
Conclusion: Although platinum agents are indispensable part of various chemotherapeutic regimens for childhood malignancies, sensorineural hearing loss is major late effect on long term follow up. Detection of ototoxicity in younger survivors is a challenge and early detection may help in earlier interventions to minimize developmental delay.

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DOSE REDUCTION IN CRANIAL PROPHYLAXIS IRRADIATION FOR HIGH RISK CHILDHOOD LYMPHOBLASTIC LEUKEMIA, THE IMPACT ON OUTCOME: SECI EXPERIENCE

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Background/Objectives: Pediatric oncologists have steadily reduced the use of this treatment modality since the late 1970s.But they are reluctant to omit cranial irradiation from protocols for high-risk patients. When radiation dose was decreased from 2400cGy to 1800 cGy it reduced the neurotoxicity to an acceptable level without decreased efficacy. Late effects on pituitary function and growth were also reported by most endocrinologists involved in the follow-up of the cancer survivors [6],they agree that cranial radiation dose lower than 16 Gy is associated withlower risk of hypothyroidism development.
Design/Methods: It includes all patients diagnosed as ALL (high risk) in the Pediatric Oncology department south Egypt Cancer Institute between the years 2000 and 2013. All patients received Whole Brain Irradiation (WBI) as part of their treatment protocol.We consider the patient as high risk ALL patients if:-age more than 10 years.-Total leukocyte count more than 50000-Slow early responder to the induction-Extramedallary presentation of the diseases.The patients will divided to 2 groups: Group A: received 1800cGy whole brain irradiation as a part of treatment prococol.Group B: received 1200cGy whole brain irradiation as a part of treatment protocol.
Results: There was no difference in CNS relapse between the two groups (p=0.845). The 1800cGy group showeda significant abnormalities in hypothalamic pituitary axis eg decreased growth hormone (p< 0.001). decreased thyroid hormones (p< 0.001).
Conclusion: Prophylactic whole brain irradiation if given for high risk ALL the recommended dose is 1200cGy due to the lower long term endocrinal abnormalities and no difference in the CNS relapse.

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ACTIVE VIDEO GAMING IMPROVES MOTOR AND PROCESS SKILLS IN SURVIVORS OF CHILDHOOD BRAIN TUMORS

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Background/Objectives: Physical activity can positively affect cognitive functions in humans and neurogenesis in animal models. We hypothesized that active video gaming (AVG) could: i) improve cognitive functions; ii) improve the execution of activities of daily living; iii) improve physical functioning, in survivors of childhood brain tumors.
Design/Methods: Children 7-17 years old who completed treatment, including radiotherapy, for a brain tumor 1-5 years earlier were randomized to either intervention or waiting-list. After 10 weeks the groups crossed-over. A motion-controlled video console (Nintendo Wii) was used during the intervention period, for a minimum of 30 minutes/day, 5 days/week. Weekly Internet based coaching sessions were held. Cognitive tests, motor tests (BOT-2), as well as testing the execution of daily activities (ADL), using the Assessment of Motor and Process Skills (AMPS) were done before and after each period, by a blinded examiner. Test scores before and after the intervention were compared. A parallel group comparison was performed as a sensitivity analysis.
Results: All 13 children (mean age 12.5 years) enrolled in the study (six boys and seven girls) completed the program. A significant improvement was seen after the intervention period compared to baseline, in Body Coordination (p= 0.020), and in the motor (p= 0.012) and process (p=0.002) parts of AMPS. In the parallel group analysis the improvement in the process part of AMPS remained statistically significant (p= 0.029), but the change in AMPS motor (p= 0.059) or Body Coordination (p= 0.28) was not. No statistically significant change in the cognitive outcome was seen although there were trends for improvement in sustained attention (p = 0.090) and selective attention (p = 0.078).
Conclusion: AVG, used as an enjoyable home-based intervention for survivors of childhood brain tumors, improved body coordination as well as motor and process skills in ADL after a 10 week AVG period.

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LATE EFFECTS OF TREATMENT IN SURVIVORS OF CHILDHOOD CANCERS : SINGLE CENTER EXPERIENCE

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Background/Objectives: With refinements in diagnostics and advances in therapeutics and supportive care the overall survival of childhood malignancy has increased. This is however at the cost of increased morbidity in the form of various long/late effects of cancer treatment. Comprehensive studies assessing the whole spectrum of late effects and their impact on the social, health and professional life of these survivors are still lacking from developing economies. We report data from a cohort of 300 childhood cancer survivors being followed at our pediatric cancer survivor clinic.
Design/Methods: Retrospective evaluation of case records was done. Details of primary diagnosis, treatment received were noted. Details of remission/relapse, growth and Myocardial function were obtained. Pulmonary function assessment thyroid profile, hearing and vision assessment was done where indicated. IQ assessment and psycho social assessment was also done. Transfusion related hazards were assessed. Details of second malignant neoplasm were noted and grades of disability recorded. Details of social adjustment into home, school, society were recorded.
Results: Commonest cancers include Hodgkin lymphoma, acute lymphoblastic leukemia and retinoblastoma. Eleven patients relapsed. Two second malignancies were recorded .69 patients had minimal disability (growth impairment), 39 had moderate disability (majority due to HBSAg positivity), 1 had grade 3 (mental retardation) and one died of liver disease (grade 5). Intelligence was affected and behavioral abnormalities identified. 25% patients had height less than 3rd centile. Hypothyroidism was seen in 2. Azoospermia was seen in one. Only three patients (4%) were found to have asymptomatic mild myocardial dysfunction.
Conclusion: Long term morbidity in childhood cancer survivors is an emerging concern: the challenge being to improve survival while reducing severity of late effects. Our study shows that late effects are of concern: Awareness towards the existence of late effects of cancer therapy is required among parents, patients and health professionals.

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OBSTRUCTIVE SLEEP APNEA IN SURVIVORS OF PEDIATRIC BRAIN TUMOURS

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Background/Objectives: Obesity has become an increasingly prevalent condition in children impacting 42 million children under the age of five today. A pediatric population at great risk of obesity are survivors of pediatric brain tumours due to post-treatment endocrine abnormalities. Obstructive sleep apnea (OSA) is a common comorbidity of obesity and little is known about OSA in survivors of pediatric brain tumours. The aim of this study was to assess the risk of OSA by evaluating sleep-related breathing disorder (SRBD) symptoms in survivors of pediatric brain tumours (cases) compared to non-cancer controls using Chervin's Pediatric Sleep Questionnaire (PSQ).
Design/Methods: One hundred participants (37 cases and 63 controls) were recruited to the Canadian Study of Determinants of Endometabolic Health in Children (CanDECIDE) from a tertiary care centre in Hamilton, Ontario, Canada. Recruitment was based on the following inclusion criteria: 5 years and older, male or female, history of surviving a brain tumour or no history of brain tumour, no previous use of immunosuppressant therapy or steroids, and 2 weeks without active infection. Participants were assigned an SRBD score using Chervin's PSQ scoring criteria.
Results: Twenty-seven percent of cases (n=10/37) and 25% of controls (n=16/63) were identified as overweight or obese (BMI-centile≥85). Cases had a mean SRBD score of 0.128 (SD±0.131) compared to the mean SRBD score of controls 0.119 (SD±0.110) (p=0.722). Linear regression correlated an increased BMI-centile to an increased SRBD score however the results were statistically insignificant (p=0.790).
Conclusion: Numerous case reports have identified SRBD in survivors of pediatric brain tumours. A cross-sectional case-control study has not been completed. OSA interventions have been used as a treatment for obesity in the general population and may be a possible obesity intervention for survivors of pediatric brain tumours. Further research is needed to determine the risk of OSA in patients who have survived pediatric brain tumours.

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WELLBEING OF CHILDHOOD BRAIN TUMOR SURVIVORS: WHAT CAN WE LEARN FROM THEIR AFTERCARE AND SCHOOL TRAJECTORIES AND WHAT ARE THE PARENTS' PERSPECTIVES?

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Background/Objectives: Children who survived a brain tumor are more prone to neurocognitive difficulties and frequent absences at school, often compromising their educational trajectory. A close monitoring by the school staff is crucial for timely intervention in case of problems. Unfortunately, most teachers and counselors are not aware of or informed about these vulnerabilities. Moreover, children are frequently referred to a professional only when obvious deficits emerge. Contemporary research on the aftercare and educational trajectories including parental and school perspectives, is scarce. Recommendations on follow up aimed at the school staff, caregivers and parents, are needed. We want to identify key events during the aftercare trajectory exploring experiences, needs and expectations of these children and their parents. In addition, we focus on the communication between the main care providers, family and school environment.
Design/Methods: A longitudinal qualitative study is carried out among a group of children, their parents, caregivers and key figures at school. We conduct semi-structured interviews and focus groups during two years. Children that are included, have finalized their treatment and returned to regular elementary school at the start of the study. Data are analyzed according to the case study design from a phenomenological perspective.
Results: Our preliminary findings reveal that psychosocial difficulties and neurocognitive sequelae have an impact on the child's wellbeing and overall development and are not monitored for in a systematic way, delaying implementation of appropriate guidance and support. Parents are highly concerned about the socioemotional functioning of their child. When confronted with poor academic results, the communication between the key figures is not always sufficient or effective and expectations, responsibilities and working methods seem to differ.
Conclusion: Drawing on the results, we hope to improve the wellbeing of children who survived a brain tumor and their families by developing recommendations for the school staff and care providers involved.

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LEFT VENTRICULAR MASS AND AMBULATORY BLOOD PRESSURE – IMPORTANT FOLLOW-UP MARKERS IN CHILDHOOD CANCER SURVIVORS

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Background/Objectives: The aim of this study was to investigate left ventricular mass (LVM) and cardiac function - predictors of cardiovascular morbidity and mortality - in young adult survivors of childhood cancer treated with intensive induction chemotherapy regimens followed by myeloablative treatment with hematopoietic stem cell support.
Design/Methods: Our national cross-sectional study cohort consisted of 19 adult (age 22.7±4.9 years, range 16-30) neuroblastoma (NBL) survivors and 20 age and sex matched healthy controls. NBL survivors were transplanted during 1984-1999 at the mean age of 2.5±1.0 years. Indexed LVM, left ventricular (LV) function and volumes were assessed with Three-Dimensional echocardiography and Tissue Doppler echocardiography. The cardiovascular risk assessment included history, body-mass index, fasting plasma lipids, glucose, and 24h ambulatory blood pressure (BP).
Results: Survivor's indexed LVM was increased compared with healthy controls (33.9 g/m2.7 vs. 28.1g/m2.7, p=0.038). In multiple linear regression analysis, the systolic BP was positively associated with LVM in NBL survivors. Increased LVM in survivors was associated with a decrease in both systolic and diastolic LV function. The end diastolic LV volume was decreased in the irradiated patient group when compared with controls suggesting myocardial fibrosis related restriction (41.1ml/m2 vs 48.5ml/m2, p=0.004).
Conclusion: LVM is increased in long-term childhood cancer survivors. The treatment of BP might prevent adverse left ventricular remodeling in these patients.

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THE EFFECTIVE STERILISING DOSE OF RADIATION FOR THE HUMAN OVARY

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Background/Objectives: To determine the dose in Gray of fractionated radiotherapy that will reduce the fixed and non-renewing population of immature eggs in the human ovary to below the threshold at which premature ovarian insufficiency (POI) ensues.
Design/Methods: Age at treatment, RT dose and age at occurrence of POI were recorded from subjects (n = 6, median age at treatment 12.6 years, range 4.9 – 15.1 years) receiving Total Body Irradiation (TBI) as conditioning treatment for a stem cell transplant. These data were analysed to derive a formula that gives the proportion of immature eggs after a given dose. Solving this formula in conjunction with a model of the decline of the non-growing follicle pool with age determines whether the dose is sufficient to reduce the immature egg population to below 1,000 for 97.5% of the female population at the age of treatment.
Results: The formula is $log_{10}(NGF) = 2 - 0.141(dose)$, where NGF denotes the percentage of non-growing follicles present at age at treatment and $dose$ denotes the radiation in Gy delivered to the ovary. Given that 97.5% of human ovaries contain 540,000 immature eggs at 5 years of age, 440,000 immature eggs at 10 years, and 330,000 immature eggs at 15 years, we report exemplar effective sterilising doses of 19.2 Gy at age 5, 18.6 Gy at age 10, and 17.8 Gy at age 15.
Conclusion: We show that if the dose of radiation to both ovaries is known, it is possible to calculate the effective sterilising dose of radiation for the human ovary. It therefore remains important for the radiation oncologist to calculate the dose received by the ovary furthest away from the radiation field. Knowledge of the effective sterilising dose provides important information for counselling females about their future reproductive potential and the potential need for fertility preservation.

Posters: Liver Tumours

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PEDIATRIC HEPATOCELLULAR CARCINOMA: A 23-YEAR EXPERIENCE AT A SINGLE INSTITUTION IN ARGENTINA

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Background/Objectives: Hepatocellular carcinoma (HCC) in childhood is rare, less than 0.5 % of all pediatric malignancies. Is the second most common primary liver malignancy of childhood after hepatoblastoma. Surgical resection remains the mainstay of treatment. To report the 23-year experience of pediatric patients (pts) with HCC treated at a single Institution in Argentina following the guidelines of SIOPEL- trials.
Design/Methods: We retrospectively analyzed 41 consecutive pts with diagnosis of HCC admitted at our Institution from January 1990 to December 2013.
Results: M/F: 1.4:1.Nine pts (22 %) had underlying disease (UD): Autoimmune Hepatitis type1 (2pts), Familiar Cholestasis (1 pt), Tyrosinemia (1 pt), Hepatitis chronic (1 pt), Cryptogenic cirrhosis (1 pt), Tyrosinemia and Fanconi Syndrome (1 pt), Glycogenosis Type 1 (1 pt), and Ataxia telangiectasia (1 pt). Median age at diagnosis: 121 months (19 -209), and 79 vs 148 months with or without UD.Most common symptoms were abdominal mass: 54% and abdominal pain: 34%. Median onset of symptoms: 2 months (1 - 32). Median serum AFP levels: 221.590ng/dL (14 - 1.226.040), elevated in 68%. PRETEXT (pretreatment extent of disease): available in 38/41. PRETEXT I: 16, II: 21, III: 31.5 and IV: 31.5%. Multifocal tumors: 51%. Vascular involvement: 34%. Metastatic disease: 27% (all lung metastasis). Twenty four pts (58%) underwent surgery, liver transplantation 10, and resection 14 pts. 55% received quimioterapy before surgery. All patients who did not undergo surgery procedure died. With a median follow up of 11 months (2.9-80.88), 5-year Overall Survival was 22 %, for the whole group, and 45% vs 6%, for localized vs metastasic disease respectively (p=0,0001).
Conclusion: HCC in children is associated with poor survival, mainly among metastatic disease and unresectable liver tumors. In contrast to adults series, in only 20% underlying diseases could be identified. Innovative therapeutic approaches are needed to improve the outcome.

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RETROSPECTIVE STUDY ON PROGNOSIS OF CHILDREN HEPATOBLASTOMA IN BEIJING TONGREN HOSPITAL FROM 2006 TO 2014

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Background/Objectives: Hepatoblastoma (HB) is a rare malignant solid tumor, but is the most commonly liver malignant tumor in children.study on clinical therapy and prognosis of children hepatoblastoma with comprehensive treatment through analysis the morbidity characters and isk factors.
Design/Methods: In this study, a total of 102 hepatoblastoma subjects were collected from September, 2006 to June, 2014. Clinical record and follow-up information of these subjects was also obtained to conduct the Kaplan-Meier survival analysis and log-rank test.
Results: (1)In 102 cases, the median age of the subjects was 1.5 years. According to clinical stage standard in CCG-POG: 4 cases of II stage, accord for 3.9%, 46 cases of III stage, accord for 45.1%, 52 cases of IV stage, accord for 51.0% . pathological type: 63 cases of epithelial, accord for 69.24%, and 28 cases of mixed, accord for 30.76% (2)In 102 cases, 52 cases were complete remission (CR), 51%, and 20 cases were partly remission (PR), 19.6%, and 28 cases were dead, 27.4% after comprehensive treatment. Follow up to January 2015, average follow up time were 27.54±19.95)months, 2-year total survival rate was 76.54%, 3-year EFS was 60.5%. 81 cases of followed up time were more than 12 months. In 81 cases, 5-year average survival time was 71.1 months, and 95% credible interval was 61.15-80.9 months by analysis on kaplan-merine. 3 Event-free survival (EFS) of II stage were: 100%,100%,0, 3-year EFS of III stage were 100%,71.4%,62.5%,0%,100%,100%, and 3-year EFS of IV stage were 66.7%,25%,33.3%. 3 EFS of IV stage with metastasis was 51.2%, and 3-year EFS of AFP less than <100ng/dl was 50%.
Conclusion: the distant organs metastasis, hepatic portal vein, central venous invasion was still important prognostic factors. It should be noted as well as younger children with early disease, AFP obvious increase in cases of early disease for reduce the relapse rate.

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SUCESFUL TREATMENT OF UNDIFFERENTIATED SARCOMA OF THE LIVER WITH SURGERY AND CHEMOTHERAPY

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Background/Objectives: Primary malignant hepatic tumors in children are rare, accounting for less than 2% of childhood cancers. Undifferentiated sarcoma of the liver (USL) constitutes the third most common after hepatoblastoma and hepatocellular carcinoma. We review our cases and present their treatment.
Design/Methods: Patient 1: In May, 2000, an asymptomatic 6 years-old girl presented with an abdominal mass. Ultrasound and CT scan disclosed a cystic hepatic tumor in the left lobe. Transaminases were elevated, bilirubin and AFP were normal. The diagnosis of Hydatid cyst was considered. A complete surgical resection was done and the diagnosis of USL was rendered. She received chemotherapy. Patient 2 presented in May 2012 at 9 years of age with progressive abdominal pain, malaise and fever. CT scan disclosed a mixed solid/cystic hepatic tumor with evidence of necrosis. She underwent total tumor resection and chemotherapy. Patient 3 is a 7 years–old boy with abdominal pain, he had a history of mild trauma and the pain increased progressively. He developed abdominal distention and underwent a partial resection of an hepatic tumor and was refered to our care in June 2014. He is undergoing chemotherapy and is scheduled for a second look surgery. All patients were treated with this chemotherapy protocol: Three cycles of PIAV alternating with 2 cycles of VAIAPIAV: Cisplatin 90 mg/m2 day 3,24, Ifosfamide 3g/m2 day 1,2,22,23,43,44, Doxorubicine day 43,44 and Vincristine 1.5 mg/m2 weekly VAIA: Vincristine 1.5 mg/m2 weeks 1 to 4 and 7, Dactinomycin 0.5 mg/m2 daily for 3 days 1-3 and 43-45, Ifosfamide 3g/m2 days 1,2,22,23,43,44 and Doxorubicine 40 mg/m2 days 22 and 23.
Results: The patients are alive, two of them off therapy for 15 and 2 years.
Conclusion: With this aproach we have had good results in our patients. It is necesary to implement an international trial in order to standardize the treatment of USL.

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PHOTODYNAMIC EFFECTS OF CURCUMIN ON PEDIATRIC HEPATOBLASTOMA AND HEPATOCELLULAR CARCINOMA CELLS LINES

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Background/Objectives: Curcumin, the yellow dye derived from the roots of turmeric, is a promising agent complementary oncology. The former low oral bioavailability of curcumin was overcome by a micellar formulation with high concentrations of curcumin e.g. in experimental pediatric hepatocellular carcinoma in vivo. The recent study analyzed the photoactive properties of curcumin on hepatoma cell lines *in vitro*.
Design/Methods: Hepatoblastoma cell lines (HuH6, HepT1) and hepatocellular carcinoma cell lines (HepG2, HC-AFW1) were treated with curcumin with increasing concentrations, the cultures were either kept in the dark or exposed to blue light (480 nm). Analysis of cell viability was performed in MTT-tests. Cellular oxidative stress was analyzed measuring the production of reactive oxygen species (ROS). Reduction of cancer stem cells population (CSC) by cisplatin, by curcumin alone, or by curcumin with PDT, was investigated with FACS analyses.
Results: In all cell lines IC50 were significantly lower after blue light exposure than after curcumin alone ($p < 0.001$, two-way ANOVA). Blue light exposure resulted in significant ROS production in all cell lines. Curcumin alone reduced HEK-6D6 positive CSC not as effectively as cisplatin alone or as curcumin with PDT.
Conclusion: Considering the strong potential of reducing viability and the proportion of cancer stem cells in hepatoma cells lines, curcumin may be developed as a potential photodynamic agent as well as a chemotherapeutic agent in pediatric solid liver tumors.

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CISPLATIN ALONE IN THERAPY OF STANDARD-RISK HEPATOBLASTOMA: FEASIBILITY OF SIOPEL-3 SR PROTOCOL IN RUSSIA

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Background/Objectives: Hepatoblastoma is a most common primary liver malignancy of childhood. Risk-adapted therapeutic approach resulted in significant de-intensification of therapy in certain subgroup of patients. The purpose of this study

was to analyze patients with hepatoblastoma treated according to SIOPEL protocols in two centers in Russian Federation.
Design/Methods: Thirty two patients with malignant liver tumors were treated during the period 01.2012 - 12.2014. Hepatoblastoma was diagnosed in 24 (75.0%) patients. Initial work-up included chest computed tomography (CT), abdomen CT and magnetic resonance imaging (MRI), alpha-fetoprotein (AFP) level. The pretreatment extent of disease (PRETEXT) system was used for staging. SIOPEL criteria were used to stratify patients to standard and high-risk group. Patients were treated according to SIOPEL treatment strategy. Fifteen (62.5%) patients were stratified to standard-risk group. Two patients received more than one drug and were excluded from the analyses.
Results: Thirteen (54.2%) patients received cisplatin monotherapy. Median age was 11.5 months (range 0.1-37.0). Seven (53.8%) patients were < 1 year. Male: female ratio was 0,44:1. Initial diagnosis was based on histology (11/13, 84.6%) or clinical data (2/13, 15.4%). Median AFP level was 349,160 (range 847-1,971,991). Distribution of patients by PRETEXT stage was the following: I - 2 (15.4%), II - 10 (76.9%), III - 1 (7.7%). Response was observed in 12/13 patients, in 1 (7.7%) case the therapy was switched to high risk protocol. Surgery was done in all 12 patients after the 4th cycle and resulted in R0 resection. 11/12 patients received 6 planned doses of cisplatin. In 1 patient two postoperative doses of cisplatin were omitted because of postsurgical complications. All patients are alive with no evidence of disease. Median time of follow-up was 14.5 months (range 3.8 – 28.5).
Conclusion: The introduction of PRETEXT system allowed reducing the therapy intensity in 50% patients with hepatoblastoma while maintaining high efficiency of therapy.

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HEPATOBLASTOMA; A SINGLE CENTRE EXPERIENCE FROM A DEVELOPING COUNTRY

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Background/Objectives: Hepatoblastoma is the commonest liver malignancy in children. Complete surgical resection is the main goal of treatment and a prerequisite for cure. Early detection, thorough diagnostic assessment and modern imaging modalities are helpful in achieving the goal of complete surgical resection. Management becomes even more challenging in a developing country with limited resources, poor framework of healthcare system and understanding of disease.
Design/Methods: Medical records of patients with hepatoblastoma treated between 2005 and 2015 were retrieved from the hospital data base and analysed retrospectively. Diagnostic labs including serum alph fetoprotein level (AFP), radiological imaging, tissue diagnosis technique, histology, staging details, treatment protocol and surgical details were recorded. Finding of repeat CT recorded for the surgical planning. The main outcome variable was survival. Results were analysed using Statistical Package for Social Sciences (SPSS 17).
Results: A total of 17 patients were treated during this period. Majority of them were males 13 (77%). More than 60% of the patients were less than 2 years at presentation. All the patients received chemotherapy according to SIOPEL. Three patients had metastatic disease at presentation and died while on chemotherapy while two were lost to follow up (presumed dead). Those patients who underwent surgery (n=12) the overall survival was 75% (n=8) after a mean follow up of 33 months. Out of the 4 observed mortalities, one developed lung metastasis, two had incomplete resection and developed local recurrence while one died due to adjuvant chemotherapy related issues. All those patients who are alive had a complete surgical resection. One patient had significant disease involving couinaud's segment 4-8 underwent associated portal vein ligation with liver partition for staged hepatectomy (ALPPS). This patient had complete resection of tumour and did not suffer liver insufficiency.
Conclusion: Long term overall survival is determined by complete surgical resection.

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IMPACT OF LIVER TRANSPLANTATION ON SURVIVAL OUTCOMES OF HEPATOBLASTOMA

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Background/Objectives: Liver transplantation (LT) permits long-term survival of the patients with unresectable hepatoblastoma, whose outcomes are extremely dismal without LT. This study was to analyze the outcomes of hepatoblastoma, highlighting on the impact of LT.
Design/Methods: We retrospectively analyzed the medical records of 64 children with hepatoblastoma treated at Asan Medical Center between 1991 and 2014. LT program for hepatoblastoma started at Asan Medical Center in 2007. Twenty-nine and 35 patients were treated before and after 2007, respectively.
Results: According to the PRETEXT staging system, 3 patients were PRETEXT I, 31 were II, 13 were III, and 17 were IV. Twenty-five patients had distant metastases at diagnosis. Of 64 patients, 5 underwent primary tumor resection, and 59 patients received preoperative chemotherapy, followed by tumor resection (including LT in 12 patients). The 5-year overall survival (OS) rate was 66.8%. PRETEX stage and metastasis at diagnosis were significantly associated with OS (PRETEXT I vs. II vs. III vs. IV: 100% vs. 79.7% vs. 55.9% vs. 43.9%, $P = 0.004$; no metastasis vs. metastasis: 79.6% vs. 47.1%, $P = 0.026$). The 5-year OS after 2007 was significantly better than that before 2007 (80.7% vs. 55.2%, $P = 0.045$). The prognostic impact of PRETEXT stage was observed only before 2007, and not after 2007 (PRETEXT I vs. II vs. III vs. IV: 100% vs. 73.3% vs. 50.0% vs. 14.3% before 2007, $P = 0.008$; 100% vs. 93.8% vs. 60.0% vs. 67.5% after 2007, $P = 0.379$). Furthermore, impact of metastasis at diagnosis on survival tended to be less prominent after 2007 (no metastasis vs. metastasis: 71.4% vs. 40.0%, $P = 0.147$ before 2007; 83.6% vs. 70.0%, $P = 0.405$ after 2007).
Conclusion: Our result demonstrated that LT could overcome previously known poor prognostic factors of hepatoblastoma such as PRETEXT stage and metastasis.

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13 - YEARS EXPERIENCE WITH LIVER TUMOURS MANAGEMENT - SINGLE CENTRE REPORT

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Background/Objectives: Liver tumors are very rare and constitute only 1-4% of all solid tumors in children. Two-thirds of these tumors are malignant. The most common primary malignant tumors are hepatoblastoma and hepatocellular carcinoma. The main objective of this report is to present 13 years experience with diagnosis, treatment and outcome in children with liver tumors at our Department of Pediatric Oncology in Bratislava. The cornerstone of longterm survival remains complete surgical resection in liver speciality center. Pre and postoperative chemotherapy increases resectability rate, decreases the risk of microscopic residual disease as well as local relapse rate.
Design/Methods: In the retrospective study we analysed 16 patients with different types of liver tumours, mainly hepatoblastoma (HB) and hepatocellular carcinoma (HCC). The children were treated according the SIOPEL protocols, and after that in a case of resectability, complete resection of the tumor, liver transplant included.
Results: In the group of the patients with HB (8) complete resection was possible in 6. In 1 patient primary liver transplant (OLT) was indicated. 5 patients are alive with follow up 60 - 142 months. 2 patients relapsed (1 after complete resection, 1 after primary OLT). 1 patient died due to progression on the treatment and 2 patients died due to relapse after primary resection. In the group of patients with HCC (5), complete resection was possible in 4 cases, these patients are alive in complete remission with follow up 44 - 129 months. 1 pt. relapsed after complete resection, curently is alive in progression of disease, 1 pt. died (non resectable tumour).
Conclusion: In a case of complete resection the outcome was better and those patients had the chance for cure. The past two decades has brought significant improvement in managment and outcome for children diagnosed with liver tumors. These improvements are the results of multidisciplinary approach and international trials.

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LIVER TUMOURS IN CHILDREN; RELATION OF HEPATOBLASTOMA WITH LOW BIRTH WEIGHT AND INCIDENCE OF HEPATOCELLULAR CARCINOMA EARLIER IN AGE?

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Background/Objectives: The most common types of liver tumors in pediatric patients are hepatoblastoma (HB, 80%) and hepatocellular carcinoma (HCC, 20%). The relationship between perinatal characteristics and hepatoblastoma as well as the outcome of liver tumors is the aim of our study.
Design/Methods: Eleven children with liver tumors who were diagnosed and treated in our unit were enrolled in our study. The age at diagnosis ranged from 2 months to 5 years for HB(med:12 months) and 7-8 years for HC. Predisposing factors such as hepatitis B,C, CMV, or metabolic disorders were tested. All patients treated according to SIOPEL protocol (plus Nexavare, in HCC) and remain in follow up.
Results: 9 cases had HB (3 with stage IV), and 2 HCC. The birth weight of patients was ranged from 1770gr-3850gr while 6 out of eleven children (66%) had birth weight lower than 2900gr. The gestational age in 4 cases was also lower than 37 weeks. Predisposing

factors were not observed in any of our cases with HCC. The a-FP level ranged from 714ng/ml to 418,846.00ng/ml in HB while from 10,520.00ng/dl to 60,500.00ng/ml in HCC. All cases are in complete first remission. One patient with HCC had reactivation of the disease. He had a second total resection of the tumour and received Nexavar. He achieved second remission.
Conclusion: 1) There is an increased risk for hepatoblastoma among children with low birth weight. 2) No predisposing factors were found in children with HCC. 3) Although the HCC is usually diagnosed at the age of 10-14 years old, our cases were diagnosed in the earlier childhood. 4) Surgical resection and the SIOPEL protocol give an excellent outcome even in stage IV, without radiotherapy.

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LAPAROSCOPIC RESECTION OF LIVER TUMORS IN A CHILDREN

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Background/Objectives: Laparoscopy for the resection of liver tumours in children has remained undeveloped in comparison to adults. Most of the indications for pediatric laparoscopic hepatic surgery have been limited to diagnostic laparoscopy and laparoscopic biopsy. Over the past ten years, however, laparoscopic liver resections for pediatric hepatic diseases have been performed successfully, and many case reports have been published.
Design/Methods: The authors report 4 cases of laparoscopic hepatic resection of benign tumors in children.
Results: In 2 patients (11-month-old boy and 3-year-old girl) an anatomical resection was performed (left lobectomy). In another 2 (12-year-boy and l6-year-old girl) a nonanatomical resection was done. There were no complications and patients were discharged on postoperative day 4, 5, 5 and 7 accordingly. The postoperative pathology of the specimens confirmed their benign nature: 1 – haemangioendothelioma infantile, 1 – „nested stromal epithelial tumor", 2 – focal nodular hyperplasia. The tumors measured 2,2 cm, 3 cm, 6,5 cm and 5 cm in maximum diameter, accordingly.The resection margins were disease-free in all cases.
Conclusion: This report demonstrates the feasibility of a laparoscopic hepatic resection in children. On the other hand, laparoscopic liver resection is challenging and teamwork and specific training are necessary.

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LIVING-RELATED TRANSPLANTATION OF A LIVER IN CHILDREN WITH HEPATOBLASTOMA

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Background/Objectives: Malignant liver tumors make 1 – 2% of a number of all tumors of the child age, with yearly incidence of 1,5 cases per million of children aged up to 15 years.
Design/Methods: At the posthoc analysis as of from 2008 to 2014 in Ukraine at the stage of surgical treatment of hepatoblastomas in children 7 living-related transplantations of a liver were performed, among them: orthotopic transplantation of the lateral section of a liver from the live relative donor (mother) was executed to five patients at the stage of surgical treatment, to one patient - hepatectomy, total pancreatectomy, gastroduodenectomy, splenectomy, extended lymphadenectomy, esophagojejunostomy, mesocaval shunting, orthotopic transplantation of the left lateral section of the liver from the live relative donor (mother) with cava portal transposition, and the transplantation concerning recurrence of hepatoblastoma after left-sided expanded hepatectomy was executed to one patient. Average age of children to whom the living-related transplantation of a liver was carried out made 2,7 years. Chemotherapy according to the clinical protocol SIOPEL 3 was carried out to all patients, group of high risk.
Results: The average time of the execution of the operation made 14,5 hours. In the postoperative period biloma of the resective surface of the graft developed in 1 patient, it was removed by way of ultrasound-controlled puncture. Complete remission of the disease was recorded in all 7 patients to whom living-related transplantation of the liver was executed. The five-year survival rate of patients with hepatoblastoma to whom transplantation of the liver was executed makes 100%, the five-year survival of the graft made 100%.
Conclusion: Executing the living-related transplantation of a liver in children with hepatoblastoma of a liver is a difficult stage of multimodality therapy demanding considerable material and technical support and it allows to achieve good remote results statistically authentically.

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THE SIGNIFICANCE OF PIVKA-II TO HEPATOCELLULAR CARCINOMA PROGNOSIS

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Background/Objectives: Hepatocellular carcinoma (HCC) is a leading cause of mortality among patients with cirrhosis. Detection of HCC at early stage is critical for good clinical outcome, as the prognosis of HCC patients is very poor.The present study was designed to study the role of prothrombin induced by vitamin absent II (PIVKA-II) in early diagnosis of liver cirrhosis, compared with alpha-fetoprotein (AFP).
Design/Methods: The patients consisted of 45 children with liver cirrhosis and 45 normal children. Female and male ratios in cirrhosis and controls were 24/21 and 26/19, respectively, and the mean ages were 12.5 and 13 years. Complete clinicopathological examination was carried out for each children to confirm diagnosis. The serum levels of AFP and PIVKA-II were determined by the ELISA methods.
Results: The results revealed a significant increase of PIVKA-II and AFP levels in cirrhosis group, compared to the controls. PIVKA-II showed a significantly higher increase than AFP level in liver cirrhosis, compared with levels in normal group.
Conclusion: Therefore, PIVKA-II can serve as an important factor in screening high risk children and early diagnosis.

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PATTERN OF CLINICO-RADIOLOGICAL CHARACTERISTICS AND RELATED BIOCHEMICAL AND PATHOLOGICAL FEATURES OF HEPATOBLASTOMA IN A DEVELOPING COUNTRY

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Background/Objectives: The aim of this study was to describe the clinico-radiological characteristics and related biochemical and pathological features of hepatoblastoma in a developing country.
Design/Methods: A prospective observational study was conducted between March, 2010 to July, 20114 in a single tertiary care centre at BSMMU in Bangladesh. The clinical features, radiological findings and biochemical and pathological changes of hepatoblastoma were evaluated. Radiological evaluation was by CT scan and serum alphafetoprotein was done as tumor marker for hepatoblastoma and histopathological evaluation was done by light microscopy.
Results: During this study periods total 50 patients were diagnosed as hepatoblastoma. The median age of diagnosis was 4 years, M:F ratio was 3:1. The median time of diagnosis after onset of symptoms was 8 months (Range – 2 months to 18 months). Of these patients 90% cases presented with abdominal mass , 95 % abdominal distension , 30% abdominal pain , 50% anorexia, 20% vomiting , 20% fever , 5% jaundice and 3% with diarrhoea .Serum alpha fetoprotein was raised in 95% of patients. PRETEXT staging at diagnosis were 5% stage – I , 15% stage – II , 50% stage – III , 30% stage – IV and 20% patient had extrahepatic involvement and 30% had pulmonary metastasis at diagnosis .On histological examination 50% fetal type , 10% embryonal , 10% mixed and 30% was anaplastic type.
Conclusion: As Bangladesh is a developing country and poverty is one of the major problem, the diagnosis of childhood cancer is challenging. In case of childhood hepatoblastoma there is delay in diagnosis, so highest proportion of patients had advanced disease at diagnosis and has bad prognosis.

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STUDY ON THE CLINICAL DIAGNOSIS AND TREATMENT OF 52 CASES IV STAGE HEPATOBLASTOMA IN CHILDREN

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Background/Objectives: Hepatoblastoma (HB) is a most common malignant liver tumor in children. The prognosis was very poor while having metastasis with some diatant organs. Our objection was to study on the clinical experience and prognosis through analysis the clinical data of IV stage HB.
Design/Methods: 52 cases of IV stage HB were collected and treated in our hospital from September, 2006 to June, 2014. Study on the clinical efficacy and prognosis factors by statistics analysis on the chemotherapy efficacy, the rate of tumor relapse, the clinical remission rate after relapse and the treatment efficacy of different metastasis condition.
Results: In 52 cases, 16 cases were 0-12 months old (30.7%), and 24 cases were 13-36 months old (46.1), and 9 cases were 3-6 years old (17.3), and 3 cases were more than 6 years old (only 5.9%). 40 cases had distant poly organs metastasis, account for 76.9%, and 12 cases had adjacent organs invaded, account for 23.1%. Followed up to 31rd, January, 2015, average followed up time was 12.4 months (3-79 months), middle followed up time was 13 months. 3 years free event survival (EFS) rate was 32.69%(17/52), and 3 years total survival rate was 61.53%,and mortality was 38.46% (20/52).In 52 cases, 31 cases had relapse during and after treatment, account for 59.61%. 2 years EFS of 31 cases with surgery and chemotherapy was 22.58%, and 3 and 5 years total survival rate (OS) of that was 32.25% and 15%, and average survival time was (45.23±4.72)months, 95% CI was 35.98-54.48 months.
Conclusion: The clinical efficacy and prognosis of IV stage HB was more poor than other stage, but the clinical remission still could be improved by personalized comprehensive treatment methods. Se, we should enhance the treatment confidence for prolong survival time and improve clinical remission.

Posters: Lymphomas

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VITAMIN D RECEPTOR POLYMORPHISM OF PATIENTS PRESENTING WITH HODGKIN LYMPHOMA

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Background/Objectives: It is well known that 1-25-OH vitamin D is inhibiting cell proliferation, angiogenesis and cell migration, while inducing apoptosis and cell differentiation. Many in vivo and in vitro studies on various cancer types indicated that binding of 1,25-OH D vitamin to its receptor (vitamin D receptor-VDR) results proapoptotic and anticancer effects. VDR polymorphism have been evaluated in different types of malignancies including breast, prostate, pancreas, colon, bladder, thyroid, skin cancers and glioma, neuroblastoma, leukemia, non-Hodgkin lymphoma. In aforementioned tumor types, mostly Cdx2, Fox1, Bsm1, Apa1 and Taq1 polymorphisms of VDR have been studied. Higher frequencies of certain VDR polymorphism in patients with cancer compared to healthy controls, suggest that these polymorphisms may in fact play a role in development of cancer. According to our knowledge no study evaluated VDR polymorphisms in patients with Hodgkin lymphoma (HL).
Design/Methods: We compared HL patients with with healthy controls in terms of VDR polymorphisms. The study included 95 patients with classic HL and 100 healthy controls. In all participants Cdx2, Fox1, Bsm1, Apa1 and Taq1 polymorphisms of VDR were evaluated.
Results: We did not observe any statistically significant difference in term of evaluated VDR polymorphisms between patients with HL and controls. Our results indicate that Cdx2, Fox1, Bsm1, Apa1 and Taq1 VDR polymorphisms did not seem to play an important role in development of HL.
Conclusion: We did not observe any statistically significant difference in term of evaluated VDR polymorphisms between patients with HL and controls. Our results indicate that Cdx2, Fox1, Bsm1, Apa1 and Taq1 VDR polymorphisms did not seem to play an important role in development of HL.

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HIGH DOSE CHEMOTHERAPY AND PERIPHERAL HAEMATOPOIETIC STEM CELLS TRANSPLANTATION FOR YOUNG PATIENTS (AGE ≤20 YEARS) WITH RELAPSED/REFRACTORY HODGKIN LYMPHOMA: SINGLE CENTRE

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Background/Objectives: The current standard therapy for relapsed/refractory Hodgkin lymphoma (RR-HL) is salvage chemotherapy followed by high dose chemotherapy (HDC) and autologous stem cell transplantation (ASCT). This standard is extrapolated from the results of 2 randomized trials in the adult population. Reports from younger patient population series can add valuable information. This study reports a single centre experience.
Design/Methods: All patients aged ≤20 years with RR-HL and underwent HDC & ASCT between years 2001 and 2013 were included. Data was collected retrospectively by the investigators. Relevant imaging was reviewed and reported by an independent radiologist.
Results: 28 patients were identified and reviewed. Median age was 18 (4-20) years. 15 were males and 13 were females. 23 (82%) patients underwent HDC & ASCT after achieving radiological response to salvage chemotherapy. The rate of radiological complete response (CR) to salvage chemotherapy was 10.7% and improved to 46.2% within 3 months after ASCT. After median follow up of 35 months, 14 (50%) are still alive with no evidence of relapse or progression. Median EFS was 24 months (95% CI: 9.3-38.7), 3 years EFS was 42% and median overall survival was not reached. CR after HDC (P=0.01) and serum haemoglobin ≥10 g/dl (P=0.01) were associated with longer EFS on univariate analysis. These 2 factors and Time to first relapse (TTR) ≥ 12 months were associated with longer EFS on multivariate analysis (P=0.009, 0.009 & 0.02 respectively). One hundred day transplant related mortality was 7%.
Conclusion: The value of HDC & ASCT for younger patients remains to be defined. TTR and serum haemoglobin predict the outcome. Large scale international collaboration should identify other predictive factors to better select patients for this intensive approach.

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RETROSPECTIVE STUDY OF CHILDHOOD BURKITT LYMPHOMA IN CENTER OF TUNISIA

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Background/Objectives: Burkitt lymphoma (BL) is a malignant tumor of B-cell lymphocyte origin and is the most frequent non-Hodgkin lymphoma in children in Tunisia. This study aimed to describe the epidemiological characteristics and survival of children presenting with BL in the center of Tunisia.
Design/Methods: This retrospective study reviewed all pediatric cases of Burkitt lymphoma confirmed by histology between 1994 and 2014. The patients were treated with the LMB 89, LMB 96 and LMB 2001.
Results: A total of 39 patients with Burkitt lymphoma were analyzed. Their age ranged from 2 to 16 years (mean of 6.5 years). The male to female ratio was3.3. According to Ann Arbor Classification, 21 of them (54%) had III stage disease, 9 (23%) had IV stage disease and the most common primary site was the abdomen (82%). The majority of patients (87%) were treated with the LMB 89 protocol with three therapeutic arms A, B and C respectively in 0%, 94% and 6% therapeutic group disease. All patients had grade 4 hematologic toxicity. Lysis syndrome was observed in two cases after the first cycle of COP which indicated to re-challenge another cycle of COP. Four children (10.4%) died (two after hematologic toxicity, one by his cancer and one par another cancer). Thirty four patients (87%) achieved complete clinical remission and all of them were alive at the last contact. The overall survival rate was 87%. No late sequel was noted.
Conclusion: Our findings confirm the favorable prognosis of children with Burkitt lymphoma with multi agent chemotherapy. Outcome needs a further challenge for decreasing intensity and duration of therapy especially in patients with central nervous system involvement and medullary infiltration.

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A COLLABORATIVE PROTOCOL FOR NEWLY DIAGNOSED INDIAN CHILDHOOD HODGKIN LYMPHOMA PATIENTS

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Background/Objectives: Previous information on childhood Hodgkin lymphoma in India has been restricted to a few single centres reports, mostly retrospective in design with non-uniform approaches to stratification, chemotherapy and radiotherapy. The Indian Childhood Hodgkin Lymphoma collaborative protocol (ICHL-1) is an initiative to overcome these limitations.
Design/Methods: The study team developed a protocol which was scientifically sound, locally acceptable and deliverable, stratified for risk, accounted for late effects, and considered treatment cost and risk of abandonment. A systematic review of published and grey literature of relevant studies from India was undertaken, along with a survey of treatment practices at treating centres in India. The initial protocol was reviewed by national experts in paediatric oncology, radiation oncology, pathology and nuclear

medicine. The final draft was reviewed by international experts from resource-rich and resource-limited settings. The primary aim was to develop a protocol to prospectively collect data on staging, risk-stratification, management, outcomes and to form a standardised therapeutic strategy with regards to chemotherapy, radiation and late-effects monitoring.
Results: A prospective, observational protocol ICHL-1 was developed. It evaluates ABVD chemotherapy, used in a risk-stratified fashion: early stage patients will receive 4 ABVD cycles, and advanced stage patients 6 cycles. Guidelines for consolidative radiation therapy (involved-field radiotherapy reserved for bulky disease and slow/non-responders) and follow-up are given. Till date 23 centres have joined the protocol. The newly structured Indian Pediatric Oncology Group has been approached to register ICHL-1 under their umbrella of studies. Ethics approval is ongoing in individual centres and recruitment is expected to start in spring 2015.
Conclusion: A prospective, observational ABVD-based protocol for management of Hodgkin lymphoma in Indian children has been successfully developed and found acceptance. This is the first step in improving standards of care in managing this disease in India, thus improving outcomes and stimulating research.

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THE ROLE OF ANTHRACYCLINES IN THE TREATMENT OF ENDEMIC BURKITT LYMPHOMA

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Background/Objectives: Endemic Burkitt lymphoma is the most common childhood cancer in Malawi, one of the world's poorest countries. At the Queen Elizabeth Central Hospital in Blantyre approximately 100 children present annually with this disease. Children are treated on a 28 day regime using cyclophosphamide, vincristine, prednisolone and intrathecal methotrexate with an event free 1 year survival rate (EFS) of 48%. Children presenting with stage 3 and 4 disease however had poor one year EFS of 24% and 32% respectively. In an attempt to improve the outcome for higher stage disease doxorubicin (60 mg/m^2/dose) was added in week 2 and 4 of the regime.
Design/Methods: The event free and overall one year survival for 76 children treated for Burkitt lymphoma on the updated protocol were analysed. In addition univariate analysis of other clinical and co-morbidities were performed.
Results: The one year EFS of children presenting with stage 3 and stage 4 Burkitt lymphoma were 53% and 55% respectively, compared with 24% and 32% in the previous protocol which was identical except for the addition of doxorubicin at day 21 and 28. No significant increase in toxicity was seen with the addition of doxorubicin. Univariate analysis demonstrated an improvement in EFS with decreasing total white blood cell count prior to day 15 of chemotherapy (Hazard Ratio 1.24 (95% CI 1.08 – 1.42) p=0.003).
Conclusion: Anthracyclines play an important role in the treatment of children with higher stage endemic Burkitt lymphoma. These results also suggest that in the Malawian setting the benefit of increasing dose intensity for higher stage disease may outweigh the risk of increased toxicity.

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POST KIDNEY TRANSPLANT EBSTEIN-BARR VIRUS ASSOCIATED DIFFUSE LARGE B CELL LYMPHOMA: A SUCCESS STORY

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Background/Objectives: Posttransplant lymphoproliferative disorder (PTLD) is a serious complication of organ transplantation that represents an uncontrolled proliferation of lymphoid cells. Epstein-Barr (EBV) is closely involved in the pathogenesis of PTLD. We present a patient, who developed Epstein-Barr virus (EBV)-related PTLD in the abdomen after renal transplantation.
Design/Methods: A 10-year-old girl with chronic renal failure underwent a renal transplantation. She was EBV-seronegative and under EBV prophylaxis. After one year of posttransplantation, she had a pelvic mass in the periodic abdominal screening.
Results: Tru-cut biopsy of the lesion resulted in diffuse large B-cell lymphoma that was compatible with PTLD. We stopped all immunosupressive agents other than prednisolone. Rituximab was initiated before chemotherapy administration. Partial response (60% regression) was achieved after four doses of Rituximab. Low dose chemotherapy consisting of six courses of cyclophosphamide, vincristine and prednisolone was applied with four more Rituximab doses. The mass totally resolved and she is in full remission and under follow up for six months.
Conclusion: PTLD is one of the most important complications of organ transplantation. Even with treatment, the mortality rate is high. Various treatment approaches have been used. Rituximab and low dose chemotherapy deserves mentioning in achieving succesful outcome.

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DIAGNOSIS,TREATMENT AND OUTCOME OF PATIENTS WITH BURKITT LYMPHOMA IN AUCKLAND ,NEW ZEALAND FROM JANUARY 2000 TO DECEMBER 2014

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Background/Objectives: To determine the effect of Rasburicase® (Urate oxidase) in prevention of tumour lysis syndrome (TLS) and the correlation with serum chemistry parameters. To document surgical interventions and complications and outcome in these patients.
Design/Methods: A retrospective chart review was performed on 29 patients.Data collected included histology, molecular biology, serum chemistry levels, presenting site, surgical interventions, treatment and outcome.
Results: There were 20 males & 9 females in this group, of European(15), NZMaori(7), Samoan(2), Tongan(4), and Asian(3) descent. There were 13 Abdomen, 4 head and neck, 1 stomach, 1 CNS with secondary kidney involvement, & 1 mediastinal site of presentation. Only 4/29 had Burkitt Leukaemia. There were 7 lymph node biopsies performed in the oropharyngeal region. There were 14 biopsies taken from solid masses; 1 was a mediastinal mass and 13 were abdominal masses. In the majority of patients, (22/29) bone marrow aspirates and trephines were utilised as staging/diagnostic procedure. Surgical complications occurred in 7 of the patients. Four were related to the line insertions and 3 patients had complications relating to surgery. Biochemical data determined that 20/29patients were at risk of developing TLS and 15 received Rasburicase® treatment. The 3 patients that did not receive Rasburicase® required multiple days' worth of allopurinol treatment. No information was available on 1 patient & another patient received no TLS preventative treatment.
Conclusion: The results showed that Rasburicase® is effective in preventing the onset of TLS. Allopurinol alone was not as effective at normalizing calcium levels after the 1st or 2nd cycle of Chemotherapy (COPADM1).Surgical complications were limited and no death occurred during or following surgical interventions. Four patients (2 stage III and 2 stage IV patients) with refractory or recurrent disease passed away (EFS 9.5 months median). The 25/29 remaining patients continue in 1st CR 10 – 180 months after treatment (m= 60).

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HODGKINS DISEASE: A SURVEY OF CHILDREN AND ADOLESCENT TREATED AT A SINGLE INSTITUTION

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Background/Objectives: We implemented a risk-adapted, gender-based approach to treat children and adolescents with Hodgkin lymphoma (HL) in our center.
Design/Methods: Data of HL patients treated at King Hussein Cancer Center (KHCC) between July2006 until January2015 was retrospectively analyzed. During the study period, we adapted a risk stratification system according to stage, presence of B symptoms and bulk of disease. Patients were stratified to Low Risk (LR) group, treated with 4 cycles of ABVD; Intermediate Risk (IR) group, treated with 4 cycles of ABVD followed by 2 cycles of COPP or COPDac according to gender; and High Risk (HR) group, treated with intensive regimen that was adjusted according to response. Radiotherapy was omitted in LR and IR patients demonstrating rapid early response (RER).
Results: We identified 173 children (101 Males) in this study. Median age at diagnosis was 12.7 years (range, 3.2 to 17.9). Stage distribution was as follows: stage I (10%), stage II (46%), stage III (27%), and stage IV (17%). Fifty patients had bulky disease and 77 had B-symptoms. Patients were stratified LR (35%), IR (31%) and HR (34%) groups. The 5- year EFS and OS were 92% ±2.5% and 99% ±0.7%, respectively. No patients died of treatment toxicity and one patient developed secondary AML. The 5-year EFS of patients in different risk groups were as follows: LR (90% ±4.3%);IR (93% ±3.9%) and HR (92% ±4.9%) with no statistically significant difference (P=0.89). We couldn't identified prognostic factors using log-test.

Conclusion: Hodgkin lymphoma patients treated at KHCC have excellent outcome regardless of their risk group. Omission of radiotherapy is safe in LR and IR patients with RER. Treatment intensification in HR patients was feasible and resulted in excellent cure rates.

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INITIAL RESULTS OF A PROSPECTIVE PILOT STUDY EVALUATING FEASIBILITY AND UTILITY OF ECG-GATED CT ANGIOGRAPHY FOR CORONARY-SPARING RADIATION THERAPY PLANNING IN PEDIATRIC HODGKIN LYMPHOMA

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Background/Objectives: Cardiovascular morbidity and mortality is common among survivors of mediastinal Hodgkin lymphoma (HL) treated with radiation therapy (RT). Toxicity data suggests that mean heart doses of less than 15 Gy and 25 Gy are sufficient to cause accelerated atherosclerosis and valvular disease, respectively. Dose to cardiac substructures likely influence toxicity but most RT plans evaluate heart as a single structure. ECG-gated CT angiography (E-CTA) could allow for accurate RT dose calculation and possible dose reduction to critical heart structures.
Design/Methods: After providing informed consent, patients receiving RT for mediastinal HL underwent E-CTA in breathhold in addition to conventional breathhold imaging. E-CTA was used to identify cardiac vessels and valves, accounting for position on both diastolic and systolic phases. Target and organ-at-risk (OAR) structures (including heart) were contoured on conventional imaging. Two volumetric intensity-modulated arc RT plans were generated for each patient. A conventional RT (CRT) plan was generated by optimizing target and OAR dosimetry without heart substructure constraints. A coronary-sparing RT (CSRT) plan was optimized with the same target coverage normalization but with coronary and valve structure constraints included. OAR D0.03cc (an estimate of maximum dose to a structure) and V15Gy (volume of a structure receiving 15 Gy or more) were calculated.
Results: Four patients with HL underwent RT planning as above. Patient characteristics include median age 15.7 (range 14.6-16.9), Stage IIA (n=2), IVA (n=1), or IVB (n=1) HL with complete response (n=3) or partial response (n=1) after chemotherapy. Average D0.03cc and V15Gy for CSRT vs CRT plans, respectively, were: left main (14.1 vs 17.8 Gy and 0.02 vs 0.66 cc), left anterior descending (13.7 vs 16.6 Gy and 0.01 and 1.20 cc), and aortic valve (18.6 vs 19.4 Gy and 2.7 vs 5.9 cc).
Conclusion: RT planning using E-CTA was feasible and decreased dose to cardiac structures compared to conventional planning.

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CLINICAL OUTCOME OF CHILDREN WITH HODGKIN LYMPHOMA AFTER CHEMOTHERAPY ALONE- THE RED CROSS CHILDREN'S HOSPITAL EXPERIENCE

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Background/Objectives: To assess the efficacy of hybrid chemotherapy protocol for Hodgkin lymphoma.
Design/Methods: The 35 accessible documents of patients treated for Hodgkin lymphoma between 2005 and 2012 at Red Cross Children's Hospital, were reviewed to evaluate overall survival (OS), Event free survival (EFS) and cause of death. The protocol used included chlorambucil, vinblastine, prednisolone, procarbazine (ChlVbPP) alternating with adriamycin, bleomycin, vincristine, dacarbazine (ABVD). Relapsed or refractory patients received six courses of etoposide, prednisolone, ifosfamide and cisplatin (EPIC) with involved field radiotherapy (IFRT). Autologous stem cell transplant (ASCT) was treatment of choice for patients who had poor response to the first four courses of EPIC.
Results: Median age was 9.5 at diagnosis and 25 (71%) were male. Two (6%) patients were HIV infected. The cervical region was the commonest site of primary disease and 14 (40%) had bulk disease. Seven (20%) had bone marrow involvement and Stage IV disease was recorded in 11 (31%) patients. Twenty two (63%) had Nodular Sclerosing histology. Thirty one were alive, including two lost to follow up in remission, including two patients with Stage III disease who relapsed off treatment and were salvaged. One Stage IV patient died soon after admission, and four Stage IV patients had refractory disease, one of whom was salvaged with EPIC, ASCT and IFRT. OS and EFS were 87% and 79% respectively for the whole study group. OS for stage I, II and III was 100% declining to 59% in Stage IV (p=0.02). EFS was 100% for stage I and II, 68% for stage III, 55% for stage IV (p=0.02).
Conclusion: Hybrid chemotherapy is associated with good outcome in stage I, II and III Hodgkin disease. Refractory Stage IV disease remains a problem and earlier evaluation with a view to adopting alternative strategies is warranted.

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USE OF F-18-FLUORO-2-DEOXY-D-GLUCOSE POSITRON EMISSION TOMOGRAPHY / CT IN THE MANAGEMENT OF PAEDIATRIC POST-TRANSPLANT LYMPHOPROLIFERATIVE DISEASE

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Background/Objectives: Post-transplant lymphoproliferative disease (PTLD) may arise following transplantation secondary to immunosuppression.
F-18-Fluoro-2-deoxy-glucose positron emission tomography/Computed Tomography (PET/CT) is an imaging modality useful in the staging and evaluation of treatment response in adult and paediatric lymphoma. Our objective is to evaluate the use of PET/CT in paediatric PTLD.
Design/Methods: Paediatric patients diagnosed with PTLD referred to our institution between July 2002 and October 2014 (n=13) were reviewed retrospectively. Those who had undergone PET/CT at diagnosis and/or follow-up were included.
Results: Seven patients were identified. Four were male, median age 6.3 years (range 1.8-14.5). Six patients were post-solid-organ transplant while one patient had non transplant-related immunodeficiency. Monomorphic disease was present in 6, with extranodal disease in 4. All except one were Epstein-Barr virus positive. Mean follow-up was 43 months (range 8-99), although 2 patients were lost to follow-up. Patients were treated with a combination of reduction in immunosuppression, chemotherapy ± rituximab. Four patients had PET/CT at diagnosis. All lesions seen with staging CT were identified. All seven patients had at least one PET/CT during follow-up. Five still had FDG-avid lesions, in 3 cases confirmed with biopsy. In one case, PET/CT showed increased uptake in areas that were unclear on CT alone. However, in another case PET/CT did not identify additional central nervous system involvement demonstrated on magnetic resonance imaging. Treatment was continued for all five PET/CT-positive patients. Five patients had a negative PET/CT, including two cases where CT alone showed persisting abnormalities of uncertain significance. In all five patients treatment was stopped and they remain in remission.
Conclusion: In this small cohort PET/CT was found to be a valuable tool in staging and assessing treatment response in PTLD. It was also helpful in clarifying equivocal findings on other imaging modalities. Larger cohort studies would better define the potential role of PET/CT in paediatric PTLD.

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CHILDHOOD HODGKIN LYMPHOMA IN MOROCCO: AN EPIDEMIOLOGICAL STUDY

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Background/Objectives: Hodgkin lymphoma (HL) is a rare malignancy in Northern Africa, with an incidence of 1.4 per 100 000 in 2012. It is the 18th most common cancer and the 18th leading cause of cancer-related death in both sexes, with an estimated 3 107 new cases of HL (1 758 men and 1 349 women) and 1 698 deaths from HL in 2012 (GLOBOCAN 2012). The aim of this study is to determine the frequency and the epidemiological characteristics of pediatric Hodgkin lymphoma in Morocco.
Design/Methods: This is a descriptive retrospective analysis of pediatric Hodgkin lymphoma cases, diagnosed and treated at Al Azhar Oncology Center in Rabat between 1994 and 2004.
Results: There were 18 children under the age of 15 years diagnosed with Hodgkin lymphoma at Al Azhar Oncology Center, which was 40.9% of all new cases of pediatric hematologic malignancies and 14.3% of all cancers in children collected during the study period. More than one-half of the cases were boys, with a male-female ratio of 1.25. The average age at diagnosis was 10.7±3.5 years (range 5-14 years). More than two-thirds of the cases were diagnosed in children aged 10-14 years (66.7%), while the highest rates for boys were noted between 5 and 9 years and for girls between 10 and 14 years of age. Among the cases for whom the outcome was known, a 14-year-old girl died during the study period.
Conclusion: Although rare, cancer in children has a substantial impact on public health in Morocco. A national cancer registry will assist in better planning, resource allocation and management including psychosocial support to improve the quality of life of childhood cancer survivors and their families.

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A RURAL PAEDIATRIC CANCER SERVICE IN CAMEROON - A SUCCESSFUL TWINNING PROJECT

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Background/Objectives: A Burkitt lymphoma treatment program started at Banso Baptist Hospital (BBH) in 2003. This was extended to Mbingo (MBH) and Mutengene Baptist Hospitals (BHM), 400 km away. In 2007 treatment of Wilms Tumour (WT) commenced, followed by SIOP recommended protocols for retinoblastoma and (RB) and Kaposi sarcoma (KS), and ad hoc protocols for other cancers.The only available children's cancer service in Cameroon was at Chantal Biya Hospital in Yaounde.
Design/Methods: Start–up funding was by the Lisa Thaxter Trust, followed by BTMAT, the NRF, Swiss Cancer League. In 2012 a twinning agreement was signed between the CBCHB, BTMAT, Stellenbosch University and WCC. Each hospital has a dedicated research nurse, supervising physician and registry office, using POND. Regular site visits and expert advice are provided by PBH and PW.Guardians only pay a basic admission fee. Hospitalisation, investigations, protocol approved drugs and supportive care is free. Parents/patients are supported with food and public transport. Three rural parent support groups provide advocacy and do farming projects (chickens, pigs, maize). A palliative care outreach program commenced in 2013. The research nurses' duties include counselling, performing basic investigations, chemotherapy administration, POND registration, long term follow and advocacy. Members of staff are trained locally and abroad. Each hospital has dedicated beds. Basic laboratory services (including a resident pathologist), radiology, surgeons, internists and ophthalmologists are available.
Results: Long term survival in ± 1000 BL patients is 50%. During 2014 our 111 new patients included BL 55%, RB 19%, WT 9%, other malignancies 17%. New patients live as far as 400 km distant, and in surrounding countries.Nurses acquired new skills to provide the backbone of this service.
Conclusion: A South to South collaboration between an academic institution, local health care providers, research foundations and NGO's has resulted in an effective, low cost children's cancer service in rural Cameroon.

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CAN USE OF PET SCAN REDUCE THE BURDEN OF TREATMENT FOR CHILDREN WITH HODGKIN LYMPHOMA

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Background/Objectives: Current treatment paradigms can cure most children with Hodgkin lymphoma, even in the developing world. In India, ABVD remains the most preferred chemotherapy regimen. This is due to its good tolerance despite its known cardiac and pulmonary late effects. PET scans are expensive and have become available only in recent years. This study was planned to evaluate if the additional cost of PET scan can be justified by reduction in burden of therapy.
Design/Methods: Medical records of 148 children <18 yrs of age, treated between 1998 and 2013 were reviewed. In the pre PET scan era, most patients received six cycles of ABVD with involved field radiotherapy being reserved for bulky or residual disease. Burden of treatment was assessed by number of cycles of chemotherapy and use of radiotherapy.
Results: Median age of the 140 evaluable patients was 9 years (range 2-18 years), 11(7.8%) were girls and mixed cellularity was the commonest histology 71(51%). B symptoms, bulky disease and advanced stage was observed in 24(17%), 58(41%), and 79(56%) patients respectively. PET scans were available for 30/140 patients whose demographic and disease characteristics were similar to the remaining cohort. Fewer patients received radiotherapy in the PET subgroup, (4/30,13% versus 37/110,33%, p0.02). They also received fewer (<6) chemotherapy cycles (10/30, 33% versus 16/110, 14%, p0.04). The 5 year overall and event free survival of the subset with and without PET scan was 90% and 79% versus 91% and 86% (p,0.8) respectively and median follow up was 60 months.
Conclusion: Trends of this small analysis suggest that better response assessment with PET scans are likely to lead to reduction in burden of therapy while maintaining excellent survival in pediatric Hodgkin lymphoma. This should encourage pediatric oncologists in developing countries who often tend to over treat due to fear of abandonment at relapse.

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CLINICAL CHARACTERISTICS AND TREATMENT OUTCOMES OF PERIPHERAL T-CELL LYMPHOMA IN CHILDREN AND ADOLESCENTS

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Background/Objectives: Peripheral T-cell lymphoma (PTCL) is rare non-Hodgkin lymphoma (NHL) which is usually associated with an inferior outcome to those of B-cell lymphomas. Data in children with PTCL are particularly rare, and optimal therapy has not been defined. This study was to analyze the clinical characteristics and treatment outcomes of children with PTCL.
Design/Methods: In this study, we retrospectively investigated 19 cases of PTCL diagnosed at the Asan Medical Center from 1995 to 2014. The clinical characteristics, treatment results, and outcomes were reviewed. Those with isolated cutaneous T-cell lymphoma and anaplastic large cell lymphoma were excluded from this analysis.
Results: According to the World Health Organization (WHO) PTCL classification, 10 patients had PTCL, not otherwise specified (PTCL-NOS), 7 had extranodal natural killer/T-cell lymphoma, nasal type (ENKL), 1 had subcutaneous panniculitis-like T-cell lymphoma and 1 had angioimmunoblastic T-cell lymphoma. Patients with PTCL-NOS were treated with various multi-agent chemotherapeutic regimens designed for T-cell acute lymphoblastic leukemia and NHL. Of 7 patients with ENKL, 4 received up-front radiotherapy, followed by multi-agent chemotherapy. Two patients with relapsed PTCL-NOS underwent allogeneic hematopoietic stem cell transplantation (HSCT) and autologous HSCT, respectively, and 1 patient with relapsed ENKL underwent autologous HSCT. Of the 19 patients, 7 (36.8%) died from disease progression, and there was no treatment-related mortality. The 5-year overall and event-free survival rates were 73.7% and 50.0% in all cases, 80.0% and 56.1% in PTCL-NOS, and, 71.4% and 28.6% in ENKL, respectively.
Conclusion: Although children with PTCL experienced frequent relapse, many of them could be rescued by salvage treatment, resulting in comparable overall survival outcomes to other NHL. Multi-center trials are required to refine the prognostic factors in PTCL and further confirm the outcome of PTCL in children.

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TREATMENT RESULTS OF ANAPLASTIC LARGE CELL LYMPHOMA IN CHILDREN AND ADOLESCENTS ACCORDING TO "MODIFIED ALCL-BFM 2003 PROTOCOL": SINGLE CENTER EXPERIENCE

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Background/Objectives: The results of anaplastic large cell lymphoma (ALCL) treatment in children and adolescents are not satisfactory in comparison with other non-Hodgkin's malignant high-grade lymphomas. According to the data of different protocols (NHL-BFM 90, CCG5941, SFOP-LM 89/91, UKCCSG, ALCL99 vinblastine, POG APO 9315, AIEOP LNH - 92, AIEOP LNH 97) 5-year overall survival and event-free survival are not more than 85 and 76%, respectively.
Design/Methods: From 2003 to 2014 years twenty children and adolescents with ALCL were included in trial «Modified ALCL-BFM 2003». Male/female ratio was 1/1. Median age - 11.3 years (range from 5 till 17). Stage I-II were revealed in 7 patients (35%), stage III-IV – in 13 patients (65%), intermediate-risk group (K2) – in 8 patients (40%), high-risk group (K3) – in 12 patients (60%). Patients without T-cell antigen expressed ALCL samples received chemotherapy by B-NHL-BFM 95, while patients with T-cell antigen expressed ALCL samples received chemotherapy by high-risk courses ALL-IC-BFM 2002 including L-asparaginase. All patients received maintenance therapy with vinblastine 6 mg/m^2 once every 3 weeks during 6 months.
Results: ALK-positive variant ALCL was revealed in 19 out of 20 cases (95%), T-cell antigen expression – in 12 out of 20 cases (60%), pSTAT3-positive variant ALCL – in 5 out of 7 cases (71%), t(2; 5)(p23; q35) – in 8 out of 9 cases (88%). We have got an excellent results. Five-year overall survival and event-free survival were 100%, a median follow-up was 63 months (range from 5 till 145).
Conclusion: «Modified ALCL-BFM 2003» protocol can be regarded as optimal therapeutic approach in treatment children and adolescents with ALCL.

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PROGNOSTIC INFLUENCE OF C-MYC, BCL2, PSTAT3 EXPRESSION, GCB/NON-GCB SUBTYPE ON TREATMENT RESULTS OF DIFFUSE LARGE B CELL LYMPHOMA IN CHILDREN AND ADOLESCENTS

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Background/Objectives: At the present time results of some pediatric protocols (FAB/LMB96 with and without rituximab (± R), B-NHL-BFM90/95, B-NHL-2004m) were published but prognostic significance of markers, such as: non-GCB DLBCL

subtype, C-MYC, pSTAT3, BCL2/C-MYC coexpression, *C-MYC*, *BCL2*/*C-MYC* gene rearrangements in childhood DLBCL is unknown.
Design/Methods: From 2003 to 2014 thirty children and adolescents with DLBCL were included in trial «B-NHL-BFM 95 ± R». Male/female ratio was 2/1. Median age - 9 years (range from 2 till 16). Stage I-II were revealed in 17 patients (56.7%), stage III-IV – in 13 (43.3%), R1-R2-risk group – in 17 (56.7%), R3-R4-risk group – in 13 (43.3%). GCB/non-GCB DLBCL subtypes were assessed by Hans, Tally and Visco-Young immunohistochemical algorithms. Cutoff values of 40% for MYC, 70% for BCL2, 50% for pSTAT3 were established. *MYC* gene rearrangement was assessed by FISH using locus-specific *IGH*/*MYC*/*CEP8* tricolor dual-fusion probes and locus-specific *MYC* dual-color breakapart probes.
Results: GCB/non-GCB DLBCL subtypes were revealed in 10 and 11 out of 21 cases (47.6 and 52.4%, Hans, Visco-Young), in 11 out of 21 cases (52.4 %, Tally). Ten (71.4%) out of 14 DLBCL samples were positive for MYC, 7 (36.8%) out of 19 – for BCL2, 2 (18.2%) out of 9 – for BCL2/C-MYC coexpression, 1 (9.1%) out of 11 – for pSTAT3. *MYC* gene rearrangement was revealed in 3 (21.4%) out of 14 patients. *BCL2* gene rearrangement was not revealed. Five-year overall survival (OS) and event-free survival (EFS) were 90 ± 5%, a median follow-up was 57 months (range from 4 till 142). There is not revealed any influence of investigated markers on OS and EFS.
Conclusion: Number of patients in this study is not enough to estimate authentic prognostic significance of these markers but high-intensive B-NHL-BFM90/95 ± R chemotherapy showed good therapeutic effect in our patients. This study will be continued.

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PAEDIATRIC DOUBLE-HIT LEUKAEMIA: CASE REPORT AND LITERATURE REVIEW

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Background/Objectives: Double-hit leukaemias (DHL) with complex abnormalities of the *MYC* and *BCL2* oncogenes are rare tumours in adult patients and have not been previously reported in paediatric literature. Here, we present a child with double-hit leukaemia with a literature review of this rare malignancy.
Design/Methods: A literature search was conducted in PubMed using the terms "double-hit leukaemia" and "dual-hit leukaemia", as well as MeSH terms "*MYC*" and "*BCL2*".
Results: A 7 year-old girl presented with facial and gum swelling, and difficulty walking. Bone marrow aspirate identified a leukaemic infiltration, but no evidence of central nervous system (CNS) disease on cerebrospinal fluid (CSF) analysis. Subsequent genetic analysis showed concurrent *MYC* and *BCL2* translocations; confirming DHL. The patient was treated with standard chemotherapy for Burkitt/ B-cell leukaemia according to Group C on the United Kingdom Children's Cancer Leukaemia Group (CCLG) guidelines. Chemotherapy resulted in complete disease remission at the microscopic, cytogenetic and molecular levels. The patient presented 22 days after completing chemotherapy with a left hemiparesis. An MRI scan identified an intracranial mass. CSF analysis and bone marrow examination confirmed a combined marrow and CNS relapse. The patient progressed and died 14 months after initial diagnosis. In the literature, there are no reports of DHL in children. The combination of *MYC* and *BCL2* translocations results in uncontrolled proliferation of malignant cells, and an aggressive clinical phenotype. Bone marrow, extranodal and CNS involvement is common at presentation and relapse/progression. There is no consensus on the management of these patients. Prognosis is poor with primary resistance to chemotherapy or early relapse and median survival of 4.5-18.5 months.
Conclusion: Double-hit leukaemia with *MYC* and *BCL2* translocations in childhood is a rare entity, associated with a similarly dismal prognosis as reported in adults. Further research and the development of a novel treatment strategy in this rare disease is required.

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BURKITT LYMPHOMA PRESENTING AS ACUTE PANCREATITIS - DIAGNOSTIC PROBLEMS WITH AN UNUSUAL ONSET

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Background/Objectives: Burkitt lymphoma comprises 30% of non-endemic paediatric lymphomas. Most patients are characterised by the presence of large abdominal masses, frequently involving the ileocecal region of the bowel. Involvement of pancreas is a rather rare manifestation of this neoplasm.
Design/Methods: We are concerned with a case of a 6-year-old boy who presented pancreatitis and cholestasis. It took 16 days from the first symptoms for the neoplasm to be diagnosed.
Results: First symptoms of the disease involved mild abdominal pain, icterus, and stool discoloration. The boy also suffered from lower limbs pain which was initially interpreted as reactive arthritis after upper respiratory tract infection. Laboratory tests revealed parenchymal liver damage (ALT 545U/l, AST 129U/l) with signs of cholestasis (total bilirubin 8,79 mg/dl, conjugated 8,06 mg/dl), and normal liver synthetic function (albumin 35g/l, prothrombin index 100%). Infectious diseases of the liver were excluded (HBV, HCV, EBV, HAV). Level of amylase in serum increased up to 245U/l, and in urine up to 1920U/l. Initial sonography did not reveal any abnormalities. After 7 days of symptoms onset sonography showed 3-cm lesion in pancreas, which initially was interpreted as inflammatory lesion. However, 7 days later imaging of the abdomen revealed significantly enlarged pancreas, 7mm expanded common bile duct, tumor mass in pelvis 10×5cm, and a 20mm lesion in the right kidney. Pelvic mass penetrated and filled the spinal canal. Moreover, infiltration of femur was found. On the basis of histopathologic examination of the tumor, Burkitt lymphoma IV stage with CNS involvement was diagnosed and chemotherapy according to B-NHL BFM04 was introduced.
Conclusion: Localisation of Burkitt lymphoma in pancreas is rare and might be mistaken for acute pancreatitis. Because of its very rapid growth rate, it requires prompt diagnosis for initiation of proper treatment. Therefore it is essential to consider Burkitt lymphoma when confronted with a paediatric presentation of any pancreatic mass.

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OUTCOME FROM BASIC PEDIATRIC CANCER RESEARCH IN RESOURCE LIMITED COMMUNITIES MAKES A HUGE DIFFERENCE

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Background/Objectives: Burkitt lymphoma (BL); the most prevalent children cancers in Cameroon, is lethal if not treated; but 50% curable with lone cyclophosphamide (CPD) therapy or combination with methrotrexate. Applying June 2010 - June 2012 cross-sectional community study outcome improving treatment and supportive care.
Design/Methods: Previous survey outcome that was done using questionnaires based on aspects of palliative care in relation to the cultural views and traditional beliefs of the community with special attention on paediatric oncology needs has proven to be very vital in service improvement where this care and support is provided to ascertain palliative care needs and possible practical interventions.
Results: A huge gap exists between the western palliative care and support approach, to this community because of their unique super attachment to their cultural views and beliefs; some of which are not compatible with a typical modern approach. Death rates, as much as 50% result from the late diagnosis, lack of health units, inaccessibility of treatment products and more.
Conclusion: Poverty and unhealthy cultures noted as the main hurdle in that, high percentage of children die at home either due to poverty, parents assumed child's cancer cause to superstition, child is taken to a basic health care clinic with no expert to timely diagnose or any similar reason. The study outcome guided in new treatment, support and advocacy guidelines. It is difficult to 'copy and paste' a modern approach to palliative care and support though it is evidently clear that modern treatment and support approach remain superb even in this community.

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CHILDHOOD BURKITT LYMPHOMA IN GHANA: A RETROSPECTIVE STUDY FROM THE PEDIATRIC ONCOLOGY UNIT OF KORLE BU TEACHING HOSPITAL, ACCRA

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Background/Objectives: Burkitt Lymphoma (BL) is the commonest childhood cancer in sub-Saharan Africa, where the predominant variant is the endemic type, usually presenting as a jaw tumor and historically highly chemo-sensitive to single agent cyclophosphamide or relatively minimal dose combination chemotherapy. We analyzed the clinical and demographic features of children with BL treated over a 6-year period at the main tertiary referral hospital in Ghana; a low-middle income country.
Design/Methods: Retrospective review of all confirmed cases of BL at the pediatric oncology unit, Korle Bu Teaching Hospital between January 1st 2007 and December 31st 2012.
Results: A total of 173 children with BL were diagnosed during the study period with a mean age of 6.9 years (range = 2-12 years), and a male predominance (male to female ratio: 1.5:1). The abdomen was commonest site of tumor presentation (46%), while the jaw was the 2nd commonest tumor site (31%). A significant association was observed between girls and abdominal tumors ($p < 0.05$) as well as between boys aged 0-4 years

and facial tumors (p=0.03). Most children presented with advanced/disseminated disease (stage 3, 47% and stage 4, 41%). All patients received at least 1 cycle of chemotherapy with 61% achieving an objective tumor response (≥ 50% reduction in tumor size). Forty-three children (25%) died during the course of treatment. Treatment delays were seen in 85% of all patients, with financial constraint of the families being a major contributor (75%). Treatment abandonment was observed as a first event in 94% of patients and two-thirds of children in the study were eventually lost to follow up.
Conclusion: While the demographic characteristics observed in this study remain consistent with endemic BL, the clinical features are suggestive of a changing pattern in disease presentation. Delayed health-seeking practices and abandonment of therapy remain major detriments to patient outcomes.

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DESCRIPTIVE EPIDEMIOLOGICAL STUDY OF CHILDHOOD CANCER IN PERU PERIOD 1981-2014

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[1] Rebagiati Essalud Hospital and Ministry of Heath, Oncology and Hematology, Lima, Peru; [2] Rebagliati Essalud Hospital, Hematology, Lima, Peru Background/Objectives: The epidemiological knowledge of childhood cancer is the main basis for planning health policies at national level, the cancer a disease that demands a high economic and social costs for the nation. Describe the epidemiology based on the National Register of the Ministry of Health (MINSA) and Essalud Hospital.

Design/Methods: Data were obtained since 1981 to 2014 period; children 0 to 18 years ; incidence rates, mortality rates were estimated, adjusted for age, gender and pathology and analysis for overall survival period was performed.
Results: Health coverage national is 60% from MINSA and 30% Essalud for 8 millions of children. Total accumulate 13,072 cases in thirty four years; 84% (11,049) MINSA and 16% (2,023) Essalud, an incidence of 111 new cases / million children-year. Genre masculine: 56.4% MINSA and 53.68% Essalud, students from 6 to 14 years (52.5%) in both institutions.First pathology Leukemia 44% MINSA et 30.98% Essalud ,second Brain tumors 8% MINSA and 19.42% Essalud, third retinoblastome MINSA 7.8% and NHL 13.14% Essalud , fourth NHL (6.9%)MINSA and Essalud renal tumors (7.31%), ranking fifth in both institutions bone tumors, 5.2% .Advance stages Ewing sarcoma (41.3%), melanoma (33%) and Neuroblastoma (19.9%). Coast population 66.5% Essalud and 52% MINSA. Mortality 36.3% MINSA and 28.53% in Essalud. The burden of disease from cancer 48, 960 represent 8% of the global burden of disease. Survival at 5 years 72- + 4.3.
Conclusion: The reported incidence rate is similar at Europe and America, the mortality is higher in last stages and now the remission is 75 to 80% through prevention, early diagnosis and multidisciplinary treatment of childhood cancer with full coverage.

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OUTCOME OF HODGKINS DISEASE IN CHILDREN WITH CHEMOTHERAPY ALONE IN A RESOURCE LIMITED COUNTRY, BANGLADESH

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Background/Objectives: Background: Forty Eight children with Hodgkins disease (HD) treated with chemotherapy alone were studied between January 2004 and December 2010 at the Paediatric Haematology & Oncology, department of Bangabandhu Sheikh Mujib Medical University (BSMMU). Objective: To assess the outcome of treatment of HD in all stages with combination chemotherapy alone.
Design/Methods: Study design: Prospective. Patients and methods: Forty eight children with Hodgkins disease less than 16 years of age were treated at the Paediatric Haematology & Oncology department of BSMMU with eight cycle of chemotherapy, with of ABVD (Adriamycin/Doxorubicin, Bleomycin, Vinblastine, and Dacarbazine) regime on an outpatient basis over a period of 8 months. The following data were analyzed: age, sex, stage of the disease, histopathological subtypes at diagnosis, response to therapy, relapses, and early treatment suspension by the patient.
Results: The mean age was 10.3 years (range 3-16). There were 42 males and 6 females giving a male: female ratio of 7: 1. Mixed cellularity is the commonest histologic subtype observed in 20 of 48 (42%) patients. Forty two (88%) patients achieved complete response, 5 (10%) had partial response and one patient did not respond at all. Three patients (Stages IIA, IIA, IVB) were lost after 2, 6 and 20 months of follow-up. Fifteen patients (31%) are known to be dead and the rest are alive and tumor free.
Conclusion: ABVD combination should be regarded at the present moment as the simplest and most effective drug therapy for treating childhood Hodgkins disease.

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OUTCOME WITH CHEMOTHERAPY (ABVD) ALONE IN PEDIATRIC HODGKIN'S DISEASE

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Background/Objectives: To assess the efficacy of chemotherapy alone, using six to eight cycles of ABVD in all stages of childhood Hodgkin's disease (HD).
Design/Methods: Between May 1993 and November 2011, charts of 39 Hodgkin disease patients who received ABVD only were investigated and analyzed retrospectively for remission and survival.
Results: There were 29 boys and10 girls with a median age of 9 years, 48.7% were less than 10 years old. 46.1% had advanced stage disease (IIB–IV). B symptoms were present in 35.9% of cases; bulky mediastinal mass in 3 cases (7.7%); spleen and bone marrow involvement in 10 (25.6%) and seven cases (17.9%), respectively. Mixed cellularity (MC) subtypewas found in 38.5%. Complete remission was achieved in 33 patients (84.6%), Six patients (15.3%) relapsed and three (7.6%) patients died on therapy. The 5-year overall survival (OS) was 88% and disease free survival (DFS) was 80%.
Conclusion: Although our group of patients is small,chemotherapy alone with ABVD, without additional radiotherapy, provides high rates of durable remission and effective in childhood HD.

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LONG-TERM RESULTS OF THE MILAN CHEMOTHERAPY PROGRAM FOR ADVANCED-STAGE BURKITT LYMPHOMA (BL) IN CHILDREN AND ADOLESCENTS

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Background/Objectives: The treatment strategy for advanced Burkitt lymphoma (BL) relays on short-pulse dose-intensive i.v. chemotherapy and intrathecal chemotherapy. Until 2014 we treated children with advanced-stage BL with a short chemotherapy program, which was originally designed 25 years ago, remaining unchanged (*J Clin Oncol* 2002;20:2783). We seek to monitor the continuing results of this long-lived protocol.
Design/Methods: Between June 2001-September 2014, 40 additional children with Murphy stage III (n=24) or IV (n=16) BL were enrolled into the Milan protocol. The chemotherapy consisted of a 5-week induction based on weekly infusion of vincristine/cyclophosphamide, doxorubicin, high-dose methotrexate (two courses), etoposide, alternating intrathecal methotrexate or cytarabine, followed by a consolidation with high-dose cytarabine/cisplatin.
Results: Patients' characteristics: 36 were male; the median age was 7 years (range, 3-17); LDH upper normal limits in 32 cases; B symptoms in 16 children; CNS involvement in 7 children, bone marrow involvement in 12 children (both in 4 cases). The effective median duration of the whole program was 61 days (range, 45-81 days). All the patients achieved a complete remission. One toxic death occurred (cytarabine-related acute heart failure). Four patients relapsed at 3, 3, 5 and 10 months, respectively, and all subsequently died of progressing lymphoma (two of them had CNS/bone marrow disease at diagnosis). One further relapse occurred at 29 months, and the patient achieved cure through repeating the same protocol. At a median follow-up of 69 months, 4-year overall and disease free survival rates were 87% ±5% and 86.5% ±6%, respectively. Relapse-free survival was not significantly different between children classified as stage III (87%) or stage IV (86%).
Conclusion: Our data show that the Milan regimen applied for advanced BL is still topical, despite originally designed over than 25 years ago, and not including rituximab.

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EVALUATION OF THYROID FUNCTIONS IN PEDIATRIC PATIENTS TREATED FOR HODGKIN LYMPHOMA

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Background/Objectives: We aimed to evaluate late side effects of chemotherapy and radiotherapy on thyroid functions treated for Hodgkin Lymhoma in childhood.
Design/Methods: Forty patients, followed and treated between 1994 and 2013, in Pediatric Hematology-Oncology Unit were evaluated. Demographic features, histopathologic type of tumor, stage, age at the time of radiotherapy, dose of radiation, time period after radiotherapy, TSH, free T4, thyroglobulin, antithyroid peroxydase,calcitonin,thyroid ultrasonography,occurence time of hypothyroidism and nodules were recorded. Whenever a nodule was detected in thyroid ultrasonography, scintigraphy was performed followed by a biopsy if indicated.
Results: All patients had radiotherapy and chemotherapy. Thirty four of them(85%) male and six(15%) were female. Age at diagnosis was 9.45±4.082, dose of radiotherapy was 21.48±4.48 Gy. In 72.5% of patients, the primary localization was head and neck. Seven patients(17.5%) had B symptoms and 17 patients(42.5%) had stage III+IV. Hypothyroidism was detected in twelve(30%) of forty patients (11 male, 1 female). Thyroid hormone therapy was given to five patients due to clinical hypothyroidism.None of the patients have hyperthyroidism and thyroid antibody positivity. There isn't any significant relationship according to age at the radiotherapy, time after radiotherapy, radiotherapy doses, stage and hystopathologic type between the patients with hypothyroidism and without hypothyroidism (p=0.434,0.45,0.77,0.882,0.479 respectively). Thyroid nodules were detected in 5(3 male, 2 female)(12%) patients with ultrasonography. Biopsy was performed to 3 patients according to result of USG, thyroglobuline and scintigraphy.
Results: Malignancy wasn't observed none of them. There isn't also any significant relationship according to age, dose of radiotherapy, stage and hystopathologic type (p=0.709,0.799,0.882,0.432). Time after radiotherapy was longer in patients with nodules(p=0,049). Time of developing hypothyroidism(n=12) was 3.10±2.02 years and nodule formation(n=5) was 8.90±7.10 years. Nodule formation time was significantly longer than development of hypothyroidism (p=0,048).
Conclusion: Pediatric patients treated due to Hodgkin lymphoma have increased risk for thyroid function abnormalities and long term follow-up was needed.

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IS QUALITY OF LIFE IS BETTER IN PATIENTS WHO RECEIVED CHEMOTHERAPY AFTER SURGERY IN CASES OF INTESTINAL BRKUIT LYMPHOMA?

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Background/Objectives: Primary tumors of the gastrointestinal (GI) tract are rare in children and represent less than 5% of all pediatric neoplasms. Non-Hodgkin's lymphoma (NHL) remains the most common malignancy of the GI tract in children. The abdomen is the most frequent onset site of non-endemic Burkitt's lymphoma. Three variants have been described. We are presenting our experience with 5 cases of Burkitt's lymphoma in pediatric age group in reference to their age of presentation, clinical manifestation and anatomical location and its management.
Design/Methods: We studied 5 pediatric cases of Burkitt's lymphoma (BL) of GI tract from Feb 2011 to March 2014. Following features were noted: extent of disease was determined by history, physical examination, baseline complete hemogram, liver function tests, lactate dehydrogenase (LDH) as a tumor bulk indicator, uric acid, serum electrolytes, bone marrow biopsy, abdominal ultrasound and/or contrast-enhanced computed tomography (CECT) scan of the abdomen. Quality of life in patients received chemotherapy after surgery was compared with those who required surgery during chemotherapy.
Results: In two cases presented with intususception which was resolved with conservative management, and one case which presented with subacute intestinal obstruction was managed initially with chemotherapy but required surgical intervention in between. Where as in one case had presented with intususception with suspected leak and one case which has featuresof subacute intestinal obstruction was initially treated by resection followed by chemotherapy. The group of patient which are treated surgically initially were tolrated chemotherapy better than other group.
Conclusion: Quality of life during chemotherapy is better in patients who received chemotherapy after surgery than who initially treated with chemotherapy though a detailed study is required for definitive conclusion.

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EARLY COMPLETE RESPONSE AS A FACTOR OF TREATMENT REDUCTION IN ADVANCED STAGES PEDIATRIC BURKITT LYMPHOMA

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Background/Objectives: Progress in treatment of advanced stages Burkitt lymphoma (BL) is associated with intensive chemotherapy, supportive care and rituximab use. Current studies investigate clinical and/or biologic features for treatment reduction. By literature data (C.Patte, 2007) it is possible to reduce treatment for early responding intermediate risk patients with B-NHL. In our study we reduced treatment for high risk BL pts.
Design/Methods: Forty one newly diagnosed BL pts with Murphy stage III-IV, 3-4 BFM risk groups were treated according to the r-B-NHL-BFM 95red protocol, between January 2007 and February 2015. The median age was 8,3 years (range, 3-16), male/female ratio – 4/1. Rituximab (375 mg/m2) was administrated on day 0 of block AA and BB. Therapeutic effect was estimated.
Results: 7-year event-free survival (EFS) by r-B-NHL-BFM 95red protocol was 96,6+/-2,4%. Twenty pts (48,8%) achieved early complete response (CR) after 2 blocks of chemotherapy. The following treatment consisted of blocks CC-AA-BB without rituximab. Al the 20 (100%) pts with CR are in remission with follow up 78 months. Twenty one (51,2%) pts did not get CR after 2 blocks of chemotherapy and continued treatment by protocol without block number reduction (CC-AA-BB-CC). 7-year EFS was 91,2+/-5,1%. Two (4,9%) pts died: one – of disease progression and another – of Pseudomonas aeruginosa sepsis.
Conclusion: Our results suggest that early complete response may be an important prognostic factor for treatment reduction in near 50% of advanced stages pediatric Burkitt lymphoma. Our results revealed that early responded advanced stages BL pts have the same excellent results with treatment reduction protocol (from 6 to 5 blocks).

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PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA IN CHILDHOOD

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Background/Objectives: To evaluate the clinical characteristics, treatment regimens, and outcome of the patients with primary central nervous system lymphoma (CNS).
Design/Methods: Five patients diagnosed with primary CNS lymphoma between 1988 and 2014 were retrospectively evaluated. All patients were treated with chemotherapy and radiotherapy. Chemotherapeutic regimens included LMB, LSA2-L2 and high dose cytarabine and methotrexate.
Results: All of the patients were male. The median age was 10 years (5-14 years). Tumor locations were frontal lobe (1), parietal and temporal lobe (2), thalamus (1), leptomeningeal (1). All had B cell phenotype. LMB chemotherapy protocol was used in 3 patients, 1 patient was in LSA2-L2 protocol and 1 patient received high dose cytarabine and methotrexate. Intratechal rituximab was used in two patients. All patients received radiotherapy. Three patients treated with LMB protocol relapsed and died while the other 2 patients were on disease-free follow-up.
Conclusion: Primary CNS lymphoma is very rare in childhood. Although high dose cytarabine and methotrexate seems to be efficient in one patient and LSA2-L2 protocol is effective in another, our series is small and further studies are needed.

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ROLE OF IL10 PROMOTER POLYMORPHISMS IN THE PATHOGENESIS OF PEDIATRIC HODGKIN LYMPHOMA

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Background/Objectives: IL10 is a cytokine involved in anti-inflammatory responses. Three Single Nucleotide Polymorphisms (SNPs), -1082 (A/G), -819 (C/T) and -592 (C/A) in the gene promoter display differential susceptibility to Hodgkin Lymphoma (HL) development, Epstein Barr Virus (EBV) susceptibility and treatment response.Objective: Investigate the role of IL10 gene polymorphisms in HL pathogenesis as well as EBV involvement in a population from Argentina.
Design/Methods: One hundred thirteen pediatric patients were studied: 64 HL and 49 reactive hiperplasias (RH) as controls. EBV infection was assessed by PCR and EBERs in situ hybridization, while IL10 promoter polymorphisms SNPs -1082A/G and -592A/C were genotyped by allele-specific (AS-) PCR. Based on the strong linkage disequilibrium between SNPs -819 and -592, three crossing AS-PCRs were carried out, to confirm the haplotypes ACC, ATA and GCC. Clinical outcome in 48 of the 64 patients with HL was analyzed.

Results: Both SNP-1082 and SNP -592 did not display statistical significant differences between HL and RH controls (p>0.05, $\chi 2$ test). Only the haplotype ACC was statistically overrepresented in HL versus controls (p=0.011, $\chi 2$ test). EBV was expressed in 65% HL and in 54% RH, and neither genotype distribution of SNPs -1082 and -592, nor IL10 haplotype showed a differential association with EBV+ and EBV- HL and controls (p>0.05, 2 test). The carriers of the SNPs -592 A/C had lower event free survival and global survival specifically in the HL group (EFS 62% vs 82% p=0,04/ GS 80% vs 100% p=0,026).
Conclusion: ACC haplotype was associated with increased susceptibility to HL. Even though the G allele in -1082 and ATA haplotype were protective for EBV primary infection, this decreased susceptibility was not observed in EBV-associated pediatric HL. We found statistical significant association between the carriage of SNP -592A/C and lower survival. Our study highlights the importance of analyzing IL10 promoter polymorphisms as another prognostic factor.

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ATORVASTATIN REGULATING THE AUTOPHAGY OF LYMPHOMA RAJI CELL VIA THE PI3K/AKT/MTOR PATHWAY

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Background/Objectives: To investigate the effect of atorvastatin on the autophagy of human lymphoma Raji cell line, and to explore the signaling pathway in this process.
Design/Methods: Raji cell line was divided into negative control group, atorvastatin group, LY294002(a PI3K inhibitor) group, rapamycin(a mTOR inhibitor) group, and they were co-cultured for 24h. The formations of autophagy were observed by acridine orange staining.The expressions of autophagy protein LC3- II and Beclin-1 were examined by Western blot. The expressions of phosphorylation of Akt and mTOR were detected by RT-PCR and Western blot methods, respectively.
Results: Compared with the negative control group, atorvastatin inhibited the autophagy of lymphoma Raji cell (t=3.972, P<0.05), and down-regulated the expressions of LC3- II and Beclin-1(t=4.038, P<0.05;t=3.639, P<0.05). Compared with atorvastatin group, LY294002 group increased the expressions of LC3- II and Beclin-1(t=4.772, P<0.05; t=2.939,P<0.05); rapamycin group also up-regulated the expressions of LC3- II and Beclin-1 (t=3.287, P<0.05; t= 4.316,P<0.05).Compared with atorvastatin group, LY294002 group decreased the mRNA and protein expression levels of p-Akt and
p-mTOR(t=4.578,P<0.05;t=3.767,P<0.05;t=4.565,P<0.05;t=3.633,P<0.05); rapamycin group also reduced the mRNA and protein expression levels of p-Akt and p-mTOR (t=2.916, P<0.05; t=3.815, P<0.05; t=2.995,P<0.05; t=4.079, P<0.05).
Conclusion: Atorvastatin can inhibit the autophagy of lymphoma Raji cell, the mechanism might be related to the activation of PI3K/Akt/mTOR signaling pathway.

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THE EFFECT OF ATORVASTATIN REGULATING GLYCOLYSIS METABOLISM PATHWAY ON LYMPHOMA CELL THROUGH TLR4/MYD88/ NF-KAPPA B PATHWAY

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Background/Objectives: To investigate the effect of atorvastatin regulating the glycolysis metabolism pathway on lymphoma cell line Raji, and explore the role of TLR4/MyD88/ NF-kappa B signaling pathway in this process.
Design/Methods: Raji cells were incubated with different concentrations of atorvastatin (0.1μmol/L, 1μmol/L, 10μmol/L), and Raji cells without any treatment were used as control. The glycolytic rates of Raji were investigated by glucose consumption assay when cells were cultured for 6, 12, 24 hours. The apoptosis was detected by flow cytometry after cells incubated for 24 hours. The mRNA expression of HK2, PKM2 and HIF-1 was detected by RT- PCR technique. The protein expression of TLR4, MyD88 and NF-kappa B was detected by Westernblot method.
Results: The results indicated that atorvastatin could inhibit the glycolytic activity on Raji cell. When treated with 10 μ mol/L atorvastatin after 24 h, the effect of inhibition to the glycolytic activity on Raji cell was most strikingly, the glycolytic rates reduced to (37.92±1.06)% (t=3.975,P<0.05). In addition, atorvastatin could induce the apoptosis of Raji cells. When treated with 10 μ mol/L atorvastatin, the apoptosis of Raji was most notably, at a rate of(52.39±2.72)%,(t=3.992,P<0.05).There was basal mRNA expression of HK2, PKM2 and HIF-1 gene in the control group. When treated with 10 μ mol/L atorvastatin, it showed that the mRNA expression of HK2, PKM2 and HIF-1 was down-regulated most obviously, at a decrease of (51.67±3.89)%,(63.29 ±2.69)%,(45.95±4.02)% (t=3.798,P<0.05;t=4.428,P<0.05;t=3.956,P<0.05), respectively. There was basal protein expression of TLR4, MyD88 and NF-kappa B gene in the control group. When treated with 10 μ mol/L atorvastatin, it showed that the protein expression of TLR4, MyD88 and NF-kappa B was decreased most visibly, with a decline of (61.09 ±5.37)%,(65.47±3.73)%,(49.06 ±4.62)%(t=4.615,P<0.05;t=3.773,P<0.05;t=3.292,P<0.05), respectively.
Conclusion:
Atorvastatin can inhibit the the glycolytic activity and induce the apoptosis on Raji cell, and the mechanism may be associated with the TLR4/MyD88/ NF-kappa B signal pathway.

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TREATMENT RESULTS OF PEDIATRIC HODGKIN LYMPHOMA: EXPERIENCE OF SINGLE CENTER FROM DEVELOPING COUNTRY

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Background/Objectives: The evaluation of clinical characteristics, treatment and follow up results of patients with Hodgkin Lymphoma (HL) in a developing country.
Design/Methods: Clinical characteristics, treatment and follow up results of 105 children with newly diagnosed HL were analyzed retrospectively.
Results: There were 68 boys (65%) and 37 girls (35%) with a median age of 10.5 (3-17 years). Duration of symptoms was median 120 days (3-1095) and out of 105, 39 patients had B symptoms. The most common histological subtype was mixed cellularity (52%). The percentage of patients with localized disease (stage I- II) and advanced disease (stage III- IV) were 49 and 51, respectively. The first-line treatments of patients were DAL-HD-90 (n=41), only COPP (n=31), ABVD (n=27), ABV-COPP (n=5) protocols. Radiotherapy was administered to 88 (84%) patients. Eleven patients didn't receive radiotherapy because of advanced disease and five due to decision of different consultant doctors. At a median follow-up of 51 months, the 5-year overall (OS) and event-free (EFS) survival rates of whole group were 84% and 74%. There found a statistically difference between the groups receiving radiotherapy and not (5-year EFS 78% vs. 45% p=0.01). Patients with stage III-IV disease had significantly lower OS rates when compared to stage I-II disease (5-year OS 77% vs. 91% p=0.03). Patients received radiotherapy in the first-line treatment had significantly higher OS rates then patients who didn't receive radiotherapy (5-year OS 90% vs. 52% p=0.001). In multivariate analysis only radiotherapy was found to be positively correlated with OS.
Conclusion: The treatment approaches applied in our department has successful results in general, survival rates of patients with advanced disease and treated without radiotherapy has been shown to be lower when compared to the patients with local disease and treated with radiotherapy. That's why we emphasize the necessity of radiotherapy for the patients with HL.

Posters: Myeloid Leukemias, Myelodysplastic & Myeloproliferative Syndromes

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CLINICAL PROFILE AND OUTCOME OF CHRONIC MYELOGENOUS LEUKEMIA (CML) AMONG PEDIATRIC PATIENTS IN PHILIPPINE GENERAL HOSPITAL (UP-PGH): A RETROSPECTIVE STUDY (2008-2013)

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Background/Objectives: Chronic myeloid leukemia (CML) in childhood is rare representing 2-3% of pediatric leukemias. At Philippine General Hospital, the country's national referral center, the survival rate for pediatric CML was 35% (2002-2005) without tyrosine kinase inhibitor. Since then Imatinib was made locally available through the Max Foundation Novartis Glivec International Patient Assistance Program (GIPAP). We report the outcome of our patients.
Design/Methods: Medical records of pediatric CML patients diagnosed from January 2008-December 2013 were reviewed. Demographic data were collected and outcome evaluated at study endpoint, November 2014.
Results: Thirty seven patients were diagnosed during the study period. Only 33 charts were available for review. Ages ranged from 5-18 years (mean 12 ± 5). Splenomegaly was present in 27 patients (82%). Philadelphia chromosome was documented by FISH and karyotyping in 25 (76%) and 5 patients (15%), respectively. At diagnosis 24 (73%) were in chronic phase, 6 (18%) accelerated and 3 (9%) blastic. Only 22 (67%) patients received Imatinib due to financial constraints. Of these, 20 were chronic and 2 in accelerated phase. At 3 months, 95% (n=20) achieved complete hematologic response (CHR); no data (n=2). Twenty eight percent (28%; n=6) had complete cytogenetic response at 12 months and 12 % (n=3) had major molecular response at 18 months. At study endpoint, 18% (n=4) achieved complete molecular response but 23% (n=5) had loss of CHR due to treatment abandonment and 14% (n=3) died of disease. Eleven patients did not receive imatinib. Of these, 5 died of disease, 5 abandoned hydroxyurea treatment, and 1 remained with CHR on hydroxyurea. The 6 year overall survival of all patients (n=33) is 49%, and 73% for those on Imatinib (n=22).
Conclusion: Survival rate among our pediatric CML patients has improved with imatinib availability. Better compliance and more financial support for disease monitoring studies are needed to define treatment response.

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DIFFICULTY IN THE DIAGNOSIS OF SMALL ROUND BLUE CELL TUMORS IN A LOW INCOME COUNTRY. A CLINICAL CASE

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Background/Objectives: Small round blue cell tumors (SRBCTs) are a group of malignancies that occur in children. The differential diagnosis mainly include rhabdomyosarcoma (RMS), Peripheral primitive neuroectodermal tumors (pPNETs), leukemia, lymphoma, Neuroblastoma among others. Immunohistochemistry is one of the most prevalent and convenient methods for pathological diagnosis; however, differentiation between those tumors, in a low income country is still very challenging. We present a clinical case of an 11-month-old male infant with a small round blue cell tumor.
Design/Methods: We present a clinical case of an infant with SRBCTand a discussion of the differential diagnosis of these tumors in the pediatric population, which represent a challenge in low income countries.
Results: An 11 old month male was admitted to the Pediatric Oncology Service at Centro Medico Nacional 20 de Noviembre ISSSTE in Mexico City, with a single small bluish colored skin nodule in foot plant since he was 2 month old. An excisional biopsy was made with diagnosis of Neuroblastoma. Our pathologists reviewed the biopsy and concluded pNET. Image studies were performed with no primary tumor site. We started chemotherapy according to Mexican National Protocol.After 5 cycles of chemotherapy, a subcutaneous soft tissue lesion in left gluteous appeared with hystophatologic diagnosis of pNET, bone marrow aspirate and biopsy were made with final diagnosis of Acute Myeloid Leukemia.
Conclusion: The differential diagnosis of SRBCTs isn´t easy in low income countries, where there is a lack of resources and investigation. The oncologists must perform a complete clinical investigation, but it is clear that the diagnosis of SRBCTs should be based on a comprehensive analysis involving morphology and immunoreactivity to a panel of markers. We should also investigate the ocurrence of major chromosomal translocations to validate the diagnosis. If we perform the accurate diagnosis, we can treat cancer in a proper way.

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USE OF ANTIFUNGAL AGENTS IN PEDIATRICS WITH HEMATOLOGIC DISORDERS

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Background/Objectives: Fungal infections are important causes of morbidity and mortality in pediatric patients with hematologic disorders. Antifungal resistance increases the cost of treatment and prolongs hospitalization, thus, leading to increasing adverse drug reactions in humans.This article seeks to investigate the rational use of antifungals in oncology wards, considering the radiological and mycological evidence.
Design/Methods: Besides the routine laboratory examination, blood cultures, molecular assays for *Aspergillus* and *Candida albicans* on serum samples were done for all patients by real time PCR. Clinical signs and symptoms and use of antifungal agents were studied, according to the patients' medical files.
Results: Among 44 febrile pediatric patients with hematologic disorders, 22 were males. The back grounds of patients were acute lymphoblastic leukemia in 26 cases, acute myelogenous leukemia in 9, *non-Hodgkin* lymphoma 3, Fanconi anemia 2 and Histiocytosis in 1 case. The mean of white blood cell count and age were 4491 and 8 years. Radiologic signs of infections were positive in 27 patients, *Candida albicans* were isolated from 3 (6.8%) blood cultures and sera samples were positive in 20 (45.5%) patients with real time PCR, 9 *Aspergillus* and 11 *Candida* albicans. Antifungals were started in 35 (79.5%) patients; amphotericin B in 23, Amphotericin and fluconazole in 4, Amphotericine with voriconazole in 2, amphotericin with itraconazole in 2 , itraconazole in 3 and fluconazole in 1 patient.
Conclusion: Unfortunately, the use of antifungal agents in pediatric oncology wards was not according to documented evidence, as the study revealed. Given the similar clinical, radiological features in microbial infections, mycological examination can help restrict the irrational use of antifungals and thereby control the respective resistance and save on the health costs. In doing so, further research based on clinical as well as microbiological parameters of fungal infections are suggested.

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ABANDONMENT AND OUTCOME OF CHILDHOOD ACUTE MYELOID LEUKEMIA IN A TERTIARY LEVEL HOSPITAL

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Background/Objectives: Acute leukemias are the most common child hood malignancy, of which acute myeloid leukemia (AML) are 15% to 20%. Abandonment is one of the most important causes of treatment failure in AML in developing countries. Lost to follow-up is also a big problem in low income countries. Many patients stop therapy soon after diagnosis due to cost, distance and ignorance. *Objective*: To determine the abandonment, outcome and treatment related mortality (TRM) and morbidity among children with AML.
Design/Methods: This prospective observational study was conducted in the Department of Pediatric hematology and Oncology, BSMMU, Dhaka for duration of one year. Fifty (50) patients of AML visited to out patient department (OPD) of Pediatric hematology and Oncology. Among them 11(22%) patients refuse treatment from outdoor. Thirtynine 39 (78%) patients of AML were selected as per inclusion and exclusion criteria. After proper evaluation and clinical examination of these patient, CBC and Bone marrow examination was done for confirmation of diagnosis.
Results: A total of 39 patients were recruited in this study. Seventeen (43.6%) patients were male and 22 (56.4%) were female. Mean ± SD of age was 7.80 ±4.42 and range was 6 months to 15 years. Out of 39 patients, 18(46.1%) patients were abandoned, 15(38.4%) expire, relapse 2(5.2%) & alive 4(10.3%).
Conclusion: High abandonment (46.1%) and treatment related toxic death (38.4%) has compromised the outcome of Acute myeloid leukemia. However AML can be treated with better outcome if improved the supportive care, reduce toxic death, refusal or abandonment.

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HIGH DOSE ETOPOSIDE AND CYCLOPHOSPHAMIDE FOR REFRACTORY ACUTE LEUKAEMIAS IN CHILDREN, ADOLESCENTS AND YOUNG ADULTS

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Background/Objectives: Overall 30-40% of children with acute myeloid leukaemia (AML) will experience relapse [Rubnitz 2007]. The 5-year overall survival (OS) for children with relapsed AML is 23% [Sander 2010]. High dose etoposide and cyclophosphamide (HD Etop/Cyclo) has achieved complete remission (CR) rates of 28–57% in adults with refractory/relapsed acute leukaemias [Brown 1990, Johny 2006, Trifilio 2013]. We aimed to evaluate the efficacy/safety of HD Etop/Cyclo in children, adolescents and young adults with refractory acute leukaemias treated at our institution.
Design/Methods: Retrospective study of patients aged 1-24 years with AML, acute lymphoblastic leukaemia (ALL) and/or biphenotypic leukaemia (BL) refractory to ≥1 line of chemotherapy, either at initial diagnosis or at relapse, between 2006-2014. Efficacy was assessed as per IWG criteria and adverse events according to CTCAE v4.03. Study endpoints were overall response (OR) after 1-2 cycles, event-free survival (EFS) and OS.
Results: Nine patients were included (10 cycles): all males; median age (range) 13 years (1–23); 6 AML, 2 ALL, 1 BL; refractory at diagnosis (n=3), following relapse (n=6). OR was: 1 CR, 2 CR with incomplete platelet recovery and 1 partial response (44.4%, 95%CI 13.7–78.8). All patients had grade (G) 4 neutropenia and thrombocytopenia. Other toxicities included (all G3): febrile neutropenia (n=8); mucositis (n=3); tumour lysis syndrome (n=2); and lung infection (n=1). One non-responder and 3 responders subsequently underwent allogeneic stem cell transplant. Median (95%CI) EFS for responders: 10.2 months (6.7–n/a). Median (95%CI) OS for the whole cohort: 8.7 months (1.9–n/a). One non-responder and one responder remain disease-free 1 and 2.9 years after HD Etop/Cyclo, respectively.
Conclusion: These results are consistent with those reported in adults. It is feasible to administer HD Etop/Cyclo in children with a toxicity profile similar to other regimes used in the relapsed setting. Hence, we believe HD Cyclo/Etop would merit further evaluation in prospective studies.

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COMPARISON OF IMMUNE MANIFESTATIONS BETWEEN REFRACTORY CYTOPENIA OF CHILDHOOD AND APLASTIC ANEMIA IN CHILDREN: A SINGLE-CENTER RETROSPECTIVE STUDY

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Background/Objectives: This retrospective single-center study assessed the incidence and clinical features of immune manifestations of refractory cytopenia of childhood (RCC) and childhood aplastic anemia (AA).
Design/Methods: From February 2008 to March 2013, 72 and 123 children with RCC and AA, respectively, were evaluated.
Results: RCC was associated with autoimmune disease in 4 children, including 1 case each with autoimmune hemolytic anemia, rheumatoid arthritis, systemic lupus erythematosus, and anaphylactoid purpura. No children with AA were diagnosed with autoimmune diseases. The incidence rate of autoimmune disease in childhood AA was significantly lower than that children with RCC ($P = 0.008$, $\chi^2 = 6.976$). Immune abnormalities were common in both RCC and AA; the most significant reductions were in total lymphocyte count and the relative numbers of CD3−CD56+ subsets found in RCC. Despite the many similar immunologic abnormalities in AA and RCC, the incidence rate of autoimmune disease was significantly lower in childhood AA than RCC. The relative numbers of natural killer cells were significantly lower in RCC patients than AA patients.
Conclusion: The large overlap of analogous immunologic abnormalities indicates RCC and childhood AA may share the same pathogenesis.

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CYTOGENETIC ABNORMALITIES IN CHILDHOOD ACUTE MYELOID LEUKEMIA: A SERIES FROM TERTIARY CARE HOSPITAL OF NORTH INDIA

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Background/Objectives: Karyotype is an independent indicator of prognosis in acute myeloid leukemia (AML) that is widely applied to risk-adapted therapy. Because AML is rare in children, the true prognostic significance of individual chromosomal abnormalities in this age group remains unclear.
Design/Methods: The study was taken in the Department of Molecular Biology & Transplant Immunology, Indraprastha Apollo Hospital, New Delhi, India for all pediatric AML patients referred for cytogenetic analysis between 2011 and 2014.
Results: Between 2011 and 2014, 26 children with AML were referred for cytogenetic analysis. Cytogenetic analyses was successful in all 26 cases (100%), and clonal chromosomal abnormalities were detected in 18(69.2%).The most common aberration was t(8;21)(q22;q22) (n=7, 38.8%) which was present in isolation (n=3, 42.8%) as well as a part of a complex karyotype (n=4, 57.2%). The complex karyotype involved loss of sex chromosome in 3 cases and trisomy 21 in 1 case besides the common t(8;21) in these cases. Since we regularly perform FISH analysis for all cases of AML, we were able to diagnose a case of cryptic AML-ETO which was missed in the conventional karyotype technique. 2(11.11%) cases each of Trisomy 21 and Trisomy 8 were observed. Complex karyotypes were observed in 6 cases (33.3%). A single (5.5%) case of Trisomy 6 was seen. High hyperdiploidy (96, XXY) was observed in 1 (5.5%) case. Other chromosomal abnormalities observed in isolation were 1 case of loss of sex chromosome andisochromosome 9 each.Loss of sex chromosome was present in 3 cases (37.5%).
Conclusion: Since the spectrum of chromosomal changes and their risk association seem to differ between children and adults with AML, it is imperative to perform cytogenetic analysis for all pediatric AML cases. FISH should be perform for rapid testing and wherever subtle duplications/deletions or translocations are anticipated.

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DIFFERENTIAL EXPRESSION OF NK CELL LIGANDS ON T, B AND MYELOID ACUTE CHILDHOOD LEUKEMIA

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Background/Objectives: NK cell function is finely tuned by inhibitory (iRec) and activating (aRec) receptors. Consistent with the "missing self" hypothesis, NK cells sensing the loss of self-HLA-class-I (HLA-I) through inhibitory killer cell immunoglobulin-like receptors (KIR) can eliminate tumor cells. NK cell function also depends on signals delivered through interaction of aRecs with their ligands. aRec such as NKG2D recognizes the stress-inducible MICA/B14 and ULBPs proteins, whereas DNAM-1 (CD226) specifically recognizes poliovirus receptor (CD155) and Nectin-2 (CD112).
Design/Methods: The expression of ligands for iKIR (HLA-I and HLA-C) and aRec (CD112, CD155, ULBP1 and MICA/B) was evaluated in 36 acute childhood leukemia at diagnosis (24 B-ALL, 6 T-ALL and 6 AML) using FACSCanto flow-cytometer on bone marrow tumor cells and on residual lymphocytes as a control for normal/basal expression. HLA-I and HLA-C expression was normalized as ratio (%) of mean fluorescence intensity (IMF) on tumor cells / IMF on control cells.
Results: The expression of ligands for iKIR was significantly lost in T-ALL (40% and 26%, respectively for HLA-I and HLA-C) but maintained for HLA-I or slightly decreased for HLA-C in B-ALL (123.6% and 73%) and AML (109% and 67.5%) compared to normal lymphocytes ($p<0.01$, T-ALL vs B-ALL or AML). In contrast, the expression aRec ligand was significantly ($p<0.05$) lower in T-ALL blasts (MFI: 159, 163, 125 and 27), than in B-ALL (IMF: 1643, 129, 188 and 45) or AML (IMF: 3902, 1013, 494 and 63) for CD112, CD155, ULBP1 and MICA, respectively.
Conclusion: The differential expression of ligands for NK cells inhibitory and activating receptors between B-ALL, T-ALL and AML acute childhood tumour cells, could potentially condition NK cell antitumor response on these types of tumours.

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PAEDIATRIC CHRONIC MYELOID LEUKAEMIA: A SINGLE UNIT EXPERIENCE IN KWA-ZULU NATAL, SOUTH AFRICA

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Background/Objectives: To describe patient characteristics, treatment response and survival of patients with Chronic Myeloid Leukaemia, at a single centre from 2003 – 2015.
Design/Methods: A retrospective chart review of patients with Chronic Myeloid Leukaemia diagnosed between January 2003 and March 2015.
Results: Nine patients were diagnosed with CML. There was a male predominance, M:F= 7:2 All 9 patients were Black. Eight patients presented with chronic phase disease, and one patient presented with blastic crisis. White cell counts ranged from 53–423, with a median of 330. Hydroxyurea, busulphan and mercaptopurine were used in 8/9 patients to control the white cell count at the outset. One patient was treated with interferon, and 7/9 were treated with Imatinib which made available via a donor programme. Four patients (4/8) with chronic phase disease progressed to accelerated phase. Of these, one was resistant to imatinib, and dasatinib was not available at the time. The second patient was salvaged with 2nd and 3rd line tyrosine –kinase inhibitors (TKI) and reverted to chronic phase. Three of the 4 patients with accelerated phase disease progressed to blast phase, and 2/4 had CNS disease. All 4 blastic phase patients demised. There was poor compliance in all 4 patients who progressed to accelerated phase. Difficult social circumstances and fatigue were the main causes of non-compliance. Compliance has been excellent in the subsequent 3 patients. 4/9 patients are still alive (survival of 5.6-9yrs) on TKI's. Three are on Imatininb and 1 is on Dasatininb.
Conclusion: Chronic Myeloid Leukaemia is a rare paediatric malignancy. Access to TKI's via donor programmes has improved survival of patients, and are critical especially in countries where stem cell transplantation is limited. Good compliance is pivotal to prevent progression to accelerated and blast phase. RT-PCR is more readily available, and treatment algorithims are now well defined, resulting in better survival.

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INFECTION TRENDS AND ANTIBIOTIC PROPHYLAXIS AMONG CHILDREN PRESENTING WITH ACUTE MYELOID LUKEMIA: A RETROSPECTIVE STUDY FROM PAKISTANI POPULATION

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Background/Objectives: Acute myeloid leukemia (AML) diagnosed among pediatric age group carries a great risk of immunosuppression and superimposed infections. Patients with this disease usually die of the related complications rather than the disease itself. The basic aim of this study was to rule out the beneficial role of prophylactic generalized antibiotic regimen for such patients thus to enhance the quality of life and decrease morbidity.
Design/Methods: This retrospective study was conducted at the oncology department of Rawalpindi Medical College allied teaching hospital. Data was collected for a period of 4 years Pediatric patients (aged 1-12 years) consecutively diagnosed with AML and treated from Jan 2011 through Dec 2014. Patients were treated on the International treatment guidelines per hospital policy protocol Data were extracted from hard copy or electronic chart review.
Results: A total of 11 cases were studied in detail. Staphylococcus is the major bug found among infective cases. Of the total 24 chemotherapy phases among 11 patients, each phase reported, preventive antibiotics were initiated when the daily absolute neutrophil count was falling <1000 cells/mcl and before the onset of fever. 5 episodes of

bacteremia were documented with predominantly coagulase-negative staphylococci and viridans group streptococci. 4 confirmed infection-related death occurred, primarily because of the respiratory tract infection leading to respiratory failure.
Conclusion: Antibiotic coverage should be organism specific and the commonest organism found to be was Staph group. Respiratory tract infection, neutropenia and onset of fever should be set as the starting point for bug specific antibiotic.

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LEUKEMIAS WITH ISOLATED EXTRAMEDULLARY RELAPSE AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION WITHOUT UNFAVORABLE CYTOGENETICS

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Background/Objectives: Extramedullary relapse (EMR) following allo-HSCT is a major contributor to mortality. Post-HSCT outcome continue to be challenging.
Design/Methods: Of the 38 leukemia patients receiving allo-HSCT from a matched sibling donor (MSD), 13 relapsed, five of whom (2 ALL, 3 AML) (38.5 %) had isolated EMR.
Results: All EMRs occurred median 6 months posttransplant. All 5 patients received myeloablative conditioning (4 TBI based, 1 busulfan based) and had 100 % chimerism when EMR occurred. Case 1, relapsed biphenotypic leukemia with pleural effusion at diagnosis. She experienced grade II/IV aGVHD. One year posttransplant she relapsed with pleural infiltrates. After two cycles of chemotherapy she died of sepsis. Case 2, resistant t(8;21) positive AML. Six months posttransplant she had a 10×5 cm mass in the upper right quadrant while suffering from extensive skin cGVHD. She received chemo/radiotherapy that lead to disappearence of the mass. She died of sepsis 17 months after EMR. Case 3, resistant AML while receiving donor lymphocyte infusions (DLIs) at six months posttransplant a mass in the leg appeared. He continued to receive DLIs and although the mass disappeared he developed grade III/IV hepatic GVHD and died because of progressive disease at 8 months of EMR. Case 4, resistant AML had paravertebral and hepatic masses nine months posttransplant while suffering from grade III/IV intestinal GVHD. He received chemotherapy and died of sepsis one month later. Case 5, resistant T-ALL and pericardial effusion at diagnosis, Six months posttransplant a 6×1 cm mass in the thorax appeared. She received chemo/radiotherapy and is still alive on ALL maintenance therapy.
Conclusion: EMR, which could escape from the immunotherapeutic effect of allo-SCT is a significant factor in the transplantation mortality. Neither myeloablative conditioning nor GVHD could have protected against EMR probably due to resistant nature of our leukemias. Best treatment of EMRs after transplantation is still not known.

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UNMANIPULATED HAPLOIDENTICAL FAMILY DONOR TRANSPLANTATION FOR THE TREATMENT OF CHILDREN AND ADOLESCENTS WITH HEMATOLOGIC MALIGNANCIES: A SINGLE INSTITUTION KOREAN STUDY

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Background/Objectives: Haploidentical family donor (HFD) hematopoietic cell transplantation (HCT) is an important treatment modality for patients with hematologic malignancies who require allogeneic transplant, but lack an HLA-matched donor. Here, we report our experience in treating pediatric patients with high risk hematologic malignancy with unmanipulated HFD transplant.
Design/Methods: Thirty-nine patients (13 female (33%)) received unmanipulated HFD transplant from August 2010 to July 2014 at a median age of 5.6 years (range: 0.7 – 17.4). Patient diagnoses were as follows: AML 26, JMML 8, ALL 3, mixed phenotype acute leukemia 1, dendritic cell sarcoma 1. Maternal donors were utilized for 34 (87%) of the patients. All patients received G-CSF mobilized peripheral blood stem cells. Conditioning regimen was as follows: busulfan-based 32, TBI-based 1, TBI and busulfan-based 6. Rabbit ATG was given for 4 days prior to transplant at a total dose of 5 – 10 mg/kg. GVHD prophylaxis consisted of cyclosporine and mini-dose methotrexate.
Results: Median cell dose infused was as follows: TNC 32.5 $x10^8$/kg, MNC 20.8 $x10^8$/kg, $CD34^+$ 7.9 $x10^6$/kg, $CD3^+$ 90.3 $x10^7$/kg. Cumulative incidence of grades II-IV and grades III-IV acute GVHD was 82.1±6.4% (32/39) and 25.6±7.1% (10/39) respectively. Cumulative incidence of overall chronic GVHD and extensive chronic GVHD was 47.2±8.3% (18/39) and 31.1±7.6% (12/39) respectively. Rate of relapse and transplant-related mortality (TRM) was 31.2±7,6% (13/39) and 10.8±5.2% (4/39) respectively. Event-free survival (EFS) of the cohort was 58.0±8.1% (22/39). None of the factors studied, including donor gender and degree of HLA mismatch, had a significant impact on EFS.
Conclusion: Unmanipulated HFD transplant done with rabbit ATG-based *in vivo* T cell depletion only is a feasible option for children and adolescents with high risk hematologic malignancy who require allogeneic HCT for cure. Although TRM remained low, further measures are necessary to decrease rates of acute and chronic GVHD.

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REMISSION INDUCTION IN MIXED LINEAGE T/MYELOID LEUKEMIA WITH CLOFARABINE IN PATIENTS WHO FAIL ALL-TYPE THERAPY FOLLOWED BY HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background/Objectives: Mixed phenotype leukemias are a rare subset of leukemias with a majority of B/Myeloid phenotype. There is no standard of care but some evidence that they are more responsive to acute lymphoblastic leukemia (ALL) type therapy. We report three cases of T/Myeloid mixed lineage leukemia. One patient achieved complete remission (CR) with ALL type therapy. In the two other, early initiation of clofarabine after failure of ALL type therapy led to remission. All three patients underwent successful hematopoietic stem cell transplantation (HSCT). We conclude T/Myeloid leukemia may be more common than previously reported and clofarabine may aid in achieving early remission allowing HSCT.
Design/Methods: A 15 year old female, a 5 year old male and a 18 year old male were diagnosed with acute T-myeloid leukemia between 2009 and 2014 by immunophenotyping of bone marrow aspirates using flow cytometry: Patient 1: CD3+, MPO partial+, CD34 partial+, CD117+, Tdt dim+. Patient 2: CD3+ and CD14+, CD64+, CD34 partial+. Patient 3: CD3+ and MPO+, CD4 partial dim+, CD117 partial dim+. All patients received ALL type induction chemotherapy.
Results: Only patient 1 achieved CR. Patient 2 and 3 required retrieval therapy but only achieved remission with negative minimal residual disease (MRD) after addition of clofarabine. All three underwent HSCT without relapse. The third patient died 190 days after HSCT due to transplant related complications.
Conclusion: We report three cases of acute T-myeloid leukemia that achieved MRD negativity prior to HSCT which has been associated with improved prognosis in ALL. Based on our and others experience ALL type induction regimen is reasonable. Instead of switching to acute myeloid leukemia type therapy, early initiation of clofarabine may be indicated to improve prognosis of HSCT if negative MRD is not achieved at the end of induction.

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EPIGENETIC THERAPY FOR TREATMENT PEDIATRIC ACUTE MYELOID LEUKEMIA

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Background/Objectives: Acute Myeloid Leukemia (AML) is a highly heterogeneous and poor prognosis disease with few available therapeutic options. The goal of our clinical trials was to increase survival of children with AML by using chemotherapy along Epigenetic drugs.
Design/Methods: Eight Russian Oncology Hospitals participated in our clinical trials. Chemotherapy was used in treated after AML-2002 protocol. Epigenetic drugs were added to chemo after AML-2007 protocol. There were 51 children after AML-2002 protocol. There were 70 children after AML-2007 protocol. Epigenetic drugs (valproic acid and all-trans-retinoic acid) were added to the maintenance therapy after AML-2007 protocol for Standard risk group. We used high-doses of chemo and autologous stem cell transplantation for treatment the patients in Intermediate risk group after AML-2002 protocol. AML-2002 protocol for High risk group consisted of alternate courses of chemo. The patients got epigenetic drugs from the first day of the treatment after AML-2007 protocol for Intermediate and High risk groups.
Results: The upwards going trend was seen in the increase of Disease-Free Survival (DFS), Event-Free (EFS) and Overall Survival (OS) after AML-2007 protocol: 55,3±6,7% vs 43,6±7,2% AML-2002 (p=0,11); 49,5±6,4% vs 39,2±6,8% AML-2002 (p=0,1); 53,5±6,3 vs 45,9±7,1% AML-2002 (p=0,3). The upwards going trend was seen in the increase of DFS and OS after AML-2007 protocol in all risk groups. We managed to increase OS accurately after AML-2007 vs AML-2002 protocol in High risk group (50,2 ±9,0% vs 30,8 ±12,8%, p=0,05). The survival values grew up more and accurately in children under one year old after AML-2007: DFS=83,3 ±10,8% vs 25,0 ±21,7% AML-2002 (p=0,04); OS=84,6 ±10,0% vs 25,0 ±21,7% AML-2002 (p=0,01).

Conclusion: Thanks to putting on epigenetic drugs the upwards going trend was seen in the increase of survival in children with AML.

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LEUKEMIA PREDISPOSITION: A REPORT OF CHILDHOOD ACUTE MYELOID LEUKEMIA AT MAHAK'S PEDIATRIC CANCER TREATMENT AND RESEARCH CENTER

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Background/Objectives: This study reports the epidemiology, characteristics, and outcome of pediatric Acute Myeloid Leukemia (AML) at Mahak's Pediatric Cancer Treatment and Research Center, diagnosed between 2007 and 2012.
Design/Methods: Retrospectively, 42 children meeting the inclusion criteria were enrolled in this study. Patients were treated according to the AML-BFM 83 protocol and have undergone prophylactic CNS radiotherapy after reaching a minimum age of 2 years.
Results: In 20 children (47%) a family history of malignant tumors has been reported, in 9 children (21%) occurrence of leukemia had been known. Both were associated with the risk of relapse (family history of cancer in relapse: n=11; 61%, P=0.136; leukemia: n=7; 39%; P=0.016). Treatment related mortality was 19% and associated with underweight patients (n=5; 62.5%; P=0.158). Following the 1st induction, 83.5% of the children (n=35) achieved complete remission, increasing to 95% (n=40) after the 2nd treatment element. The event-free and overall survivals were 36% (SE=3.5) and 44% (SE=3.4), respectively. The median time of event-free and overall survival were 18 ± 3.4 and 26 ± 6.8 months, respectively. Eighteen patients (42.9%) experienced relapse. Relapse rate was significantly associated with bone pain as the first clinical manifestation (P=0.012).
Conclusion: This study shows a relation of positive family history and relapse rate and warrants further studies on this subject. Improvements of diagnostics (founding a central lab), better risk stratification and supportive care, shifting to a feasible new protocol, improvement of human stem cell transplantation are crucial steps towards better outcome of pediatric AML in Iran.

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HAEMATOPOIETIC STEM CELL TRANSPLANTATION IN CHILDREN IN REPUBLIC OF KAZAHSTAN

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Background/Objectives: Pediatric haematopoietic stem cell transplantation (HSCT) department was opened in May, 2012 in Scientific Centre for Pediatrics and Children Surgery in Almaty.
Design/Methods: 5 allo-HSCT of the bone marrow stem cells from matched sibling donors (MSD) were performed in our unit for children with ALL, AML, JMML and SAA recently. First allo-HSCT was done in 14 yo boy with very SAA who was failed primarily immunosuppressive therapy. Conditioning regimen consisted of fludarabine, cyclophosphamide and rabbit ATG with cyclosporine A (CsA) and mycophenolate mofetil for GvHD prophylaxis. Due to poor graft function he underwent retransplantation with the same donor outside the country. Two HSCT were performed in patients with AML, CR2, who had history of hepatitis C. Conditioning regimen included: TreoCyMel, GvHD prophylaxis tacrolimus + methotrexate. PCR showed donor chimerism of 100% since 2 years with continuous hematological remission in first patient and chimerism of 100% since day+90 in second patient with AML. 2.8 yo girl with JMML underwent HSCT after TreoCyMel, GvHD prophylaxis with CsA. Engraftment was detected at day+24, PCR chimerism showed 100% donor cells at 1,6 years. 2.6yo girl underwent HSCT for ALL; t(4;11) after early bone marrow relapse in CR2. Conditioning regimen: TreoCyMel, GvHD prophylaxis with CsA. Engraftment was detected at day+22. PCR chimerism showed 97% donor cells on day+120.
Results: Despite our limited experience of HSCT, none of our patients suffered from early transplant mortality. Only one suffered from acute GvHD grade II (on day +24) and was treated with steroids. In one case, a patient with ALL at 120 days after allo held ascertained disease relapse. All other are alive early after HSCT (4-24 months).
Conclusion: Using of transplantation HSCT can improve the outcome of most children with different malignant and non-malignant disorders in our country.

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TET2 ALTERATIONS IN TAIWANESE CHILDHOOD ACUTE MYELOID LEUKEMIA

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Background/Objectives: Mutations in the tet oncogene family member 2 gene (TET2) are frequently found in adult acute myeloid leukemia (AML) patients and had some prognosis effect. However, reports of TET2 mutation in children are limited. We assess the prevalence of TET2 mutations in Taiwanese childhood AML and attempt to analyze the prognosis effect.
Design/Methods: Sixty-nine consecutive AML children from 1997 to 2010 were enrolled. TET2 analysis was performed by direct sequencing and assumed as mutation according to public database, literature documents and bioinformatics tools evaluation. Clinical characters and overall survival (OS) were compared between patients with and without TET2 alterations.
Results: Only intronic and missense mutations were identified and there was no nonsense or frameshift mutation. Two putative disease-causing missense mutations (S609C and A1865G) were identified in 1 patients and we estimated the prevalence of TET2 mutation in our patients was 1.4% The most common polymorphism was I1762V (45%), followed by V218M (12%), P29R (6%) and F868L (6%). Patients with polymorphism I1762V tended to have better survival rate then patients without I1762V (48.4% vs 25.7%, $p = 0.049$) thought the OS was no different by the Kaplan–Meier method ($p = 0.104$).
Conclusion: The prevalence of TET2 mutations in childhood AML patients was lower and the mutations were less complex than in adult AML. The prognosis effect of TET2 mutation needs further investigations to confirm the role in childhood AML.

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COMPLETE CLINICAL, HEMATOLOGICAL, CYTOGENETIC AND MOLECULAR TRANSCRIPT PROFILE AND OUTCOME ANALYSIS OF PEDIATRIC AND ADOLESCENT CHRONIC MYELOID LEUKEMIA CASES

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Background/Objectives: CML comprises 3% of all pediatric leukemias, with an annual incidence of 1 per million children and adolescents < 20 years of age.
Design/Methods: A total of 20 pediatric and adolescent CML cases (0-18 years) prospectively diagnosed on cytogenetic and RT-PCR analysis over four years (2010-2014) were enrolled.
Results: 7/20 (35%) were pediatric (0-12 yrs) and 13/20 (65%) adolescent (12-18 yrs) cases. Male: Female ratio was 1:1. All (100%) presented with massive splenomegaly. 19/20 (95%) were in chronic phase, and one (5%) presented in blast crisis. All had high TLC at diagnosis, with 7/20 (35%) having a WBC count more than 200×10^9/L. 13/20 (65%) had normal platelet counts, 6/20 (30%) high ($>500 \times 10^9$/L) and one case (5%) had a low platelet count. High absolute basophil count ($> 0.5 \times 10^9$/L) was seen in 19/20 (95%) cases. 15/20 (75%) cases had a low LAP score. Ph positivity on cytogenetic analysis was noted in 16/20 (80%) cases. No case had any other numerical or structural genetic change. All cases (100%) were positive for BCR-ABL transcript (p210 type) by RT-PCR analysis. 12/20 (60%) had a b2a2 type of p210 transcript while 8/20 (40%) had a b3a2 transcript. 18/20 (90%) cases received imatinib (200 mg-OD), 2/20 (10%) developed relapse, while 1/20 (5%) died and 1/20 (5%) did not respond to treatment. The event free survival was 78% at a median follow up of 30 months while the overall survival in responders was 85% at 30 months.
Conclusion: Pediatric CML though rare, needs to be considered in cases with high TLC and high absolute basophil count. BCR-ABL studies are necessary for a confirmed diagnosis. The overall outcome with imatinib treatment was very good as 85% of them were in remission at 30 months of follow up.

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TREATMENT OF ACUTE MYELOID LEUKEMIA IN DOWN AND NON DOWN SYNDROME CHILDREN. SEVENTEEN YEARS EXPERIENCE AT A TERTIARY CARE INSTITUTION

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Background/Objectives: Patients of Down syndrome (DS) with Acute Myeloid Leukemia (AML) have an overall good outcome compare to Non DS.
Design/Methods: Medical records of 27 DS AML patients who received chemotherapy between 1998 and 2013 were reviewed. Their outcome was compared to the 134 Non DS AML patients treated during the same time period.
Results: In the DS group 20 patients were males (74%). Median age at diagnosis was 24 months (range 1.32-153.24). Four patients were below the age of 12 months (14.81%). 7 were FAB M7. Mean WBC count was 32.73(range 1.80-219.96). Two patients were CNS positive. 22(81.48%) were in remission at the end of induction .Seven (25.9%) patients relapsed with a median relapse free time of 3.96 months (range1.8-16.08). Seven patients (25.9%) died (PD in 6 and Infection in 1).23 patients (85.1%) develop different chemotherapy related toxicities. Amongst the Non-DS AML, 74 (55.22%) patients were males. Median age at diagnosis was 74.16 months (range 3.36-165.96).17 patients (12.68%) were below the age of 12 months.15 had M7 and 21 had M5. Mean WBC count was 45.23(range1-539). Nineteen patients were CNS positive. 42 patients (31.34%) relapsed with a median relapse free time of 9.24 months (range0.96-39.36). 62 patients (46.26%) died (PD in 46 and infections in 16).123 patients (91.79%) develop different chemotherapy related toxicities .The OS of DS AML group was 71.4% compare to Non DS AML group of 43% and EFS of the DS AML group was 65.8% compare to Non DS AML group of 40.2%.
Conclusion: Our results show a favorable outcome in DS AML group compare to Non DS AML group treated at our institute.

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ACUTE MYELOID LEUKEMIA - M7 IN DOWN SYNDROME; DOSE IT MAKE A DIFFERENCE?

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Background/Objectives: AML-M7 is a rare form of childhood leukemia which is characterized by a poor response to therapy compared to patients with AML-M7 in children with Down syndrome (DS).
Design/Methods: We compared 7 DS AML- M7 with 15 Non DS AML-M7 patients treated at KFSHRC, Riyadh, Saudi Arabia between 1987 and 2013. Data were analyzed for clinical characteristics of the patients and their outcome.
Results: The 2 groups received institutional AML protocol. In the DS group 6 patients were males (85.7 %). Median age at diagnosis was 20.52 months (range 7.93-27.51). Two patients were below the age of 12 months (28.57%). Mean WBC count was 25.03(range 3-138). All patients were CNS negative. 6 patients (85.7%) were in remission at the end of induction .No relapses. One patient (14.28%) died due to progressive disease. Six patients (85.7%) had infectious toxicities during the induction (BI 5,FI 3,F/N 5) and 2 patients(28.57%) in post induction phase(BI 1,FI 1,F/N 1) . Amongst the Non-DS AML, 10 patients (66.6%) were males. Median age at diagnosis was 15.31 months (range 3.34-84.72). Seven patients (46.6%) were less then 12 months. Mean WBC was 14.60(range5-32). All were CNS negative. Ten patients (66.6%) achieved remission at the end of induction. 3 patients (20%) relapsed with a median relapse free time of 2 months (range1.18-2.72). 6 patients (40%) died (PD in 3 and infections in 3). 9 patients (60%) develop infectious toxicities during induction (BI 3, FI 3, F/N 8) and 8 patients(53.3%) in the post induction phase(BI 5, FI 2,F/N 5) . The OS in Non-DS group was 57% compared to 85.7% in DS group (p=0.484) and EFS was 58.3% compared to DS AML group of 85.7 %.(p=0.014).
Conclusion: Our results support a favorable outcome of DS AML M7 group compare to Non DS AML M7 group.

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REDUCED INTENSITY CONDITIONING TRANSPLANTS WITH POST TRANSPLANTATION CYCLOPHOSPHAMIDE FOR RELAPSED LEUKEMIA - A BELIEVABLE OPTION IN THE DEVELOPING WORLD!

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Background/Objectives: High non-relapse mortality (NRM) of myeloablative hematopoietic stem cell transplant (HSCT) in leukemia patients with comorbidities, has led to increased interest in Reduced intensity conditioning transplants(RIC). Post-transplant cyclophosphamide (PtCY) with RIC is a new strategy which decreases graft versus host disease (GvHD) without compromising graft versus leukemia (GvL) effect. We report here the feasibility and outcome of these RIC transplants in a developing world setting.
Design/Methods: Five children with relapsed leukemia and co-morbidities (Intracranial bleed-1, Invasive fungal infection-2, hepatitis C-1, poor general condition-1) from Dec2013 to Dec2014 underwent PtCY RIC HSCT. The clinical records and investigation sheets were analyzed retrospectively. Patient's follow-up ranged from Day+83 to Day+305.
Results: Mean age was 11.4 year (6-19 years). All had relapsed leukemia (Acute myeloid leukemia-1, chronic myeloid leukemia-1, acute lymphoblastic leukemia-3) and all except one were in complete remission (CR). Conditioning was Fludarabine (160 mg/m^2), Cyclophosphamide (29 mg/kg), ATG (4.5 mg/kg), Thiotepa (8 mg/kg) and TBI (2Gy). Three patients had matched sibling peripheral blood stem cell (PBSC) graft, one had haploidentical PBSC and one had double cord blood (DCB) graft. Mean CD34$^+$ cell dose was 6.6×10^6/kg for patients with PBSC graft and 2.1×10^5/kg for DCB graft. PtCY was given on Day+3 and Day+4 at dose of 50 mg/kg/day. All patients engrafted. Mean neutrophil engraftment was on 18.6 day. Chimerism studies showed fully donor in 4 and mixed chimerism in 1. Child with mixed chimerism was treated successfully with donor lymphocyte infusion, GVHD grade3 was seen in 1 and grade2 in 2 patients. There were two deaths. The patient with DCB transplants died on D+83 due to BK virus and cytomegalovirus infection with GVHD and second patient relapsed post-transplant and died during re-induction on Day+88. Day-100 mortality was 40% and overall survival was 60%.
Conclusion: In relapsed leukemia patients with co-morbidities, RIC HSCT with PtCY constitutes a feasible and effective option.

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DIFFERENT MODES TO INACTIVATE THE SECOND ALLELE OF TP53 IN THREE INDEPENDENT MALIGNANCIES IN A YOUNG FEMALE PATIENT WITH LI-FRAUMENI SYNDROME

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Background/Objectives: Li-Fraumeni syndrome, a cancer predisposing syndrome, caused by germline mutations in TP53, is associated with the development of various tumors at a young age.
Design/Methods: Here we investigated the inactivation of the second allele of TP53 by sequencing, TOPO TA cloning, karyotyping and FISH, in three different malignancies that developed in a female child with Li-Fraumeni syndrome: a choroid plexus carcinoma at the age of 4 months, a secondary acute myeloid leukemia (AML) by the age of 4 years, and a Wilms tumor at the age of 5 years.
Results: The de novo heterozygous TP53 germline mutation c.818G>A; p.Arg273His (rs28934576) located within the DNA binding domain of TP53 is a first and important step towards tumorigenesis. Investigating the TP53 mutation status in all three tumor tissues, we show that 1) in the choroid plexus carcinoma, the known germline mutation was detected in a homozygous state as a result of loss of the wild-type allele and a duplication of the mutant allele due to copy-number neutral LOH/uniparental disomy, 2) in the secondary AML, a complex karyotype indicating an increased genomic instability led to the loss of TP53 - most probably the wild-type allele - due to a deletion of 17p, and 3) in the Wilms tumor, the somatically acquired mutation c.814G>A was identified leading to compound heterozygosity.
Conclusion: The findings show that the complete inactivation of TP53 either by loss of the wild-type allele or by compound heterozygous mutations is the decisive step towards tumorigenesis in this young patient with Li-Fraumeni syndrome.

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CO-EXPRESSION OF MULTIPLE ABC-TRANSPORTERS IS STRONGLY ASSOCIATED WITH TREATMENT RESPONSE IN CHILDHOOD ACUTE MYELOID LEUKEMIA

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Background/Objectives: To analyze whether expression of ABC-transporters is associated with remission rate and long term outcome in a prospective clinical study of childhood acute myeloid leukemia (AML).
Design/Methods: The expression of four ABC-transporter genes (ABCA3 encoding drug transporter ABCA3, ABCB1 encoding multidrug resistance protein 1, ABCC3 encoding multidrug resistance-associated protein 3 and ABCG2 encoding breast cancer

resistance protein) was measured by TaqMan real time PCR in pretreatment samples from 112 children with AML. Patients were treated according to multicenter study AML-BFM 2004.
Results: ABCC3 (p=0.009) and ABCG2 (p=0.03) were associated with a lower chance to achieve remission after the first course of chemotherapy. ABCC3 was associated with lower relapse free survival (p=0.02). ABCG2 was expressed at higher levels in subtypes of AML with favorable outcome but within standard and high risk patients it was associated with poor outcome (p=0.02). A strong association was observed between the number of overexpressed ABC-transporters and the chance to achieve remission (p=0.01) or the chance of relapse free survival (p<0.001).
Conclusion: Modern and intensive treatment regimens do not readily overcome drug resistance caused by ABC-transporters. Inhibition of ABC-transporters could be particularly useful in patients who express multiple of these genes.

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ISOLATED CENTRAL NERVOUS SYSTEM RELAPSES OF CHRONIC MYELOID LEUKEMIA AFTER ALLOGENEIC STEM CELL TRANSPLANTATION SUCCESSFULLY TREATED WITH CRANIOSPINAL RADIATION, A CASE REPORT

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Background/Objectives: Hematopoitic stem cell transplantation (HSCT) was considered as one of the curative treatment for chronic myeloid leukemia (CML), a rare hematologic malignancy among pediatric population. Isolated extramedullary relapse in central nervous system (CNS) of CML in pediatric patient after HSCT have never been reported.
Design/Methods: A 5–year old Thai boy presented in 2008 with fever, marked splenomagaly was diagnosed with chronic phase CML in our institute.
Results: His initial blood counts showed anemia with hyperleukocytosis while CSF cytology was negative. A bone marrow (BM) karyotype showed, 46,XY,t(9,22) and BM pathology was compatible with CML in chronic phase. He was treated with hydroxyurea follow by Imatinib. Repeated BMA and cytogenetic revealed normal study three months after treatment. Eleven months later, he developed an episode of myeloid blast crisis. He received induction of remission chemotherapy according to ThaiPOG protocol for AML which consist of intravenous idarubicin, cytosine arabinoside with concurrent intrathecal metrotrexate, cytosine arabinoside and hydrocotisone. Subsequently, he achieved remission and underwent HSCT from matched related donor. He received busulfan plus cyclophosphamide as a conditioning regimen. Twelve months after transplantation, he developed ataxia. MRI of the brain and spine revealed an infiltrative lesion sized 4×3×2 cm. involving superior cerebellar vermis with leptomeningeal enhancement along conus medullaris. BM examination revealed remission. A biopsy of a cerebellar tumor showed the infiltration leukemic cells with mixed phenotype of B lymphoblastic and myeloid. IHe received whole brain (3,060 cGy) and spinal (3,170 cGy) radiation. Currently, he is in remission 4 years after the relapse.
Conclusion: Risk factors of isolated CNS relapse in this patient include conditioning regimen without total body irradiation and poor CNS penetration of imatinib. Given its rarity, treatment for this entity is not yet well defined. In summary we report our treatment experience in pediatric patient with isolated CNS relapse CML following HSCT.

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ACUTE MYELOID LEUKAEMIA (AML) TREATED ON THE RED CROSS WAR MEMORIAL CHILDREN'S HOSPITAL (RCWMCH) TREATMENT PROTOCOL RX 2071 (ADAPTED FROM MRC-AML15)

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Background/Objectives: Due to the poor outcomes achieved in Acute Myeloid Leukaemia (AML) treatment, the Red Cross War Memorial Children's Hospital (RCWMCH) Oncology service changed from a protocol based on BFM-87 to one based on MRC-AML15.This study was to assess the outcomes and treatment – related toxicity among children treated with RCWMCH protocol Rx 2071.
Design/Methods: This was a retrospective review of AML patients treated with R_X2071 between 2007 and 2012 at RCWMCH. Patients with Acute Promyelocytic Leukaemia (APL) and trisomy 21 were excluded. Patients with APL are treated with All Trans Retinoic acid (ATRA), and since 2009 their protocol also includes 6- Mercaptopurine and Methotrexate in the maintenance phase. Risk was assigned by cytogenetics. Good risk patients were those with translocations t(8; 21) and inv(16). Poor/standard risk included all other cytogenetics according to MRC-AML15.Data pertaining to toxicity was obtained and captured from patient folders.
Results: Thirty five children were treated on Rx 2071. Males comprised 51.43% (18/35) and females 48.57% (17/35). Ages ranged from 0.33 to 12.51 years with the median age being 5.68 years. Off-treatment follow up ranged from 1 year 7 months to 6 years 8 months. Fifteen patients had favourable cytogenetics, 14 with t (8; 21) and 1 with inv(16). Event free survival (EFS) for the good risk group was 86.7%.Twenty patients presented with standard/poor risk cytogenetics: four did not achieve remission and were deemed poor risk while 16 were standard risk. EFS in this group was 39.7%. Patients had a median of 4 neutropaenic fevers, and required a median of 8 packed cell transfusions and 11 platelet transfusions. There were 38 positive blood cultures, one patient needed inotropic support and there were no toxicity-related deaths.
Conclusion: Results are superior to those achieved with the previous regime, and the toxicity is not excessive.

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OUTCOME OF HIGH HYPERDIPLOIDY IN INDIAN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Background/Objectives: High hyperdiploid ALL (hHALL) (51- 65 chromosomes per cell) is a good risk subgroup that accounts for 25 – 30% cases of Pre B ALL.
Design/Methods: We analyzed the clinical presentation and outcome of children with hHALL diagnosed at our center between 1995-2013.
Results: Two hundred and eleven children diagnosed pre B ALL with evaluable cytogenetic and follow up data were included in this study. 58 patients (27%) had hHALL.Those who had t(9:22) along with hHALL were excluded from the analysis. Median age at diagnosis was 4 years. High WBC count (>20,000 cells/mL) was observed in 19% hHALL and 25% of non-hHALL. There was no difference in median age or sex ratio between both groups. Median duration of follow up was 4 years. 3 children with hHALL relapsed (5.7%) compared to 13 in the other group. Chromosome 21 was most commonly affected (60%) followed by 17, 6, 10, 14, 4, 5 and X. Triple trisomy (+4, +10, +17) was observed in 4 patients.Six patients had additional structural abnormalities. Three children with hHALL relapsed (5.7%) compared to 13(8.1%) in the non-hHALL group. One had isolated CNS and 2 had combined relapses. No significant difference was noted regarding the site of relapse between the two groups. Early relapses (< 18 months) were more common in non-hHALL cases (75%). Six out of 58 hHALL patients had additional cytogenetic abnormalities and had poor outcome compared to those without. There was no significant difference in EFS (hHDALL 68.2 ± 8.8% vs. non hHALL 74.3 ± 4.4 %) and OS (78.3 ± 6% vs 79.8 ± 3.9%) between the two groups.
Conclusion: The prevalence of hHALL and chromosome 21 involvement was similar to previously published literature. Pattern of relapse seems to be different in hHALL although not statistically significant.Additional structural abnormalities reduce the prognostic benefit of hHALL.

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EMERGING ROLE OF MICRORNA-106B~25 CLUSTER IN RELAPSED MLL-REARRANGED PEDIATRIC AML

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Background/Objectives: Mixed lineage leukemia (*MLL*) rearrangements represent about 15-20% of pediatric acute myeloid leukemia (AML) cases. Survival rates have increased over the past decades, still, approximately 30-40% will relapse during or after therapy. The role of microRNAs (miRNAs) in leukemogenesis of *MLL*-rearranged AML, especially towards the development of relapse, is unknown.
Design/Methods: To determine whether specific miRNAs are involved in relapse development, we performed miRNA profiling, using TaqMan Low Density Array (TLDA) in 6 paired initial diagnosis–relapse pediatric AML samples with *MLL*-rearrangements. An independent set of 8 paired initial diagnosis-relapse cases was used to confirm the identified miRNAs using single stemloop RT-qPCR. Expression of predicted targets of differentially expressed miRNAs were determined with RT-qPCR (n=14) and Western blot (n=3) in paired samples. Samples were based on material availability.

Results: Fifty-three miRNAs were significantly differentially expressed (FDR <0.1) in the 6 paired cases. miR-106b, miR-93 and miR-25 (miR-106b~25 cluster), located as a cluster in intron 13 of MCM7, were overexpressed in relapse patient samples, as well as in 8 additional paired samples (n=14, p<0.05). E2F1, a transcription factor, acts a as an upstream regulator of MCM7. *MCM7* and *E2F1* expression based on RT-qPCR was significantly higher expressed in relapse samples compared to initial (n=14, p=0.008 and p=0.006, respectively). On protein level, a decrease of two targets of the miR-106b~25 cluster, $p21^{WAF1/CIP1}$ and BIM protein was found at relapse in 2/3 paired samples, although no difference in mRNA expression was found.
Conclusion: $p21^{WAF1/CIP1}$ and BIM are important proteins for the cell cycles and apoptosis, respectively. Overexpression of miR-106b-25 cluster and decreased of $p21^{WAF1/CIP1}$ and BIM protein at relapse may play an important role in relapse pediatric AML with *MLL*-rearrangements. Further research is warranted to identify the role of this cluster for clinical resistance and as treatment target.

Posters: Neuroblastoma

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I131 META-IODOBENZYLGUANIDINE THERAPY IN CHILDREN WITH ADVANCE NEUROBLASTOMA. THE EXPERIENCE OF A HOSPITAL

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Background/Objectives: Survival rate of advance neuroblastoma is low therefore, improved therapeutic strategies are necessary. I^{131} meta-iodobenzylguanidine (MIBG) has been used as treatment for advance or relapse neuroblastomas in an attempt to improve prognosis. This study describes our experience with MIBG.
Design/Methods: Retrospective study of patients diagnosed with neuroblastoma, younger than 21 years, treated with MIBG in our hospital. We collected data about age, stage of disease at diagnosis, previous treatment, disease at the time of MIBG therapy, toxicity and follow up.
Results: Ten patients received MIBG therapy. Two of them had N-myc amplification. Stages at diagnosis were: one patient stage II, other stage III and eight stage IV. Three of those 10 patients received a second dose of MIBG, thus a total of 13 treatments were considered: eight received treatment at first relapse/progression; two at second and the three remaining at third relapse/progression. Adverse events were: one acute thyroiditis, four oral mucositis (none of them required parenteral nutrition), neutropenia grade 4 in 7 patients (with no severe infections), all patients had grade 4 thrombocytopenia (without hemorrhagic complications), one patient had grade 4 anemia, six grade 3, and three patients grade 2. Eight out of 10 died from the disease: one of them at 90 and 3 months after the first and second doses of MIBG; another at 43 and 8 months after the administration of treatment; a third one at 14 and 7 months after the respective doses; and the remaining five patients died within 30, 22, 6, 5 and 5 months of therapy; one patient is in complete remission and other alive with disease progression at the time of the study.
Conclusion: Treatment with MIBG has benefits in neuroblastomas in relapse/progression improving survival rates without severe toxicity.

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DETERMINATION OF THE EXPRESSION OF ALK PROTEIN IN NEUROBLASTIC TUMORS (NT) IN CHILDHOOD. ASSOCIATION WITH PROGNOSIS DETERMINANTS

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Background/Objectives: Recently, changes in the ALK gen (mutation, amplification, translocation) have been implied in the oncogenic pathways of neuroblastic tumors (NT), through the inhibition of apoptotic mechanisms, with the consequent adverse outcomes. The over-expression of ALK (ALK+) is, for some authors, an independent adverse prognostic determinant. To systematize the study of ALK status in NT, would allow the identification of those cases that might evolve in adverse ways and to modify the treatment. The use of Crizotinib would be a therapeutic target for these patients. To determine the expression of ALK protein by inmunohistochemistry in NT and associate it with other known prognosis determinants.
Design/Methods: Clinical charts and histopathological reports were evaluated in 23 patients with primary NT, diagnosed between January 2007 and December 2014. The International Classification for NT was used. The variables evaluated in patients with ALK + were: age, gender, stage, histology and NMYC amplification. Overall Survival (OS) and Event Free Survival (EFS) were analyzed with the Kaplan Meier Estimator.
Results: Twenty three patients were evaluated, male 13 (54%). Median age 29 months (range 1-130). Five patients had ALK +; 3 of them were Stage IV with N-MYC non-amplified, histological type was 1 patient differentiating, 1 patient ganglioneuroblastoma intermixed and 1 poorly differentiated, all of them with adverse results and death. The remaining 2 patients were Stage 1, with non evaluated N-MYC with histological subtype undifferentiated (1 patient) and 1 differentiating, both in complete remission today. Median follow-up 30 months (range 0.3-85). EFS and OS 40 %.
Conclusion: Although the small sample, three of the relapsed patients presented non-amplified NMYC and ALK+, these might indicate ALK as an adverse prognostic factor in these patients. It would be useful to evaluate the efficacy of Crizotinib as a therapeutic target in these patients.

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NEUROBLASTOMA IN SAUDI ARABIA: SINGLE CENTRE EXPERIENCE

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Background/Objectives: Neuroblastoma is the most common extracranial solid tumour in childhood. While the survival has improved in the last few decades, children with high-risk neuroblastoma still have very poor outcomes despite aggressive treatment, with significant Short- and long-term complications. We aimed to assess the trends of overall survival (OS) and event free survival (EFS) of patients with neuroblastoma treated at King Fahad Medical City (KFMC)nd to correlate the survival data with the clinical, pathological and biological features of the tumors.
Design/Methods: Retrospective observational study of all patients, with diagnosis of neuroblastoma, who attended on KFMC and treated on Children Oncology Group based protocol, period July 2006 to June 2014.
Results: Eight years neuroblastoma data was available for the 42 patients of which 22(52.5%) were male and 20(47.6%) were females. Age at diagnosis was in between 0 and 91 months with mean and median 26.3± 3.7 and 18.5 months respectively. Sixteen (38.1%) patients were under one year and 26(61.9%) above 1 year of age. The OS and EFS rates were 71.5% and 66.5% respectively. Patients under one year of age did better with OS and EFS 82% and 75% respectively, p<0.05 , whereas were 62% and 59% respectively, p<0.05 on patients older than one year of age. OS and EFS at the end of interval in Low Risk group was 100.0%, Intermediate Risk group was 100.0% and High Risk group was 55% and 48.0% respectively. The difference was significant (p < 0.05).
Conclusion: Our results are very encouraging and comparable with the known published of other international cohorts, with an excellent outcome for stage 1, 2,3&4s. The prognosis for advanced (Stage 4) remains rather poor. A collaborative Saudi-wide effort, with an emphasis on research in detecting biologic characteristics of aggressive disease and tailoring therapy, is needed.

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BUSULFAN/MELPHALAN CONDITIONING REGIMEN FOR AUTOLOGOUS TRANSPLANTATION IN HIGH-RISK NEUROBLASTOMA: EARLY TOXICITY AND OUTCOME REPORT FROM A SINGLE INSTITUTION

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Background/Objectives: Neuroblastoma is the most common extracranial solid tumor, accounts 8% of childhood cancer. Busulfan/Melphalan (BuMel) conditioning regimen is recommended by SIOPEN in treatment of high-risk neuroblastoma (HRNB). BuMel toxicity outcome data is lacking following COG induction. The aim of this study is to determine the toxicity of BuMel conditioning regimen in pediatric patients with HRNB at King Faisal Specialist Hospital and Research Center-Jeddah.
Design/Methods: Retrospective chart review was done and clinical, laboratory and outcome data of 19 pediatric patients with HRNB admitted between May 2011 and Oct. 2014 were analyzed.
Results: Out of 19 patients 13 (68.4%) were males. The mean age at diagnosis was 3.6 (+/-2.5) years. Seven (36.8%) patients were treated with CCG 3891 protocol while 12 (63.2%) patients with COG A3973 protocol. Mucositis 15 (78%) was the most common toxicity observed followed by bleeding 14 (74%) (10/14 had GIT bleeding), Sinusoidal obstruction syndrome (SOS) in 8 (42%) out them 6 had moderate SOS, fungal infection 7 (37%), bacterial infection 6 (31.5%), CMV reactivation 3 (16%) and hemorrhagic cystitis 1 (5%). None of them developed idiopathic Pneumonia Syndrome. The median ANC and platelet recovery was 17 (range: 12-48) days and 80 (range: 14-510) days respectively. Transplant related mortality at day +100 is 5% and overall relapsed rate is 37% with mean time of relapse 4.7 months. Event free survival is 63% and overall survival is 58% with mean duration of follow up 8.2 months.

Conclusion: Our study showed potential benefit of BuMel as a conditioning in HRNB treatment. However, we observe high incidence of SOS and delayed platelet recovery. Further large scale multi-center long term follow up study will be needed.

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OUTCOME OF CHILDREN WITH HIGH RISK NEUROBLASTOMA TREATED IN NORTHERN EGYPT

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Background/Objectives: The long-term survival probability for children with high-risk disease historically was less than 15%. Better results have been achieved using an aggressive multimodality approach. Despite aggressive multimodality therapy, current survival rates remain unacceptably low. Limited resources form a barrier to apply different treatment modalities and manage treatment related toxicities.
Design/Methods: A retrospective review of the clinical records of all patients younger than the age of 18 years diagnosed with high risk Neuroblastoma and treated at Alexandria University Hospital Pediatric Oncology unit according to HRNBL1/SIOPEN protocol, over a period of 4 years (2010– 2014).The primary outcome was Overall survival and a secondary outcome progression free survival rates were calculated.
Results: Out of 104 patients confirmed as Neuroblastoma, 58 patients (56%) stratified as high risk. The age at presentation varied between 9 to 72 months with a median of 37 months .There were 29 males (50%) and 29 females (50%).Primary site was Adrenals in 43 patients (75%), abdominal retroperitoneal in 13 patients (22%),Thorasic paravertebral in 2 patients (3%). Stage M was the most common in 56 patients (97%).NMYC amplification was done in 6 patients and was amplified in 3 patients (50%). surgery was incomplete in 26 patients (62%), Complete or minimal residual in 13 patients (31%) and was avoided due to major risk in 3 patients (7%). There were 33 patients candidate for Autologus Bone marrow transplantation, only 20 of them (60%) were transplanted and 13 patients relapsed before BMT, with a mean time delay to the BMT was 5.3 months. Median follows up was 17 months. The 2-year PFS and OS were 29% and 34% respectively.
Conclusion: The outcome in our setting is better than reported outcomes without BMT but worse than reported outcomes with BMT, this could be attributed to the delay between end of induction therapy and the BMT.

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OUTCOME OF CHILDREN WITH NON HIGH RISK NEUROBLASTOMA TREATED IN NORTHERN EGYPT

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Background/Objectives: Neuroblastoma is a disease exhibiting extreme heterogeneity varying in location, histopathologic appearance, and biologic characteristics. Multimodality therapy including chemotherapy and/or surgery are the mainstay for therapy in very low, low and intermediate risk Neuroblastoma or even observation in some patients with stage MS Neuroblastoma. Recent focus has been to reduce therapy for low and intermediate risk Neuroblastoma while maintaining survival rates at 90%.Limited resources can be challenging in diagnosis, risk stratification and treatment.
Design/Methods: A retrospective review was made of the clinical records of all patients younger than the age of 18 years diagnosed with very low, low and intermediate risk Neuroblastoma and treated at Alexandria University Hospital Pediatric Oncology unit according to SIOP Europe Neuroblastoma (SIOPEN) study protocol, over a period of 4 years (2010 – 2014).The primary outcome examined was Overall survival and a secondary outcome progression free survival rates were calculated.
Results: Out of 104 patients histologically confirmed as Neuroblastoma, 46 patients (44%) stratified as very low, low and intermediate risk. The age at presentation varied between 1 week to 120 months with a median of 9 months .There were 30 males (65%) and 6 females (35%).Primary site was Adrenals in 26 patients (56%), abdominal retroperitoneal in 8 patients (17%) ,Dumbell tumour in 6 patients (13%) and others in 6 patients (14%). Stage was L2, MS, L1 & M (54%,26%, 18% & 2%) respectively .NMYC amplification was done in 12 patients (26%).surgery was incomplete in 15 patients (48%) Complete in 14 patients (45%).Median follow up was17 months. The 2-year PFS and OS were 77% and 82% respectively.
Conclusion: Our results in a limited resource country, is close to published data, when multimodal treatment was applied.this reflects the non demanding nature of the treatment of low/intermediate risk Neuroblastoma.

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RESPONSE TO RE-VACCINATION IN CHILDREN AFTER TREATMENT FOR SOLID TUMORS

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Background/Objectives: The aim of this study was to examine effectiveness of re-vaccination in pediatric patients with solid tumors at least 6 months after the cessation of the of treatment.
Design/Methods: The study was performed prospectively in 35 patients with solid tumors. Diphtheria, tetanus, acellular pertussis, hepatitis B, hepatitis A, measles-mumps-rubella (MMR) and varicella vaccines were applied to patients.
Results: In patients with various solid tumors, 80% of patients had complete protection against diphtheria and 88,5% against tetanus before vaccination, but only 28,6% against hepatitis A. All seronegative patients achieved protective antibody levels after one dose against diphtheria, tetanus and hepatitis A. Before vaccination, 54.3% of patients were protected against pertussis and 66,7% against hepatitis B. For pertussis, 60% of patients achieved protective antibody levels after one dose, but 64,2 % for Hepatitis B. Before vaccination, 34.4% of patients were seropositive against measles. After one dose, 73.3% of seronegative patients achieved protection. Before vaccination, 78.1% and 71,9 % of patients were seropositive against rubella and mumps respectively, all seronegative patients achieved full protection against rubella and mumps after one dose. Fifty-nine point four percent of patients were seropositive against varicella before vaccination. 87,5 % became seropositive after one extra dose.
Conclusion: In our study, patients had very good antibody response against diphtheria, tetanus, hepatitis A, rubella and mumps vaccines at least 6 months after the cessation of therapy. Performing one booster dose of these vaccines appeared to be sufficient for all groups. Protection after pertusis, hepatitis B, measleses and varicella zoster vaccines were in moderate levels. The patients showed different antibody responses to vaccines, depending on age, the time passed after the cessation of treatment and their primary vaccination status. Antibody levels should be followed to evaluate the response obtained. A booster should be considered when there is a decrease or loss in antibody levels.

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VENETOCLAX IS A PROMISING DRUG FOR THE FUTURE PERSONALIZED TREATMENT OF NEUROBLASTOMA PATIENTS WITH HIGH BCL-2 EXPRESSION

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[1] Academic Medical Center University of Amsterdam, Oncogenomics, Amsterdam, Netherlands Background/Objectives: The anti-apoptotic B cell lymphoma proteins are highly expressed in numerous cancer types and have been shown to play an oncogenic role. BCL-2 is highly expressed in neuroblastoma tumours. Previous studies showed that BCL-2 knockdown with shRNA or inhibition with small molecule inhibitor navitoclax induced a strong apoptotic response in neuroblastoma cells expressing high BCL-2 levels. Additionally, navitoclax delayed the onset of neuroblastoma tumour formation in vivo. Unfortunately, navitoclax causes dose-limiting thrombocytopenia in patients due to inhibition of BCL-XL. We therefore studied in vitro and in vivo responses of neuroblastoma cells treated with the new and more specific BCL-2 inhibitor venetoclax.

Design/Methods: We used in silico analysis of the BCL-2 family members mRNA levels, protein expression and the BIM/BCL-2 complex levels of neuroblastoma lines (n=24) as selection biomarkers for sensitivity to venetoclax. Immunoprecipitation of BIM displaced from BCL-2 in vitro and in vivo served as an efficacy biomarker for sensitivity to venetoclax. In vivo experiments were performed in NMRI nu/nu mice with subcutaneous KCNR xenografts.
Results: We show that venetoclax induces strong apoptotic responses in cell lines with high BCL-2 expression levels, indicated by dose-dependent cytochrome c release from the mitochondria into the cytoplasm and PARP cleavage. The in vitro efficacy of the compound was ascertained by BIM displacement from BCL-2. Combining venetoclax with cytostatics used in neuroblastoma treatment showed synergistic responses. Venetoclax significantly inhibited the growth of high BCL-2 expressing neuroblastoma xenografts in mice. Despite complete displacement of BIM from BCL-2 and increased cleaved caspase 3 levels, complete tumour regression was not observed.
Conclusion: Taken together, our findings suggest that BCL-2 inhibition with venetoclax strongly induces cell death in neuroblastoma cells expressing high BCL-2 levels. However, resistance to the compound does occur, indicating the necessity of combination treatment with other targeted inhibitors and cytostatics to overcome neuroblastoma resistance to venetoclax.

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COMPARISON OF THE SIOPEN AND MODIFIED CURIE SCORING AND CORRELATION WITH THE PROGRESSION FREE SURVIVAL IN STAGE IV NEUROBLASTOMAS:SINGLE INSTITUTIONAL EXPERIENCE

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Background/Objectives: Semi-quantitative studies using MIBG scoring have been devised that are easy to use with short training time, reliable and reproducible, facilitates comparison between results obtained by different investigators and centres ,readily adapted to multi-center use and have been validated for this purpose. Initial evolved scoring system included the French group Curie scoring by Curie Institute in France and the recently evolved SIOPEN scoring .The aim of the present study is to comparison between the Modified Curie and the SIOPEN scoring in Indian patient population in terms of inter-score and inter-observer reliability and correlate with the progression free survival.
Design/Methods: Data of 92 MIBG scans of 60 patients was retrospectively analyzed in patients diagnosed or suspected to have stage IV high risk neuroblastomas at initial staging, post induction, follow up and suspected recurrence (known MIBG avid disease).These scores were assessed for interscore and inter observer variability using the Spearman's coefficient of variation .Absolute and relative scores (post therapy scores divided by the pre therapy scores were obtained). Correlation with the progression free survival using Kaplan Meier survival analysis was done.
Results: Scoring results were highly correlated between both methods, and inter observer reliability was excellent at both initial staging and at post induction. A Curie score </= 2 and a SIOPEN score </= 4 (best cut off) at post induction were correlated to significantly better progression free survival.Patients with lower initial scores were more likely to reach complete remission at the end of induction. Achieving a low MIBG score is more important than achieving a specified reduction in the MIBG scores.
Conclusion: The modified Curie score and SIOPEN score have an excellent inter observer reliability with an excellent inter-score comparison. Both the scoring systems at post induction correlates with event free survival.

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BORTEZOMIB BASED CHEMOTHERAPY IN RELAPSED NEUROBLASTOMA AS A BRIDGE TO MIBG THERAPY WITH STEM CELL TRANSPLANT

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Background/Objectives: Bortezomib is a proteasome inhibitor and inhibits cell growth and angiogenesis in neuroblastoma cells. The aim of the study was to evaluate safety and efficacy of Bortezomib based chemotherapy for relapsed neuroblastoma as a bridge to MIBG therapy and autologous stem cell transplant (SCT).
Design/Methods: All children with relapsed neuroblastoma were treated with at least 2 courses of chemotherapy Bortezomib 1 mg/mt^2 day1, 4, 8, 11, Cyclophosphamide 440 mg/ mt^2 day1-5, Etoposide 100 mg/ m^2 day1-5 and All-Trans Retinoic acid (ATRA) 25 mg/ mt^2 day1-28 after taking informed consent of the parents. Data regarding side effects (NCI Grading) was collected prospectively and response was assessed after 2 courses by PET-CT scan and bone marrow (BM) examination.
Results: Three children who had relapsed after autologous SCT (male-2, female-1) were given a total of six courses. Median age was 4.5 years. Sites of relapse were abdominal-3, BM-3, Bone-1 and Brain-1. Mean duration of hospital stay was 7.3 days/cycle. Grade-3 oral mucositis and thrombocytopenia was noted in all. Grade-3 neutropenia seen in each cycle. Sepsis workup negative in 2 children (4 cycles). One child (cycle 2) developed invasive aspergillosis; one had Grade -1 neurotoxicity in the form of self-limiting hallucinations with normal MRI Brain. PET-CT post 2 cycles could be done only in 2 as third child moved to another centre showed no to markedly decreased FGD avidity in the lesions. BM was negative for tumor cells in both these cases. They both successfully underwent MIBG therapy combined with myeloablative chemotherapy followed by autologous SCT in one and haploidentical SCT in other.
Conclusion: Bortezomib based chemotherapy can be safely used to treat relapsed neuroblastoma with acceptable side effects. Its efficacy seems to be good as a bridge to MIBG and SCT but it needs to be confirmed in a setting of multi-centric clinical trial.

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CONGENITAL NEUROBLASTOMA PRESENTING WITH SYMPTOMATIC EPIDURAL COMPRESSION AT BIRTH

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Background/Objectives: Seven-10% of neuroblastoma present with symptoms of epidural compression (SEC). The optimal treatment of this condition is undefined. More than a half these patients develop permanent sequelae. Occasionally, SEC are discovered at birth. The related literature is limited to few cases with short follow-up. None of the survivors recovered neurologically, with the exception of the two described most recently, delivered prematurely. The three cases described herewith were followed for a minimum of 5 years.
Design/Methods: Of 1,436 patients aged 0-18 years diagnosed with neuroblastoma between 2000-2011 enrolled in the Italian Neuroblastoma Registry, 75 (5.2%) presented with SEC, and 3 (0.28%) had SEC at birth.
Results: The three patients were born at term of pregnancy. Third trimester ultrasound was performed in all and was read normal. Details on clinical presentation, therapy, neurologic response and sequelae are summarized as follows. Case 1/F/ 2008; Gestation weeks 40; Symptoms of SEC: limbs hypotonia and poor motility; Therapy: 2 CARBO/VP, 2 CADO, steroid Neurologic response: improved; FU mos 168; Sequelae:neurologic bladder, paraparesis, walking with casting, scoliosis. ; Case 2/F/ 2008; Gestation weeks 39; Symptoms of SEC: limbs hypotonia, no spontaneous movement and reflexes; Therapy: 2 CARBO/VP, steroid; Neurologic response: improved; FU mos: 81; Sequelae:neurologic bladder, walking with casting, constipation. Case 3/M/ 2011; Gestation weeks 38; Symptoms of SEC; limbs hypotonia and gluteal muscles hypotrophy; Therapy:4 CARBO/VP, 2 CADO, steroid; Neurological response: improved; FU mos: 77; Sequelae:neurologic bladder, leg hypotrophy, right equinus-varous foot.
Conclusion: These three cases confirm that newborns with neuroblastoma and SEC are destined to develop permanent sequelae. However, two cases described on 2008, who were delivered prematurely following ultrasonic detection of an intracavitary paraspinal tumour, survive free of sequelae. Routine third trimester ultrasound should take into greater account the possibility of detecting paravertebral tumours. Following foetal-MR scan the interdisciplinary team should discuss the possibility of anticipating patient's delivery.

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ITCC BIOLOGY: PRE-CLINICAL TARGETED DRUG DEVELOPMENT FOR HIGH-RISK PEDIATRIC CANCERS

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Background/Objectives: The European consortium *I*nnovative *T*herapies for *C*hildren with *C*ancer (ITCC) has been created in 2003 and aims to develop novel therapies for pediatric cancers. Within the consortium, ITCC Biology endeavours to supply the biological rationale for targeted drug trials in children with cancer. Therefore, a stepwise pipeline for the pre-clinical testing of targeted drugs across high-risk pediatric cancer types has been set-up, from drug selection to *in vivo* evaluation. Currently, ITCC Biology focusses on opportunities for further expansion and development of the pre-clinical drug development pipeline.
Design/Methods: The bioinformatics platform R2 (http://r2.amc.nl) will be expanded with genomics data for (not yet covered) pediatric cancer types and gene signatures that can predict the activation status of actionable signaling pathways. To quickly analyze protein expression levels of drug targets in large series of primary tumour samples, a new tissue-microarray facility is being developed. In addition, a robotic platform allowing high-throughput drug testing across multiple cell lines is being set-up.
Results: Targeted inhibitors venetoclax, cobimetinib, binimetinib, selumetinib, trametinib, alectinib, crizotinib, LDK378, ribociclib, RG7388, TH588 and AT7519 have been selected for the first cytotoxicity screen in a panel of 33 cell lines representing 6 types of pediatric cancer. The bioinformatics platform R2 has been expanded with mRNA profiling data for primary Ewing sarcoma and osteosarcoma and gene signatures predicting the activity of the PI3K-mTOR and RAS-MAPK pathways. Preliminary tests to study manual versus robotic drug screening showed similar results with both techniques. Currently, the optimal seeding densities and growth rates for all cell lines are being determined. The first screen will be performed within the next 6 months.
Conclusion: Proposed improvements in pre-clinical drug testing should eventually lead to more drugs entering clinical trials for pediatric cancer treatment and the faster discovery if drugs might be useful for more than one cancer type.

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INHIBITION OF RHO-ASSOCIATED KINASE 2 INHIBITS MALIGNANT PROGRESSION IN NEUROBLASTOMA BY INDUCING DIFFERENTIATION AND MYCN DEGRADATION

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Background/Objectives: The non-canonical Wnt/planar cell polarity (PCP) pathway regulates cytoskeletal organization, migration and neuritogenesis. Signaling is characterized by activation of the GTPases Rho and Rac, and the downstream Rho-associated protein kinases (ROCKs). Neuroblastoma is a malignant embryonal tumor of the sympathetic nervous systems, often with poor prognosis. The need for novel therapeutic approaches is great. Genetic analyses have revealed mutations and aberrations in the regulators Rho/Rac in neuroblastoma. The aim of this study was to characterize the Wnt/PCP signaling and the effects of ROCK inhibition in neuroblastoma.
Design/Methods: Cytotoxic activity of ROCK inhibitors was studied in cell viability assays. Morphology and invasion were studied with microscopy. The molecular mechanisms were characterized using cell- and molecular biology techniques. *In vivo* studies in mice were carried out to validate the therapeutic effects and toxicity.
Results: Several mediators in the pathway were differentially expressed in cell lines and patient samples. Using compounds blocking ROCK1 and ROCK2 activity revealed that the ROCK2 inhibitor HA-1077 effectively repressed proliferation and reduced cell viability in neuroblastoma. Additionally, HA-1077 inhibited migration and induced differentiation through initiating neural outgrowth. Furthermore, HA-1077 reduced the growth of established neuroblastoma xenografts in nude mice.
Conclusion: These results suggest that non-canonical Wnt signaling in general and ROCK in particular is a promising new therapeutic target for high-risk neuroblastoma.

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EXOSOMES FROM MYCN-AMPLIFIED NEUROBLASTOMA CONTAIN ONCOGENIC MICRORNAS

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Background/Objectives: The MYCN oncogene is frequently amplified in neuroblastoma and is associated with aggressive disease and treatment failure. MYCN induces expression of different miRNAs, which are posttranscriptional regulators of gene expression with established roles in neuroblastoma development.
Design/Methods: We have isolated and characterized exosomes from MYCN amplified cell lines, and here demonstrate their ability to be taken up by other cells.
Results: In this study, we show that MYCN -amplified cell lines not only express miRNAs with functions inside the cell, but also secrete populations of miRNAs inside small vesicular structures called exosomes, with the ability to shuttle to other cells. By profiling the miRNA expression, we demonstrate high expression of a group of established oncomirs in exosomes from two MYCN- amplified cell lines. Despite the fact that other studies have demonstrated the ability of exosomal miRNAs to regulate their targets in recipient cells, we did not observe this with exosomes from MYCN -amplified cells. However, exosomes were able to induce in vitro angiogenic tube formation, suggesting that they can have tumorigenic properties.
Conclusion: These new findings reveal a potential new way for MYCN -amplified neuroblastoma cells to interact with their environment.

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MICRORNAS AND CHEMORESISTANCE IN NEUROBLASTIOMA

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Background/Objectives: Neuroblastoma represents the most frequently diagnosed solid tumor in infants. Chemoresistance is a major obstacle in treating high risk neuroblastoma. Several studies indicate that deviant expression of certain miRNAs correlate with poor clinical outcome in neuroblastoma. However, the role of miRNAs in neuroblastoma cell resistance to chemotherapeutic drugs is poorly understood. The understanding of biological and molecular aspects of miRNA-mediated drug resistance in neuroblastoma may provide exciting opportunities for therapy of aggressive neuroblastoma. The aim of this study is to determine potential miRNAs that could be linked to chemoresistance in neuroblastoma.
Design/Methods: To investigate the role of miRNAs for drug resistance in neuroblastoma, ten neuroblastoma cell lines were used. These cell lines consisted of five isogenic pairs isolated from the same patient before treatment and after relapse.
Results: A miRNA cDNA library was been generated from all neuroblastoma cell lines used in this study. To identify differentially expressed miRNAs between cell lines deriving from patients before and after chemotherapy, a deep sequencing analysis (SOLiD sequencing) was performed using the miRNA cDNA library. To analyze miRNA expression data in the context of known biological functions, "Ingenuity Pathway Analysis" (IPA) was used.
Conclusion: Differential expression of miRNAs upon chemotherapy in neuroblastoma cell lines is predicted to alter biological functions associated with drug resistance. Manipulation of one or more of these miRNAs could be a potential new therapeutic approach to overcome neuroblastoma chemoresistance.

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EXPERIENCE WITH HIGH RISK NEUROBLASTOMA IN JORDAN

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Background/Objectives: High risk neuroblastoma (HRNB) carries poor prognosis despite multimodal treatment. The management of HRNB in developing countries is controversial.
Design/Methods: We conducted a retrospective analysis of children (<18 years) with HRNB who presented from July2006 until December2014. Patients' characteristics, treatment modalities and outcome were analyzed. All cases were discussed in multidisciplinary clinic that included pediatric oncologists, radiologists, pediatric surgeons and radiation oncologists.
Results: We identified 61 patients (31 males) who presented with HRNB to our center. The median age at diagnosis was 3.1 years (range 0.3 to 11). Four patients had stage III disease, 4 stage IVs, and 53 stage IV. MYCN was amplified in 45% of tested patients (23 of 51). Forty two patients underwent High dose chemotherapy with stem cell rescue (HDC/SCR). The 5-year EFS and OS were 27%±7.1% and 34%±7.5%, respectively. The following factors were significantly associated with better survival: HDC/SCR (P=0.0094) and diagnosis year after 2010 (P=0.037). In a separate analysis of patients who had BMT, patients diagnosed after 2010 had a better outcome although not statistically significant (48%±16% vs. 24%±10%, P=0.18). Of note, doses used for HDC/SCR were increased after 2010.
Conclusion: There is improvement over time in the outcome of patients with HRNB; this can be attributed to multidisciplinary care and improvement in supportive care as well as optimization of chemotherapeutic doses used.

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CLINICAL AND BIOLOGICAL FEATURES OF POOR RESPONDERS TO INITIAL TREATMENT DEFINED BY SEMI-QUANTITATIVE MIBG SCORING IN METASTATIC NEUROBLASTOMAS

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Background/Objectives: ^{123}I-mIBG scintigraphy has proven its clinical value for staging and response evaluation of patients with neuroblastoma (NB). Any residual mIBG-positive metastases after 4 cycles of chemotherapy indicate an extremely poor prognosis, and early prediction of poor response is warranted. We performed a retrospective institutional review of stage 4 NBs to investigate the correlation between post-treatment mIBG scores and clinical / biological features at diagnosis.
Design/Methods: Nineteen stage 4 NB patients treated in two regional pediatric oncology centers from 2005 to 2014 were included. Extent of metastatic disease was evaluated at diagnosis and after 4 cycles of induction chemotherapy using the established semi-quantitative mIBG scoring method (SIOPEN score). Patient were treated with induction chemotherapy consisting of vincristine, cyclophosphamide, cisplatin and pirarubicin, following the group study protocols in which each patient had been enrolled.
Results: The median of SIOPEN score at diagnosis was 36. After 4 cycles of induction chemotherapy, 5 had at least one SIOPEN score (positive group) and 14 had a score of zero (negative group). The positive group consisted of older patients compared to the negative group, with 3 out of 5 cases over 8 years of age in the positive group (P=0.0160). There were no differences in pretreatment tumor markers. Initial SIOPEN score did not differ between the two groups (P=0.211). Out of 8 *MYCN* amplified cases, 7 were in the negative group, whereas only one was in the positive group, although the *MYCN* status was not statistically different between the two groups (P=0.153). DNA index did not correlate to SIOPEN score.
Conclusion: Older patients showed poor response to initial chemotherapy. In the majority of the younger cases, despite the high scores observed at diagnosis, the scores

sharply decreased to zero after induction chemotherapy. A prospective study with a larger cohort is needed to verify our results.

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NON-INVASIVE DETECTION OF MYCN AMPLIFICATION IN PLASMA CELL-FREE DNA DIGITAL PCR IN NEUROBLASTOMA

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Background/Objectives: Amplification of neuroblastoma derived (avian) v-*myc* myelocytomatosis viral related oncogene (*MYCN*) is an important risk-stratified indicator in neuroblastoma. In noninvasive measurement of *MYCN* amplification using plasma cell-free DNA, we have used quantitative real-time PCR (qPCR). In this study, we used Digital PCR (dPCR), which is a highly accurate method of determining DNA concentration, for detecting *MYCN* amplification in stored blood plasma samples.
Design/Methods: We used 10 ng of plasma-derived DNA for qPCR and 2-4 ng DNA for highly sensitive droplet dPCR to determine *MYCN* copy numbers in 10 healthy volunteers and 47 neuroblastoma cases. The copy number was calculated as the ratio of copies of *MYCN* to those of a reference gene(NAGK2.
Results: In 27 neuroblastoma cases with non-amplified tumors, *MYCN* copy numbers of *MYCN* were was 1.05 ±0.27 and 1.06 ±0.13 in both qPCR and dPCR, respectively. In 20 cases with amplified tumors, calculated copy numbers *MYCN* were 12.0-110.9 and 13.6- 194.0 copies, respectively. The correlation coefficients between *MYCN* copy numbers in tumor tissue and in blood plasma using qPCR and dPCR were approximately 0.9 and 0.94, respectively.
Conclusion: We can detect *MYCN* amplification of neuroblastoma tissue noninvasively and quantitatively by measuring the *MYCN* copy number in the plasma DNA digital PCR. This dPCR system is more accurate method using smaller amount plasma-free DNA than qPCR. Determination of *MYCN* copy number in plasma DNA digital PCR may be useful when evaluating risk-stratified indicator in neuroblastoma before surgery.

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RESULTS OF TREATMENT OF PATIENTS WITH NEUROBLASTOMA STAGE 3 HIGH-RISK GROUPS

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Background/Objectives: At the moment, the survival of patients with stage III neuroblastoma high risk does not exceed 50%. Current approaches to the treatment of patients in this group may improve survival of these patients and 65%.
Design/Methods: From 2013 to the present time in the Institute of Pediatric Oncology examined and treated with 4 children with neuroblastoma stage III high-risk groups aged 1 to 3 years. Three of the children had a tumor of the adrenal gland, one - in the retroperitoneal space. Three of the children had metastases in retroperitoneal lymph nodes. All patients on the first biopsy of the tumor was performed. In one case - the tumor was removed radically. Were carried out histological and molecular genetic studies to determine gene amplification MYCN, deletion 11q23 and 1p36. After due diligence and risk assessment for all patients was conducted treatment program that includes an inductive combination chemotherapy, surgery, high-dose chemotherapy with ASCT, radiation therapy, and biotherapy 13-cis-retinoic acid.
Results: At the moment, 3 out of 4 children have completed treatment and are in dynamic observation with no signs of recurrence of the disease, with follow-up of 12 to 18 months. One of the children currently receiving special treatment, his condition is clinical remission.
Conclusion: Conducting comprehensive treatment that includes intensive inductive chemotherapy, high-dose chemotherapy with ASCT, radiation therapy, and biotherapy in patients with neuroblastoma stage III high-risk groups can improve survival in this group of patients up to 65-70%.

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ARE NEUROLOGIC DISORDERS CAUSED BY THE TUMOR ITSELF OR BY SURGICAL INTERVENTIONS IN PATIENTS WITH NEUROBLASTOMAS/ GANGLIONEUROMAS OF THE SMALL PELVIS?

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Background/Objectives: Neuroblastomas (NB)/ Ganglioneuromas (GN) localized in the small pelvis are a rare entity and account for less than 5% of all NB/ GN. In some cases, neurologic disorders, like bladder or rectal dysfunctions, are one of the first clinical signs. Notwithstanding, neurogenic bladder or rectum is a known complication after NB/ GN resections in the small pelvis. Aim of this analysis was to review our patients in regard to neurologic outcome after NB/ GN resection in that region.
Design/Methods: Medical charts were reviewed of patients with NB/ GN of the small pelvis, who were operated in our institution between 2004 and 2014. All patients were treated according to the NB2004 trial protocol of the GPOH. Cystomanometry was performed in addition to the standard preoperative diagnostic work-up and in cases of postoperative symptoms of neurogenic bladder.
Results: 9 out of 209 patients (m:f 1:1.5) had tumor resection due to NB/ GN of the small pelvis. Tumors were located between L4 to S5. Complete or near total resection was feasible in 6 cases. Histology revealed NB in 2 cases, only. Others were GN. All were negative for MYCN amplification. Neurologic disorders were seen in 4 patients (3 neurogenic bladder, 1 cauda equine syndrome, 1 injury of ischiadic nerve). 3 of these patients had tumor extension to spinal canal.
Conclusion: While oncological outcome of NB/ GN of the small pelvis is superior compared to other locations, these patients are at risk to develop neurologic deficiencies. Apart from surgical trauma of nerval structures, tumor extension to the spinal canal might be negative predictive factor for the development of neurogenic disorders. Therefore, the impact of surgery resp. tumor extension to the spinal canal should be analyzed for more cases to adapt the surgical strategy for these patients.

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ANALYSIS OF SETUP ERROR IN RADIOTHERAPY OF PEDIATRIC NEUROBLASTOMA WITH CONE BEAM CT

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Background/Objectives: To evaluate the setup error for pediatric patients with neuroblastoma using cone beam CT imaging (CBCT) and discuss margin between CTV and PTV. It can be a reference for treatment plan design.
Design/Methods: Ten neuroblastoma patients were selected between October 2012 and May 2013 underwent daily pretreatment localization CBCT and post-treatment CBCT. Localization was based on CBCT to treatment planning CT registration, setup errors in the medial-lateral (ML), superior-inferior (SI) and anterior-posterior (AP) directions were obtained. Interfraction and intrafraction positioning errors were calculated based on weekly and daily images.
Results: A lateral, longitudinal and vertical setup error of 5.3 mm, 5.7 mm and 5.2 mm is required with weekly CBCT. When daily CBCT was incorporated, the setup error was reduced to 2.1mm, 1.7 mm and 1.4 mm.
Conclusion: Daily localization based on CBCT can reduce the required setup error for neuroblastoma patients and reduce margin between CTV and PTV, thereby reducing normal tissue exposure for the patients. This is particularly important to pediatric patients. The internal margin needs further investigation for margin between CTV and PTV.

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TREATMENT OF LOW-RISK NEUROBLASTOMA: SINGLE CENTER EXPERIENCE IN RUSSIA

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Background/Objectives: Patients with low-risk neuroblastoma represent up to 40% of all patients. Surgery is the main method of therapy and reducing proportion of patients requiring chemotherapy is a priority. The purpose of this study was to analyze treatment outcomes in a group of patients with low-risk neuroblastoma treated in a single oncological center in Russia.
Design/Methods: During the period 01.2012-12.2014 243 patients with neuroblastoma were observed and treated. International neuroblastoma staging system criteria were used for staging and response evaluation. Patients were allocated to the risk groups based of the criteria of German neuroblastoma study group and treated according to NB2004 protocol.
Results: Low-risk group included 132 (54.3%) patients. Median age was 5.5 months (range 0.5-103.3). M:F ratio was 1.1:1. The distribution by the site of the primary tumor: adrenal gland - 65 (49.2%), retroperitoneum – 31 (23.5%), mediastinum – 30 (22.7%), other – 6 (4.6%). Stage distribution: stage 1 – 55 (41.7%), stage 2 – 38 (28.8%), stage 3 – 11 (8.3%), stage 4S – 28 (21.2%). Initial therapeutic modalities included observation - 4 (3.0%), surgery - 99 (75.0%), chemotherapy and other modalities - 29 (22.0%). Disease progression was observed in 14 (10.6%) and relapses in 8 (6.0%). Median follow-up was 15.7 months (range 0.5-35.1). Outcomes: 127 (96.2%) patients are alive, 5 (3.8%) died. 2-year overall survival was 0.96±0.017, 2-year event-free survival (EFS) 0.77±0.03. 2-year EFS by stage: stage 1 – 0.83, stage 2 - 0.82, stage 3 – 0.41, stage 4S – 0.69. Cause of death included tumor progression in 2/5 and treatment-related death in 3/5. All deaths were registered during the first three months from diagnosis.
Conclusion: In our study the majority of patients with low-risk NB patients had localized stage 1-2 tumors and treatment was limited only by surgery. Chemotherapy required for patients with the presence of life-threatening symptoms.

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PROGNOSTIC SIGNIFICANCE OF miRNAs EXPRESSION INVOLVED IN THE EPIGENETIC REGULATION OF P53/MDM2 PATHWAY IN CHILDHOOD NEUROBLASTOMA

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Background/Objectives: Much of the difficulty in devising effective therapies lies in the biologic and clinical heterogeneity of neuroblastoma, which can be attributed largely to the interaction of multiple genetic and epigenetic factors. ; The aim of our study was to investigate prognostic significance of miRNAs expression involved in the epigenetic regulation of p53/MDM2 pathway in childhood neuroblastoma.
Design/Methods: The case group comprised 80 patients with histologically confirmed neuroblastoma (median age: 39.6 months; range: 1.5–204 months; I-II stages: 12; III stage: 26; IV stage: 42; MYCN-amplified tumors (MNA): 27%). Patients were treated according to a risk groups under the international standard protocols. MYCN gene amplification, MDM2 and miR-34-family, miR-885-5p, miR-380-5p gene expression level were detected in tumors by FISH and TaqMan real time RT-PCR methods.
Results: Tumors were categorized into groups according to high or low miRs expression levels based on cutoff point - optimal criterion, that was determined by ROC analysis. It has been found that downregulation of miR34-family associated with significant reduction of 3-year overall survival (OS) in patients with MDM2 overexpression regardless MNA. In not-MNA neuroblastomas with low MDM2 expression 3-year OS was on 44 % lower in downregulated miR-34a cases compared to miR-34a high expressed neuroblastomas which excludes their impact in p53 regulation. It has been found that high levels of miR-380-5p expression are correlated with a significant decrease in OS. The 4-year OS rate for patients with high miR-380-5p expression was 80% compared to 21% for low miR-380-5p expression ($p<0,001$). The 5-year event free survival (EFS) rate for patients with high miR-885-5p expression was 53% compared to 12% for low expression ($p<0,04$). No effect of miR-885-5p expression on OS rate for neuroblastoma patients has been revealed.
Conclusion: Our results suggest the possibility of using the level of miR-34-family, miR-885-5p, miR-380-5p expression in neuroblastoma as prognostic and risk group stratification markers.

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THE COX/MPGES-1/PGE2 PATHWAY DEPICTS AN INFLAMMATORY DEPENDENT HIGH-RISK NEUROBLASTOMA SUBSET AVAILABLE FOR NOVEL SPECIFIC ANTI-INFLAMMATORY TREATMENT

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Background/Objectives: High-risk neuroblastoma often have poor prognosis. Older children with 11-q deleted tumors show resistance to induction chemotherapy, late relapses and poor outcome despite intensified treatment. Although adult cancers show an inflammatory microenvironment knowledge is limited on potential significance of inflammation in childhood malignancies.
Design/Methods: Human tumors were analysed for expression of pro-inflammatory lipid mediators. Xenografts in nude mice and spontaneous tumors in transgenic mice were treated with specific inhibitors of the COX/mPGES-1/PGE2 inflammatory pathway.
Results: High-risk neuroblastomas showed high expression of enzymes involved in the production of pro- inflammatory lipid mediators including microsomal prostaglandin E synthase-1 (mPGES-1) the major enzyme converting prostaglandin H2 (PGH2) to prostaglandin E2 (PGE2) and lack of expression of the PGE2 metabolizing enzyme 15-hydroxyprostaglandin dehydrogenase (15-PGDH) resulting in high PGE2 concentrations. High mPGES-1 and low 15-PGDH corresponded to poor survival. 11-q deleted tumors showed significantly higher PGE2 than other subsets. Neuroblastoma microenvironment showed abundant occurrence of immunosuppressive CD163+ M2-polarized macrophages and CD11b+ myeloid-derived suppressor cells. mPGES-1 expressing cells were indicated cancer associated fibroblasts (CAFs) expressing vimentin, fibroblast activation protein (FAP), alpha smooth muscle actin (αSMA), and platelet-derived growth factor receptor beta (PDGFRβ). Specific PGE_2 targeting by Cox-inhibiting celecoxib or a novel specific mPGES-1 inhibitor significantly delayed tumor growth *in vivo*. Tumor weights were reduced at sacrifice both in transgenic TH-MYCN mice and nude mice with11-q deleted xenografts compared to untreated control animals. Treated tumors showed significant decrease of M2-polarized macrophages and reduced angiogenesis.
Conclusion: We found that high prostaglandin E_2 production and expression of microsomal prostaglandin E synthase-1 (mPGES-1) is coupled to high-risk neuroblastoma tumors with 11q-deletions. Infiltrating cancer-associated fibroblasts contribute to neuroblastoma inflammation microenvironment. The inflammatory COX/mPGES-1/PGE_2 pathway plays a crucial role in cancer-related inflammation providing specific therapeutic targets. Anti-inflammatory drugs combined with current treatment should be considered for novel high-risk neuroblastoma therapy.

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ARSENIC TRIOXIDE POTENTIATES THE CYTOTOXICITY OF CHEMOTHERAPEUTIC AGENTS AGAINST HUMAN SK-N-SH NEUROBLASTOMA CELL LINE

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Background/Objectives: The aim of this study was to investigate whether arsenic trioxide combined with mitosis-phase-specific antineoplastic agent or non mitosis-phase-specific antineoplastic agent has synergistic effects of cytotoxicity in human SK-N-SH neuroblastoma(NB) cell line.
Design/Methods: At first, we investigated the exposure time that arsenic trioxide could arrest NB cell cycle in G2/M phase with the highest proportion by flow cytometry, then we monitored the ability of arsenic trioxide combined with four various chemotherapeutic agents including vinorelbine, docetaxel, etoposide and cisplatin to induce NB cells apoptosis. There were two different ways that arsenic trioxide combined with one of the four drugs, NB cells were either incubated with another drug simultaneously, or firstly incubated with arsenic trioxide and then with another drug when cell cycle was arrested in G2/M phase with the highest proportion.
Results: Our results showed that arsenic trioxide induced NB cells apoptosis in a time- and dose-dependent manner, and arsenic trioxide arrested NB cell cycle in G2/M phase with the highest proportion after 48 hours incubation. Arsenic trioxide potentiated the apoptotic rate of NB cells induced by chemotherapeutic drugs. We further determined that the combination of 48 hours of arsenic trioxide followed by the addition of mitosis-phase-specific antineoplastic agent (vinorelbine, docetaxel) caused a synergistic increase in cytotoxicity of NB cells, while less effective caused by arsenic trioxide combined with non mitosis-phase-specific antineoplastic agent (etoposide, cisplatin).
Conclusion: Our in vitro study shows that co-application of arsenic trioxide with mitosis-phase-specific antineoplastic agent (vinorelbine, docetaxel) may potentiate the curative effects against NB. Arsenic trioxide shows a very good prospect in NB treatment.

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LOW DOSE OF ARSENIC TRIOXIDE INHIBITS MULTIDRUG RESISTANT-RELATED P-GLYCOPROTEIN EXPRESSION IN HUMAN NEUROBLASTOMA CELL LINE

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Background/Objectives: The present study aimed to investigate arsenic trioxide (As_2O_3), cisplatin (DDP) and etoposide(Vp16) on the anticancer effects and P-gp expression in NB SK-N-SH cells.
Design/Methods: The potential influence of As_2O_3, DDP and Vp16 on cytotoxicity in SK-N-SH cells was assessed by Flow cytometry with Annexin V-PI staining and drugs IC50 were established. Moreover, chemotherapeutic agents-mediated the changes of cellular expression levels of resistant-related P-gp were analyzed using Western-blotting.
Results: (1) Data showed that As_2O_3 had a dose- and time-dependent toxic effect on SK-N-SH cells via induction of apoptosis in manner. Furthermore, As_2O_3, DDP and Vp16 were observed with their IC50s on SK-N-SH cells being 3umol/L, 8ug/ml and 100ug/ml respectively. (2)As_2O_3 in SK-N-SH cells led to enhanced accumulation of cell populations in G2/M phase with increasing the exposure time. In contrast, we observed that SK-N-SH cells populations arrested in S phase by DDP and Vp16. (3) Following pretreatment of SK-N-SH cells with As_2O_3, the expression of P-gp was not increased. The expression of P-gp down-regulation was noted following pretreatment of SK-N-SH cells with As_2O_3, and these changes were statistically significant with As_2O_3 in the concentration of 2umol/L and 3umol/L($P<0.05$). 3umol/L As_2O_3 for 72h induced significantly decreased the expression of P-gp than 2umol/L As_2O_3 for 72h in SK-N-SH cells($P<0.05$). However, the expressions of P-gp were up-regulated in SK-N-SH cells by DDP and VP16 on different concentration.
Conclusion: In summary, SK-N-SH cells were responsive to drugs-induced apoptosis in a dose- and time-dependent manner. These findings showed that low dose As_2O_3 reduces the P-gp expression in human NB cell line. Taken together, these results indicated that the effect of As_2O_3 on reducing the expression of P-gp may make the drug as an excellent candidate in chemotherapy regimens for MDR NB.

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RACK1 GENE SILENCING INDUCES APOPTOSIS IN MYCN GENE AMPLIFIED NEUROBLASTOMA CELL LINES

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Background/Objectives: To evaluate the role of Receptors for Activated C- Kinases (RACK1) in the apoptosis of Neuroblastoma (NB).
Design/Methods: Expression of RACK1 was evaluated by immunofluorescence in MYCN gene amplified NB cell lines, SK-N-BE (2) and IMR32. RACK1 gene was silenced by RNA interference (RNAi). Then cell apoptosis and expressions of pro- and anti- apoptotic Bcl-2 members and caspases were detected by flow cytometry and western blotting respectively.
Results: RACK1 expressed in SK-N-BE(2). RACK1 gene silencing significantly increased the apoptosis ratio of SK-N-BE(2), and increased the cleavage of Caspase-3, -7, -9, but not -8. RACK1 RNAi decreased the expressions of Bcl-2, Bcl-xl and Mcl-1, while increased the expression of Bim.
Conclusion: RACK1 gene silencing induced NB cell apoptosis via activating intrinsic pathway and repressing anti-apoptotic Bcl-2 family members.

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THE PPM1D ENCODED PHOSPHATASE WIP1 IS A NOVEL ONCOGENE AND POTENTIAL THERAPEUTIC TARGET IN NEUROBLASTOMA AND MEDULLOBLASTOMA

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Background/Objectives: The most common cytogenetic lesions in the embryonal neural tumors medulloblastoma (MB) and neuroblastoma (NB) affect chromosome 17, with 17q+ or isochromosome 17q, in approximately one-third of MB with these aberrations being a significant indicator of poor clinical outcome. Similarly, in NB gain of 17q is the most powerful genetic predictor of adverse clinical outcome. 17q+ correlates with poor survival in our population-based material where we found aberrations of chromosome 17 in 85% of primary neuroblastomas, specifically, gain of PPM1D/Wip1 at 17q23. Wip1 is a serine/threonine phosphatase encoded by the gene *PPM1D*, described as a gatekeeper in the Mdm2-p53 regulatory loop involved in genetic stability, inflammation and a potential oncogene contributing to carcinogenesis.
Design/Methods: Comparative genomic hybridization (CGH) was used to examine PPM1D/Wip1 in neuroblastoma and medulloblastoma tumors and cell lines. Wip1 knockdown SK-N-BE(2) cells were generated by shRNA transfections and tested in vivo in tumor xenografts. Pharmacological inhibition with the p53-mdm2 modulating inhibitors RITA, Nutlin-3 and a new PPM1D/Wip1 inhibitor, was used to evaluate the function of PPM1D/Wip1 in preclinical models.
Results: CGH-array analysis detected PPM1D/Wip1 extra copies in all tumors and cell lines containing 17q-gain. Tumor neuroblastoma xenograft development was significantly delayed showing median tumor development (0.10 mL) to be more than doubled (median 15 days, vs. 33 days, $p<0.001$) after Wip1 downregulation compared to scrambled controls. A novel Wip1 inhibitor was highly potent in cytotoxic/cytostatic effect in a variety of neuroblastoma and medulloblastoma cell lines. Furthermore, this Wip1 inhibitor significantly inhibited growth of established human neuroblastoma- and medulloblastoma tumors in nude mice after treatment ($P<0.01$).
Conclusion: Our results show that PPM1D/Wip1 is oncogenic in neuroblastoma and medulloblastoma development and provides a novel therapeutic target in these two childhood cancers of the nervous system. More studies investigating the effects of PPM1D/Wip1 inhibition are needed to evaluate its clinical significance.

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CLINICAL BEHAVIOR, AND EPIDEMIOLOGICAL, DEMOGRAPHIC AND THERAPEUTIC ASPECTS OF THE DESMOID TUMOR IN CHILDREN OF CALI–COLOMBIA

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Background/Objectives: Desmoid-Tumors(DT) or
Aggressive-Fibromatosis-Juvenile(AFJ) are tumors with low grade of malignancy, low potential to produce soft-tissue metastases, and high rate of recurrence.Prevalence is unknown with a very low incidence. The etiopathogenic mechanism is unknown, literature register that may be multifactorial involving genetic, hormonal, surgical and trauma factors. The clinical presentation is non-specific and there are not enough reports. Describe the clinical behavior, demographic, epidemiological and therapeutic variables of Children with DT in Cali, Colombia-South America.
Design/Methods: A retrospective descriptive cross-sectional study of pediatric patients with histopathological diagnosis of DT/AFJ deposited in the clinical database from the Department of Pathology at Hospital Universitario del Valle between the period of January 2000-May 2014.Among the factors that describe the behavior of the disease were taken into account: median age at diagnosis, ethnicity, sex, location of the lesion, (total resection of the lesion -partial), treatment outcome after surgical technique. Surgical and traumatic personal history and family history of cancer was also considered.
Results: Sample from universe of this study consists in 4 patients diagnosed during this period of time: three Africancolombian children and one Caucasian showed a diagnosis median age of 3.25 years, ratio female-masculine: 3:1, location: 1extremities, 2head and neck, one buttock. Three patients had complete resection of the tumor with negative margin, one patient relapse after radiotherapy received, none received cytostatic treatment, hormonal or chemotherapy; 3 patients had relapses and required surgery again, none was amputated. None had a history of traumatic significance. One patient had a family history of brain cancer and cancer unspecified. None reported associated metastases.
Conclusion: From our screening the most important risk factors for poor control are: early age of onset, size, recurrence, surgical margin requirement radio-chemotherapy. Finally, since there are tumors of low incidence, prospective multicenter studies are needed to clarify epidemiological behavior.

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EFFICIENT ADAPTIVE RANDOMISED TRIAL DESIGN IN NEUROBLASTOMA: THE BEACON-NEUROBLASTOMA TRIAL

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Background/Objectives: Running clinical trials in relapsed neuroblastoma is challenging due to its rarity. There remains uncertainty as to the best treatment for children with relapsed/refractory neuroblastoma and randomised trials will be essential to evaluate new treatments reliably. There have been many single arm, but few randomised, phase II trials in this patient group. This lack of reliable evidence risks the introduction of ineffective new agents into standard clinical practice.
Design/Methods: Adaptive trials using novel methodology, such as multi-arm multi-stage (MAMS), can increase the efficiency of trials, enabling more agents to be

evaluated more quickly, without gaps between studies. The evolution of the BEACON-Neuroblastoma trial in relapsed/refractory neuroblastoma is described here.
Results: BEACON-Neuroblastoma started as 2×2 factorial trial investigating the role of two agents added to a backbone of temozolomide as chemotherapy for relapsed/refractory neuroblastoma: 1) bevacizumab (Jung design); 2) irinotecan (likelihood-based Bayesian design). The phase II trial to obtain initial evidence of activity (response) will become a Phase III trial to evaluate efficacy (event-free survival) in agents/regimens that meet the Phase II success criteria. As result of recently published promising results on the combination of topotecan and temozolomide (TOTEM), BEACON-Neuroblastoma was amended to a 3×2 factorial design to evaluate this combination in addition to the two existing questions. The recruitment target was initially 120 patients (60 for each comparison); the amendment will increase the sample size to 160 patients (60 for each comparison) and duration of the study from two to four years. The successor to BEACON-Neuroblastoma will expand on this approach and become an ongoing MAMS trial.
Conclusion: The adaptive design of BEACON-Neuroblastoma and its successor will allow multiple agents to be evaluated quickly and efficiently, with ineffective ones being dropped and new ones brought in as they become available, in a rolling programme of research.

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INTRAABDOMINAL MALIGN MASSES: EXPERIENCE OF 406 CASES IN 24 YEARS TREATED IN A SINGLE CENTRE

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Background/Objectives: The diagnosis, treatment and follow up of intraabdominal tumors have a special importance among all pediatric malignancies. In this study, we aimed to evaluate the demographic, clinical and pathological properties of intraabdominal tumors followed by our department.
Design/Methods: Intraabdominal malign tumors account for 31.7% of all pediatric malignancies followed by our department. Medical records of 406 children with intraabdominal malign tumor diagnosed in the Department of Pediatric Oncology, Gazi University Medical Faculty during 1991-2015 were reviewed.
Results: The mean age at diagnosis was 5.4 ± 4.6 years (10 days-17 years). The mean duration of symptoms until the diagnosis was 25.4 ± 24.3 days (1-200 days). In 43% of the patients, the masses were noticed by parents. The most common symptoms were abdominal mass (47.7%), abdominal pain (34.2%), constipation (16%), fever (19%) and hematuria (%3.9). The tumor was most commonly located in the upper right quadrant (27%) followed by pelvis (21.1%), widespread abdominal (15.5%) and upper left quadrant (18.9%). The first five tumor types causing intraabdominal mass were neuroblastoma (20.9%), non-Hodgkin lymphoma (18.2%). Wilms tumor (17.4%), germ cell tumors (16.7%) and hepatoblastoma (4.4%). The most common tumors under 12 months of age were neuroblastoma (31.1%) and germ cell tumor (25.2%) and was non-Hodgkin lymphoma (29.7%) above 5 years of age. There were spinal cord compression symptoms in 7.1%, bone marrow infiltration in 12% and tumor lysis syndrome in 8.3% of the patients at the time of diagnosis.
Conclusion: In our series, the most common abdominal malignant tumor was determined as neuroblastoma in infants and non-Hodgkin lymphoma above 5 years of age, as consistent with the literatüre.

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TANDEM PERIPHERAL BLOOD STEM CELL TRANSPLANTATION AS TREATMENT OF NEUROBLASTOMA IN CHILDREN

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Background/Objectives: Currently investigate the feasibility of using tandem high-dose chemotherapy in the treatment of many malignant solid tumors: medulloblastoma, germ cell tumor, soft tissue sarcomas and high-risk neuroblastoma. Nevertheless effectiveness convincing results haven't been obtained.
Design/Methods: From 2012 to 2015 year in the Department of Pediatric Oncology at the National Cancer Institute have been carried out 15 tandem transplantations (TT) in children with high-risk of neuroblastoma. Patient's age was 1-14 years. 10 pts. with primary neuroblastoma got TT after chemotherapy on HR-NBL-1/ESIOP protocol, 5 pts. as a consolidation of relapse second-line therapy. The first part of tandem transplantation was BuMel in all patients. Twelve patients had topotecan-based regimens as the second part of tandem transplantation and three patients had CEM regimen. A time interval between parts of tandem was 1-3 months. For autologous transplantation have been used only peripheral stem cells. All patients received 13-cis retinoic acid after of conventional treatment.
Results: All patients successfully completed high-dose chemotherapy. There were neutropenia and thrombocytopenia 4th rate, oral mucositis with different degrees of severity in all patients. WBC count recovered more then 500/μL after first cycle on +10-15 day, PLT count recovered on +13-28 day. In 2 patient was observed neurotoxicity like short clonic and tonic seizures after second cycle. WBC count recovered more then 500/μL after second cycle on +9-14 day, PLT count recovered on +10-22 day. Currently, 7 of 15 patients are in CR, 3 patients had early relapse and continue treatment, 5 died of PD. The follow-up period after accomplishment of TT is 2-26 months.
Conclusion: Application of TT in children with high-risk neuroblastoma resulted to three-year disease-free survival rate of about 46.4% and the overall four-year survival rate to 66,3%. With no possibility of mIBG therapy and antibody therapy, the use of tandem transplantation provides an opportunity to improve outcomes.

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LYMPHATIC LEAKAGE (LL) AFTER RESECTION OF NEUROBLASTOMA

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Background/Objectives: Lymphangiogenesis and lymphangiogenic vessel remodeling is known to play an important role in cancer progression. Little is known about the impact of lymphangionesis in neuroblastoma. From a surgical point of view, lymphatic fistula is a potential complication after neuroblastoma surgery. Aim of this study was the evaluation of frequency and impact of lymphatic leakage in a center for neuroblastoma surgery.
Design/Methods: Between 2003 and 2014, 210 patients (pts) were resected for neuroblastoma in our department for neuroblastoma. Out of these, 200 patients were eligible for this study. Patient charts were reviewed for INSS stage, surgical radicality, duration of abdominal or thoracic drainage and maximum amount of fluid drained per 24 h.
Results: Out of 200 patients, 73 patients (37%) had a duration of drainage of 7 or more days. Maximum amount of drainage was 4 liters per day; longest duration of intraabdominal drainage was 91 days. In case of chylous fistula, all patients were treated with a conservative approach. Duration of drainage was significantly associated with surgical radicality (p=0.000). Furthermore, the duration of drainage was significantly associated with the maximum amount of fluid drained per 24 h (p=0.000). Lymphatic fistula was significantly associated with INSS stage (p=0.000). Overall Survival (OS) demonstrated a better OS for patients without LL (87% alive) than pts with LL (72% alive). OS was significantly associated with the maximum amount of fluid drained per 24 hrs (p=0.009), but not with duration of drainage.
Conclusion: LL is a frequent complication after neuroblastoma surgery and in some cases with substantial loss of fluids and proteins. It can be treated in nearly all cases conservatively. One major problem is the delay of further chemotherapy and radiation which however does not seem to have a great impact on the prognosis.

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MIBG (METAIODOBENZYLGUANIDINE) CROSSES BLOOD BRAIN BARRIER ADEQUATELY? REALITY OR ILLUSION

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Background/Objectives: Even after high dose chemotherapy, the overall survival of Relapsed Stage 4 Neuroblastoma patients remain inconsequential. MIBG (Metaiodobenzylguanidine) appears to be a suitable option but its penetrability across Blood brain barrier (BBB) is largely unknown. We describe a case with CNS changes after MIBG therapy.
Design/Methods: A patient with Relapse Neuroblastoma underwent MIBG with Autosomal stem cell transplantion (AutoSCT) in a tertiary hospital. The clinical records were retrospectively analyzed.
Results: A 5 year old boy Stage 4 Neuroblastoma (Poorly differentiated) with abdominal mass with bilateral pelvic bone involvement and received 6 cycles of chemotherapy followed by AutoSCT. Then received 20G radiation followed by Cis-retinoic cycles. After 4th cycle, patient developed bone pains and MRI showed increase in abdominal tumor size along with Bone marrow metastasis. He developed seizures. PET-CT showed 6.1×7.4×9 cm mass in retro peritoneum with multiple lymph nodes with bilateral brain metastases. He received 3 cycles of Cyclophosphamide, Etoposide, Vincristine and Bortezomib. Stem cells collected after two cycles. Surgical resection not possible so biopsy taken which showed Ganglioneuroblastoma. He underwent MIBG with AutoSCT. MIBG was given @ 12mCi/kg BW on Day-21, complicated by hypertension within 24 hrs. After four days of MIBG, seizures reoccurred and CT showed cerebral edema, hemorrhage surrounding the metastatic lesion and necrosis within the lesion. He received Melphalan (140 mg/m^2), Carboplatin (1500 mg/m^2) and Etoposide (1200 mg/m^2) from Day-7. Dose of stem cells 10.6 × 10^6/kg. Day+12 Neutrophil engrafted. On Day+17 repeat PET-CT revealed marginal reduction in size of retroperitoneal mass

with no FDG avidity and calcification.Follow-up CT head revealed absence of edema with tumour necrosis. One month post-transplant, patient is fine.
Conclusion: Necrosis within brain lesions with perilesional edema and hemorrhage suggest that MIBG has brain penetration and can cross BBB. Thus, MIBG with AutoSCT can also be used for relapse and refractory CNS Neuroblastoma.

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CURETTAGE FOR FOCAL HIGH-RISK SKELETAL NEUROBLASTOMA RESISTANT TO CHEMOTHERAPY AND RADIOTHERAPY

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Background/Objectives: High-risk neuroblastoma (HR-NB) refractory to, or relapsed after, high-dose induction chemotherapy is considered incurable, even when focal. Our initial strategy to eradicate this resistant disease is local radiotherapy followed by anti-GD2 immunotherapy. In a subgroup of patients with focal skeletal NB refractory to radiotherapy, surgical curettage was performed. We now report on their outcome.
Design/Methods: After obtaining IRB waiver, we retrospectively reviewed the records of patients with metastatic HR-NB who underwent surgical curettage between 2007 and 2011 of a single chemoradiotherapy-resistant skeletal site.
Results: Six patients (age 1.5 - 8.5 years at diagnosis, 2 - 11.5 years at curettage) underwent surgical curettage of their single site of persistent skeletal NB. Three patients each had refractory and relapsed NB, respectively. Sites of disease were humerus (n=2 patients) and tibia (n=4), documented by MIBG and MRI. All 6 patients had received intensive induction chemotherapy and second-line chemotherapy, and 5/6 had received radiotherapy (2100-3600cGy) to the site of persistent disease. Curettage was not associated with any surgical complications. Active NB was detected histologically in all samples. Post-operatively, MIBG scan normalized in all patients. Post-curettage therapy included radiotherapy, 3000-3600cGy (n=6), chemotherapy (n=4), and immunotherapy with anti-GD2 antibody 3F8+GM-CSF (n=6). Three patients subsequently relapsed: only 1 at the site of curettage. Median 5-year progression-free survival was 50±20% post-curettage. Two of 3 patients achieved a further remission and continue to remain disease-free 56+ and 87+ months post-curettage; one died of progressive multifocal disease. Five-year overall survival for the 6 patients was 83±15%.
Conclusion: Surgical curettage as part of a multi-modality strategy represents safe, effective local therapy for focal skeletal HR-NB resistant to chemoradiotherapy. This experience suggests that, with current treatment modalities such as anti-GD2 immunotherapy, focally chemoradioresistant HR-NB is not necessarily a harbinger of widespread disseminated disease, potentially changing the therapeutic paradigm for this group of patients.

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CAN FDG PET/CT BE A SURROGATE MARKER FOR MYCN EXPRESSION IN NEUROBLASTOMA

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Background/Objectives: N mYC amplification is one of the factor utilized for risk stratification of neuroblastomas. This molecular profiling takes a few days and hence the possibility of predicting the expression through surrogate marker could help early management decisions. To evaluate the possibility of Flurodeoxy glucose positron emission tomography/computed tomography (FDG PET/CT) uptake using the semiquantitative maximum standard uptake value (SUV max) as a surrogate marker for MYCN expression in neuroblastoma.
Design/Methods: Method: Retrospective analysis of 22 patients of neuroblastoma (13 male & 9 female; 12 patients > 18 month age) who were a part of hospital protocol was done to correlate SUV max of the primary tumor on a baseline FDG PET/CT study with MYCN expression. The SUV max of the primary tumor was noted and compared with the MYCN amplification done using PCR or FISH on biopsy sample. These 2 parameters were analysed using the Mann Whitney U test. Cut off value for SUV to predict expression of MYCN dentified using the ROC curve method.
Results: The SUV max range for 21 patients was 2.4 -30.1 (mean :7); 1 patient showed no FDG uptake. MYCN was expressed in 7 patients whose SUV ranged 5.8 -30.1 (median 9) while those with no MYCN expression the range was 2.7 -10.6 (median 3.6) Statistical analysis using Mann Whitney test revealed a higher SUV paramenter correlating with a MYCN expression. The SUV Cut off for a positive MYCN was calculated to be 6.9 with a specificity of 80% and sensitivity of 75%.
Conclusion: The pilot study shows a correlation of SUV and MYCN. Patients expressing MYCN tend to show a higher SUV level. The small sample size derived a SUV cut off of 9 to predict MYCN expression this however needs further validation with a prospective large population.

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13-CIS RETINOIC ACID INDUCES DIFFERENTIATION OF THREE TYPES OF HUMAN NEUROBLASTOMA CELL LINES IN VITRO

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Background/Objectives: To investigate the effects of 13-cis retinoic acid (13-cis RA) in inducing differentiation of three types of human NB cells in vitro.
Design/Methods: The status of N-MYC gene amplification of cultured SH-SY5Y, SK-N-SH and SK-N-BE2 cells was detected by fluorescence in situ hybridization (FISH). After treatment with different concentrations of 13-cis RA, morphological changes were observed by phase-contrast microscope, and neuron-specific enolase (NSE) concentrations were determined by ELISA. The cell viability was measured through cell counting kit-8(CCK-8) assay, and the cell apoptosis was assayed with flow cytometry (FCM).
Results: The morphological changes characteristic of differentiation were observed in all 3 types of NB cells after 13-cis RA treatment. N-MYC amplification was detected in SK-N-BE2 cells even after 13-cis RA treatment, while the other two cell lines were amplification-null. After different concentrations of 13-cis RA treatment, NSE concentration increased with prolonged time, especially for SK-N-BE2 cell($F=27, P<0.0001$).13-cis RA stimulated cell proliferation within 48 hours of treatment, and then inhibited cell growth. FCM indicated that the degree of apoptosis in SH-SY5Y cell were significantly higher after 13-cis RA treatment of 10μM concentration for continuous 96h($F=16.21, P=0.011$) and 120h ($F=16.04, P=0.016$)as compared to the control group. Cell apoptosis of SK-N-SH cell after 13-cis RA treatment of 1μM and 10μM concentration for 48h, while SK-N-BE2 cell with different concentrations of 13-cis RA for 120h were significantly higher than that of the control groups.
Conclusion: The present study showed that 13-cis RA could induce differentiation of human NB cells in vitro. It induces cell proliferation within 48 hours of 13-cis RA, and thereafter suppresses cell growth. No improvement of N-MYC amplification cells with the detection of DNA level after 13-cis RA treatment, which suggests that combination treatment is possibly needed.

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THE PD-L1 EXPRESSION INCREASES AFTER CONSECUTIVE MULTIMODAL THERAPIES IN NEUROBLASTOMA

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Background/Objectives: Programmed death 1 (PD-1) protein, a T-cell co-inhibitory receptor, and one of its ligands, PD-L1, play a pivotal role in the ability of tumor cells to evade the host's immune system. We investigated the expression of PD-L1 on neuroblastoma cells by immunohistochemistry.
Design/Methods: Forty-one NB patients diagnosed and treated between 1993 and 2014 were included in this study. Ten patients underwent a primary operation (PO). Of the remaining 31 patients, 6 patients received biopsy alone, while 25 patients underwent a delayed primary operation (DO) after chemotherapy. The PD-L1 protein expression was detected by immunohistochemistry of formalin-fixed paraffin-embedded specimens using an anti-human PD-L1 monoclonal antibody (5H1). PD-L1 tumor positivity was defined as ≥5% tumor cell membrane staining. Statistical analyses were performed using Fisher's exact test.
Results: Four out of 10 neuroblastoma sections collected with PO were positive for PD-L1. Only one of 31 biopsy specimen was positive for PD-L1, thus demonstrating that PD-L1 was positive in only 5 out of 41 specimens obtained before chemotherapy. However, 14 out of 25 specimens obtained from DO were positive for PD-L1 ($p<0.01$; biopsy specimen vs DO specimens). Of these 14 PD-L1 positive specimens obtained from DO, relapse occurred in 7, while no relapse was observed in 7 patients. In contrast, recurrence occurred in 4 patients according to the findings of 11 PD-L1 negative specimens. No statistical correlation between the PD-L1 expression and the incidence of relapse was thus observed (n.s.).
Conclusion: Our results indicate that most primary neuroblastomas do not express PD-L1, and its expression was found to increase after chemotherapy. Although the expression of PD-L1 does not correlate with recurrence, PD-L1 may nevertheless be

associated with the survival of tumor cells, and therefore still be a potential target for the treatment of neuroblastoma after multimodal therapy.

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A TREATMENT OPTION OF CONGENITAL NEUROBLASTOMA WITH EXTENSIVE HEPATIC METASTASIS: TRANSARTERIAL INFUSION CHEMOTHERAPY

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Background/Objectives: Due to the possibility of spontaneous regression, Stage IVs neuroblastoma generally confers a good prognosis. However, neuroblastoma with extensive hepatic metastasis is frequently life-threating because of its massive hepatomegaly and thoracoabdominal compression. The authors report 6 cases of congenital neuroblastoma with extensive hepatic metastasis and introduce our experience in controlling this lession.
Design/Methods: Between September, 2013 and August, 2014, six cases of congenital neuroblastoma with extensive hepatic metastasis were admitted to our institution. Six patients aged from 2 weeks to 13 weeks at time of diagnosed. 1 case refused chemotherapy. 5 cases received chemotherapy and 2 of them accepted transarterial infusion chemotherapy (TAIC) later on.
Results: The case refused chemotherapy died from thoracoabdominal compression and renal failure at the age of 14 weeks. In the 5 cases underwent systematic chemotherapy, 4 cases still suffered from gradually increased abdominal distension. 2 cases died at the age of 15 weeks and17 weeks respectively. Other 2 cases accepted TAIC 3 weeks after systematic chemotherapy. Hepatomegaly was relieved in both cases after TAIC therapy. 1case survived by systematic chemotherapy only.
Conclusion: Extensive hepatic metastasis in congenital neuroblastoma is a life-threating sign. TAIC is a considerable treatment option in cases despite systematic chemotherapy.

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HIF-1A COULD PROMOTE THE PROLIFERATION AND MIGRATION ACTIVITY OF NEUROBLASTOMA CELL LINE SK-N-SH

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Background/Objectives: HIF-1a plays a significant role in some tumors' process. The purpose of our study is to investigate the influence on the growth and development of neuroblastoma that HIF-1a has.
Design/Methods: The neuroblastoma cell line SK-N-SH was cultured and treated with 100uM $Cocl_2$ for making hypoxic microenvirenment. There were two groups (control group and $Cocl_2$ group) and three time points(0h,12h and 24h). CCK8 Kit, cell scratch test was used for testing the cell proliferation and migration activity, respectively. Real-Time PCR and Western Blot were used for measuring the content of HIF-1a mRNA and HIF-1a protein, respectively.
Results: During 0 to 12 hours, the proliferation activity and migration activity of SK-N-SH in $Cocl_2$ group were both stronger than that in control group. The difference value of OD value(`x±s) in control and Cocl2 group was 0.251±0.113 and 0.646±0.207, respectively($P<0.05$) .The difference value of wound width in control and Cocl2 group was 50.367±9.085 and 108.87±7.86, respectively($P<0.01$). While during 12 to 24 hours, the proliferation activity of SK-N-SH was weaker than that in control group, and there was no significant difference about the migration activity of SK-N-SH between control and $Cocl_2$ group.The difference value of OD value(`x±s) in control and Cocl2 group was 1.361±0.15 and 0.367±0.084, respectively($P<0.01$) .The difference value of wound width in control and Cocl2 group was 30.29±13.67 and 20.45±11.991, respectively($P>0.05$). HIF-1a mRNA and HIF-1a protein increased in 12 hours($P<0.01$), while HIF-1a mRNA increased in 24 hours($P<0.01$), and HIF-1a protein had no obvious increasing during 12 to 24 hours($P>0.05$).
Conclusion: Hypoxia probably promotes the malignancy activities of neuroblastoma. And HIF-1a might be the most important factor in hypoxic microenvironment that promotes the malignance of neuroblastoma cells.

Posters: New Drugs/Experimental Therapeutics

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SUCCESSFUL MANAGEMENT OF CHEMOTHERAPY INDUCED HYPERTRIGLYCERIDEMIA IN ACUTE LEUKEMIA WITH OMEGA 3 FATTY ACID

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Background/Objectives: To study the effect of presecribing omega 3 Fatty acids for treatment of hypertriglyceridemia in ALL instead of invasive procedures like plasmapheresis and demonstrating its efficacy.
Design/Methods: Two Patients who developed severe hypertriglyceridemia while on chemotherapy for ALL were prescribed Omega 3 Fatty Acids. Triglyceride and Cholesterol levels were monitored sequentially on days 2,4, 6 and 10 along with clinical assessment for development of complications due to hypertriglceridemia.
Results: A 15-year-old male child who was a case of T cell ALL on reinduction chemotherapy as per BFM 95 protocol, presented with symtoms of neuropathy and myopathy. His seum sample was lipemic. His S.Triglyceride levels were >4870 mg/dl and cholesterol level was 655 mg/dl. He was started on Omega-3 capsules (300 mg) thrice a day. Triglyceride levels dropped to 1,980 mg/dl, 1120 mg/dl ,540 mg/dl, 326 mg/dl and 250 mg/dl on days 2,4,6,10 and 12 respectively. His cholestrol levels decreased from 380 mg/dl to <150 mg/dl within 10 days. The patient recovered clinically and his neurological as well as laboratory parameters remained stable. A 4 year old patient, who was a case of B cell ALL was being treated on BFM95 Protocol developed hypertriglyceridemia which was detected during routine sampling while on induction chemotherapy. His Triglyceride levels were equal to 2489 mg/dl. He was started on omega 3 fatty acids. His triglyceride level decreased to 1500 mg/dl, 840 mg/dl and 437 mg/dl and 250 mg/dl on days 2,4,6 and 10 following starting of therapy. We were able to avoid plasmapheresis in both these patients and successfully treat them conservatively.
Conclusion: Severe hypertriglyceridemia may be conservatively managed with omega 3 fatty acids as an adjunct to diet. Plasmapheresis may be reserved for symptomatic patients with very high triglyceride levels not responding to conservative therapy. The availability of omega-3 fatty acids, has demonstrated efficacy, safety and is valuable for the medical management of hypertriglyceridemia in ALL patients.

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THE "TRIALGAP": REDUCED ACCESS TO CANCER TRIALS FOR CHILDREN AND YOUNG PEOPLE IN SCOTLAND

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Background/Objectives: The Scottish Government recommends that all children and TYA (teenage and young adults aged 16-24 years) with cancer should be able to participate in clinical trials due to reported benefits in survival and patient experience. We sought to determine how Scottish children and TYA fared in this regard compared to peers in the rest of the UK.
Design/Methods: Information on available clinical trials by cancer diagnosis was collected from: NCRI Portfolio Maps; the UK Clinical Research Network Database Portfolio; Edge Database (regional directory of clinical trials); hospital data managers.
Results: *Trials (UK vs Scotland)*: The UKCRN site designates 22 UK cancer trials that are only for "TYA Cancer" and 39 trials as "paediatric". Respectively, only 11 and 19 of these designated trials are available in Scotland. Further, we found 712 studies that could recruit TYA, of which only 215 are available in Scotland.*Treatment in Scotland (TYA vs paediatric)*: Treatment of children with cancer (aged 0-15 years) is concentrated in 3 centres while TYA may be treated in one of 19 centres (2 TYA units, 17 adult hospitals).
Conclusion: Children and TYA in Scotland have reduced access to trials of cancer therapy compared to the UK as a whole. This "trial gap" is exacerbated by incomplete listing of available trials and, for TYA, by their dispersion amongst numerous treatment centres.

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MYOSTATIN AS A MARKER FOR SHOWING DOXORUBICIN INDUCED CARDIAC DAMAGE

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Background/Objectives: Doxorubicin (DXR) is an effective chemotherapeutic agent but causes severe cardiac failure over known doses. Thus, early detection and prevention of cardiac damage is important. Various markers have been tested for early detection of cardiac damage. Myostatin is a protein produced in skeletal muscle cells inhibits muscle differentiation and growth during myogenesis. We evaluated the role of myostatin as a marker for showing DXR induced cardiac damage and compared with well known cardiac markers like NT-proBNP, hs-TnT and CK in a rat model of chronic DXR cardiotoxicity.
Design/Methods: The study was performed with 32 male rats and divided into four groups. Group 1 received one month, group 2 two month, group 3 tree months of adriamycin therapy and group 4 served as control.
Results: There was no statistically significant difference between study groups and the control group in terms of CK, AST, LDH, MDA, SOD, GSH-Px and IL-1 levels. Myostatin levels were significantly increased in Group 3 in comparison to the control, and there was no difference between Group 1, 2 and 3. Myostatin levels in Group 1 and 2 were not significantly higher than the levels in the control group. High sensitive troponin levels were significantly increased in Group 2 and 3, compared to those in the control group (no change in Group 1), and there was no statistical significance between Group 1, 2 and 3 regarding the myostatin levels. The proBNP level was higher in Group 3 than it was in the control group, and there was no statistical significance between group 1, 2 and 3 regarding the proBNP levels. There was a 9.56, 3.00, and 2.30 fold increase in the first month of ADR administration on NT-proBNP, hs-TnT and myostatin levels, respectively.
Conclusion: Myostatin, NT-proBNP, and hs-TnT but not CK rose significantly during DXR treatment.

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PEDIATRIC AND ADULT SUBGROUP RESULTS FROM AN ONGOING DEFIBROTIDE EXPANDED ACCESS PROGRAM IN THE US FOR PATIENTS WITH HEPATIC VENO-OCCLUSIVE DISEASE

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Background/Objectives: Hepatic veno-occlusive disease (VOD), or sinusoidal obstruction syndrome, is an unpredictable, life-threatening complication of hematopoietic stem cell transplantation (HSCT). Severe VOD (sVOD) is associated with >80% mortality; it is characterized clinically by multi-organ failure (MOF). In the European Union, defibrotide is approved for treatment of sVOD in HSCT. In the United States, defibrotide is available through an ongoing, expanded-access, protocol-directed treatment IND (T-IND) study. T-IND *day+100* survival post HSCT/chemotherapy was analyzed for pediatric/adult subgroups.
Design/Methods: Patients received defibrotide 25 mg/kg/day, ≥21 days recommended. Eligibility: Originally, sVOD with MOF (renal/pulmonary) by Baltimore criteria post HSCT; amended to include patients post HSCT/chemotherapy with non-sVOD (without MOF), VOD per modified Seattle criteria, or biopsy-proven VOD.
Results: Of 641 patients enrolled through 2013 receiving ≥1 dose (median treatment duration, 21 days), 636 had age data: 58% were pediatric (aged <16y) and 42% adult (>16y). Among pediatric and adult patients post HSCT, day+100 survival was 58% (163/283) and 45% (109/243), respectively. sVOD occurred in 55% of children and 50% of adults. Among sVOD and non-sVOD post-HSCT subgroups, respectively, pediatric survival was 50% (79/157) and 67% (84/126); adult survival was 38% (46/122) and 52% (63/121). For pediatric and adult patients post chemotherapy, survival was 83% (39/47) and 60% (9/15), respectively; sVOD subgroup rates were 77% (20/26) and 67% (4/6). Adverse events (AEs) occurred in 61% (227/372) of children and 76% (200/264) of adults, with treatment-related AEs in 19% and 24%, respectively. Serious AEs occurred in 45% of children (most common non-VOD/non-MOF: pulmonary hemorrhage [8%]) and 53% of adults (most common non-VOD/non-MOF: hypotension [5%]).
Conclusion: Defibrotide was generally well tolerated, with manageable toxicity. The higher survival rates in the non-sVOD subsets indicate further study is warranted to determine the impact of treatment earlier in the course of VOD. T-IND enrollment continues. *Support*: Jazz Pharmaceuticals.

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MOBILISATION OF HAEMATOPOIETIC STEM CELLS IN PAEDIATRIC PATIENTS, PRIOR TO AUTOLOGOUS TRANSPLANTATION FOLLOWING ADMINISTRATION OF PLERIXAFOR AND G-CSF

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Background/Objectives: Plerixafor is a selective reversible antagonist of CXCR4, capable of interfering with CXCR4 interaction with Stromal cell-derived factor 1 alpha (SDF-1). Therefore when used in combination with granulocyte-colony stimulating factor (G-CSF) it is capable of amplifying the effects of G-CSF in mobilizing haematopoietic stem cells. In this we retrospectively review our single centre experience with Plerixafor and G-CSF to mobilize stem cells in five extremely heavy pre-treated oncology patients, as a primary method of mobilization.
Design/Methods: All patients started G-CSF at 10microgram/kg 4 days prior to the first administration of plerixafor. Plerixafor was administered at 0.24 mg/kg on the first day of apheresis and administered on subsequent days if further stem cell harvesting was required.
Results: Patient 1 mobilized on day 1 alone and achieved 10.7×10^6/kg; Patient 2 and 3 continued to have rising CD34 levels demonstrated over the 3 days of apheresis and with an incremental number achieved each day, although the measured CD34 level pre-harvest showed a drop for Patient 3. Patient 4 and 5 mobilized extremely well on day 1 alone and yielded the CD34 positive stem cell dose required. During apheresis patient 2 developed signs and symptoms of hypocalcaemia but this corrected with oral calcium correction, whilst patient 3 during harvest required phosphate and potassium correction.
Conclusion: Plexiaflor in combination with G-CSF has shown encouraging results in this small selection of patients who were heavily pre-treated prior to undertaking the stem cell mobilisation regimen. Although this is a small cohort of patients the data obtained provides a foundation for future research within a larger patient group.

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REVIEW OF PRESCRIBED MEDICATION AND CLOSE COOPERATION WITH PHARMACIST LEADS TO REDUCTION OF MEDICATION ERRORS IN A PAEDIATRIC ONCOLOGY DEPARTMENT

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Background/Objectives: Approximately 100 children between 0-15 years are diagnosed with cancer each year and treated at Rigshospitalet, Copenhagen. A review of medication errors at the department showed that medication errors were primarily related to errors of prescription and were discovered at dispensation step by nurses or administration by parents. In order to optimize patient safety, the department and pharmacy initiated a project of pharmacist review of medication.
Design/Methods: The purposes of the project were a) to ensure that prescription errors were discovered and corrected before dispensation and administration and to correct eventual errors, through dialogue with the prescribing physicians, b) to ensure best practice of drugs prescribed and c) to ensure the most effective and appropriate use of medicines.Two pharmacists reviewed medicine prescribed for admitted children every weekday from 10-12 am. Review of medication was prioritized as follows: 1. Children with complex treatment or unstable disease. 2. Recently admitted children. 3. Children who had been transferred from other departments within the same day. In case of inappropriate prescription the pharmacists contacted the responsible physician in order to change prescription if relevant. All reviews were recorded in a central database by date, age of child, any deviance from best practice and if intervention was accepted by physician.
Results: Within the period from March1st. 2014 to February 28th 2015, 3253 prescriptions were reviewed. In 51.2% (N=1585) there was no deviation from best practice. In 12,2% (N=396) errors of prescribed dose or incorrect duration of treatment were found. Of these, 95.0% (N=375) were accepted by the physician. The remaining 36.6% of findings concerned side effects, dispensing intervals, formulation of drug and interacting drugs.
Conclusion: Review of prescribed medication in a paediatric oncology department and collaboration between pharmacists and prescribing doctors improves quality of medication and reduces adverse events.

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EFFECTIVENESS OF ANKAFERD BLOOD STOPPER IN PROPHYLAXIS AND TREATMENT OF ORAL MUCOSITIS SEEN IN CHILDHOOD CANCERS AND CORRELATION WITH PLASMA CITRULLINE LEVELS

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Background/Objectives: Oral mucositis is observed in 52-80% of the children receiving cancer therapy. Ankaferd Blood Stopper (ABS) is an herbal product that is used as a hemostatic agent. In previous studies, it was shown that ABS has anti-microbial, anti-inflammatory effects as well as positive effects on healing of tissue injury. This study aimed to investigate effectiveness of ABS in prophylaxis and treatment of oral mucositis.
Design/Methods: This was a randomized, controlled and open study which included 27 patients aged 4-17 years receiving chemotherapy regimens with strong mucotoxic effect. The patients were asked to perform standard oral care (SOC) upon first day of chemotherapy for 10 days and oral mucosa was assessed daily upon completion of chemotherapy based on World Health Organization scale for oral mucositis. Same patients receiving same chemotherapeutic agents in the second course of chemotherapy were asked to gurgle by using ABS four times daily in addition to SOC. Mucosa ratings were performed before second chemotherapy course and at the period where mucositis became most intensive, and blood samples were drawn to measure citrulline levels again.
Results: Stages of oral mucositis were found lower in the second chemotherapy course given SOC plus ABS when compared to first chemotherapy course given SOC alone ($p=0.007$). Mean plasma citrulline level obtained before and after chemotherapy decreased from 44.08 to 23.99 nmol/mL in chemotherapy course given SOC alone ($p<0.001$) while it decreased from 38.67 to 26.78 nmol/mL. When extent of decrease in plasma citrulline level was assessed, it was greater in courses given SOC alone compared to those given SOC plus ABS ($p=0.009$).
Conclusion: Based on our results, ABS exhibited beneficial effects in the prophylaxis and treatment of oral mucositis. However, multi-center experiences and further studies with larger sample size are needed for introduction of ABS into primary oral care and treatment protocols of oral mucositis.

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LIPOPLATIN; A NEW LIPOSOMAL AGENT, IN THE TREATMENT OF RELAPSED OR METASTATIC CHILDHOOD SOLID TUMORS : TOXICITY AND CLINICAL OBSERVATIONS OF EFFECTIVENESS

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Background/Objectives: Liposomal cisplatin (Lipoplatin) is a new cisplatin formulation and has been investigated in a small number of adult cancer studies to Compare with cisplatin for effectiveness and toxicity. There is no childhood studies.
Design/Methods: we aimed to investigate renal toxicity, myelotoxicity, other side effects and effectiveness of lipoplatin in highly pretreated relapsed or metastatic solid childhood tumors. Patients (were enrolled to study after july 2014) ages were between 4 to 7 years old (2 boys, 3 girls) with relapsed, metastatic solid tumors 2 rhabdomyosarcoma, 2 neuroblastoma; relapsed after high dose therapy followed by autologous peripheral stem cell transplantation, 1 condrosarcoma). Patients have been received Lipoplatin (125-175 mg /m2) and Paclitaxel (125-175 mg/m2, before Lipoplatin administration) every other week between 2 to 5 cycles, total 15 cycles. Renal function tests, blood counts, vomiting side effects, and other possible side effects have been recorded before and after each cycle besides imaging studies to asses clinical effectiveness.
Results: Creatin level range before treatment were 0.25 - 0.92 mg/ dl (median: 48) while it was between 0.38 - 0.82 mg/dl (median: 0.49) after Lipoplatin-Paclitaxel treatment. There was no renal failure or any other important side effects to restrict chemotherapy schedule. Only mild, Grade 1-2 myelosupression and grade 1 vomiting have been observed. Although, it is early to evaluate effectiveness of the treatment, it was possible to receive stable disease for 2-8 months in that advanced disease patients with better quality of life.
Conclusion: According to preliminary results of our study; Lipoplatin is effective and well tolerated by children with relapsed and metastatic cancer with no grade 3/4 nephrotoxicity, myelospression or neuropathy. It may even serve as an option as first line therapy for advanced stage, metastatic childhood solid tumors to prevent any renal or neurological side effects before they observed.

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PHARMACOTHERAPEUTIC COUNSELING BY A CLINICAL PHARMACIST ON A PEDIATRIC HEMATOLOGY AND ONCOLOGY UNIT

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Background/Objectives: Pharmacotherapy in pediatric hematology and oncology (PHO) patients is complex. To improve the quality of treatment and care, a team of 4 clinical pharmacists is involved in the PHO unit of the University Hospitals Leuven. To guarantee optimal continuity, standardization of the interviews is essential.
Design/Methods: Different types of interview are defined: first discharge interview, basic discharge interview, start-up of corticosteroids, start-up of an oral chemotherapeutic, maintenance therapy, tapering of corticosteroids. After each interview, the pharmacist registers patient and type of interview.
Results: From February 2014 until January 2015, 205 patients (0-18 years) were followed: 64 new diagnoses, 141 patients already on treatment. A total of 914 interviews were performed. The greatest attention is paid to the basic discharge interviews (n=612, 67%), followed by start-up of corticosteroids (n=73, 8%) and first discharge interviews (n=65, 7%). Most of the interviews (74%) are done during hospitalization. Only 26% of the interviews are performed at day-clinic.
Conclusion: Given the great amount of interviews, a fulltime presence of a clinical pharmacist on a PHO unit is needed. As 74% of all the interviews are discharge interviews, and performed by a team of 4 pharmacists, a structured approach of these interviews is needed to guarantee content quality. In the near future a qualitative survey will be carried out at the physicians, nurses and patients and their families to evaluate the content of the interviews.This project is funded by the NationalCancerPlan and Kinderkankerfonds Leuven.

Posters: Nursing

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EVERYONE HAS A ROLE IN INFLUENCING AND SHAPING BEST CARE PRACTICE IN PAEDIATRIC CANCER CARE: THE JOURNEY FROM CLINICAL SUPPORT WORKER TO WARD MANAGER

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Background/Objectives: Every member of the paediatric oncology nursing team play a vital role in delivering the best care to patients within paediatric oncology. From the role of clinical support worker, to staff nurse, through to senior sister. At every level of competence nursing staff can impact, influence and shape the practice that is delivered to patients and their families. The model of the service in which that is delivered is paramount.
Design/Methods: The role of the clinical support worker has undergone many changes throughout time from a clinical role to a non-clinical role and back again. With the current challenging climate of less qualified nurses available to employ, the role of the clinical support worker has needed to be developed and adapted further to underpin and support the role of the qualified paediatric oncology nurse. Through personal experience of a career starting as a clinical support worker, progressing to a ward manager the author has great insight and understanding of what the role of clinical support worker within paediatric oncology should entail.
Results: Increasing the number of clinical support workers that are employed and that undertake a trust wide education and development programme will aim to support recruitment and retention of clinical support workers and nursing staff too. Shaping and tailoring a further training and education programme within paediatric oncology for clinical support workers will endeavour to compliment this further.
Conclusion: The clinical support worker role plays an essential part in the delivery of care. They assist nursing staff with their clinical duties and also can support patients and parents through their journey. In an ever changing culture of fewer nurses coming through the nurse training programmes the role of the clinical support worker in paediatric oncology is as pivotal as ever in delivering, influencing and shaping best care within paediatric oncology.

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IMPLEMENTATION OF A NUTRITION THERAPY PROTOCOL IMPACTS IN THE USE OF PARENTERAL NUTRITION IN PAEDIATRIC ONCOLOGY PATIENTS UNDERGOING HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background/Objectives: The Hematopoietic Stem Cell Transplantation (HSCT) represents increased nutritional risk to paediatric oncology patients. Parenteral Nutrition (PN) is often used for patients undergoing HSCT, which could represent increased risk of line infections, hyperglycemia, hypertriglyceridemia and cholestasis, apart from higher cost. The use of Nutrition protocols is essential to standardise nutritional care and follow up, especially in complex procedures such as HSCT. The aim

of this study was to investigate whether the implementation of a Nutrition therapy protocol reduced the use of PN in paediatric oncology patients undergoing HSCT at a tertiary Paediatric Oncology hospital in Sao Paulo, Brazil.
Design/Methods: A retrospective study was conducted by chart review on the use and duration of PN in children and adolescents with cancer, from conditioning to 60 days after HSCT. Transplants from January 2012 to January 2015 were analysed. The data was divided in before and after the implementation of a Nutrition therapy protocol (January/2014) and the percentage of patients who received PN in both groups was compared. The protocol indicates the use of nasogastric tube feeding for patients undergoing HSCT. The chi-square test was used to verify the statistical significance of the difference between the frequencies.
Results: Data of 26 patients were analysed, 14 before (42.9% female; mean age 10.9 years) and 12 after (50% female; mean age 10.1 years) the implementation of the protocol. The frequency of use of PN dropped from 71.4% to 8.3% ($p < 0.05$) and the duration from 12.6 to 0.8 days/patient.
Conclusion: The implementation of a Nutrition therapy protocol decreased the use of PN in this group of patients.

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THE EFFECT OF FAMILY LIFE AND CHILDREN RAISING ATTITUDES TO PAIN PERCEPTION OF CANCEROUS CHILDREN

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Background/Objectives: This study was performed to determine the effect of parents' children raising attitudes in cancerous children pain perception with definitive and comparative methods.
Design/Methods: One hundred and twenty children and their parents' were taken as trial group in compliance with study criteria between the dates during the study was performed. The data were collected using child and parent data collect forms and PARI-Parental Attitude Research Instrument. In evaluation of the data, for statistical analyses SPSS Windows 10.0 sorftware used. For evaluation of study data, Kruskal Wallis test and Mann Whitney U test were used for comparing quantitative data in addition to identifying statistical methods, Chi-square test were used in comparing quantifiable data.Pearson Correlation Analysis were used for determining relations between parameters.The results were evaluated within a confidence interval of 95% an at a significance level of $p<0.05$).
Results: At the end of the study; mother's child raising attitudes didn't affect children pain perception level was found. There were a negative relation between the mothers'expression of children in Facial Pain Scale(22.4% level in negative direction,$p<0.05$) and VAS scores (24.4% level in negative direction,$p<0.01$).The result of this research showed that child raising attitudes didn't affect the pain perception of the children but effect the expression and expression manners of pain. While democratic behavior and equality respect bottom dimension points of mothers children who express pain are higher than mothers of children who don't express pain($p<0.05$).Also, emotional expressions of pain in children, whose mothers have high points from constraint and discipline bottom dimension, are significantly lower than children who express their pain behaviourally ($p=0.023$, $p<0.05$) and physically ($p=0.008$,$p<0.01$).
Conclusion: In concslusion, parents' children raising attitudes affected the children's pain expression and behaviours. Considering these effects, it is thought that the efficient analgesia chance of cancerous children will be raising with holistic nurse approach made by evaluating.

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NURSING CHALLENGES CARING FOR PRE-ADOLESCENT ONCOLOGY PATIENTS WITH ORTHOPAEDIC COMPLICATIONS

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Background/Objectives: To overcome the nursing challenges of pre-adolescent oncology patients nursed in traction due to pathological fractures.
Design/Methods: Data collected retrospectively from folder review from one patient. Another patient currently observed in hospital, while in traction. Qualitative study regarding two patients with pathological fractures.
Results: One patient currently receiving physiotherapy to improve mobility. The second patient is still in traction while receiving chemotherapy with view of limb salvage.
Conclusion: Patients at risk of pathological fractures and those who have sustained pathological fractures, can still have an equally good quality of life especially during the challenging period of immobility.

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RESILIENCE AND MENTAL HEALTH IN PARENTS OF CHILDREN SURVIVING ACUTE LYMPHOBLASTIC LEUKEMIA

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Background/Objectives: Cancer in children is a tremendous stressor that requires parents to adapt to new challenges related to the child`s illness. Research has mainly focused on psychopathology, and rarely on a resource-oriented perspective, such as resilience. The objective of this study is to assess resilience factors among both mothers and fathers of children surviving acute lymphoblastic leukemia (ALL) compared to parents of healthy children. In addition, to explore the association between parental resilience and mental health.
Design/Methods: This cross-sectional study consisted of parents (n=55) of 40 children in remission from ALL between 8 to 15 years of age, compared to parents of healthy children (n=63). Children were recruited from the Norwegian Radium Hospital, Oslo and St. Olavs University Hospital, Trondheim, Norway. The Resilience Scale for Adults (RSA) assessed parental resilience and the General Health Questionnaire (GHQ-30) assessed parents' mental health.
Results: Significant lower scores were found for the RSA total scores for both mothers and fathers compared to healthy controlgroup. No significant differences were found for mental health. The resilience factors: Perception of Self, Planned Future and Family Cohesion were significant predictors for mental health in mothers of children surviving ALL, and Social Competence was a predictor for fathers.
Conclusion: Resilience factors associated with parents' mental health may be of protective value, and should therefore be considered in a clinical setting.

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CONFIRMATORY FACTOR ANALYSIS OF THE FATIGUE SCALE-ADOLESCENT

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Background/Objectives: Fatigue is one of the most common symptoms reported by adolescents who have survived cancer. Numerous studies have indicated that it can exacerbate other late effects of cancer treatment and limit the survivors' capacity to perform daily activity, consequently affecting their quality of life (QoL). It is therefore vital for healthcare professionals to develop interventions that can help reduce fatigue. First, however, the availability of a reliable and valid instrument accurately assessing fatigue is crucial before any intervention can be planned and evaluated. This study aimed to examine the psychometric properties of the Chinese version of the Fatigue Scale for Adolescents (FS-A) and assess its factorial structure by confirmatory factor analysis (CFA).
Design/Methods: A cross-sectional study design was employed in an outpatient clinic. A convenience sample of two hundred adolescents who have survived cancer were invited to participate. The internal consistency, test-retest reliability, content validity and construct validity of the Chinese version of the FS-A were assessed.
Results: The Cronbach's alpha coefficient and intra-class correlation coefficient were 0.89 and 0.85 respectively. The content validity index was 0.92. There was a strong positive correlation ($r = –0.58$) on the scores between adolescents' fatigue and depressiveness, but a strong negative correlation ($r = 0.53$) on scores between adolescents' fatigue and QoL. The mean score of fatigue of the survivors was found to be significantly lower than that of children receiving cancer treatment, but significantly higher than that of their healthy counterparts. The result of CFA showed that a four-factor model was adequately fit the data obtained by the Chinese version of the FS-A, indicating that the factorial structure is the same as its original version.
Conclusion: The result provides further evidence to support that the Chinese version of the FS-A is a reliable and valid instrument assessing fatigue among adolescents who have survived cancer.

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ADJUSTMENT AND COPING IN PARENTS OF CHILDREN WITH CANCER

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Background/Objectives: The diagnosis and treatment of cancer is very stressful event for children and other family members, as well as causing physical, social, emotional and economic difficulties. It requires using of appropriate coping strategies to ensure adherence to treatment and to be protected from the psychopathological effects of diagnosis and long term treatment of cancer. Research has been conducted to investigate the coping in parents of cancer patients.
Design/Methods: The study was performed in Clinics of Pediatric Oncology and Hematology with participating of 187 parents of children with cancer. In collecting the data, an information form, which was developed by researchers and "Ways of coping inventory" were used. The frequency distribution, arrhythmetic average and standard deviation of the data was obtained. In analyzing the data, Student's t test, one- way ANOVA, Bonferroni and Tukey advanced level test, Pearson correlation test and Chisquare test were used.
Results: The majority of the parents were shocked when they first heard the diagnosis and felt the fear of the loss of the child. Parents use spiritual beliefs, compare their situation with others and need health care practitioners' to cope with their problems. It's shown that the factors effected the coping in parents are; the age of children, negative relations with other family members, the way to get the medical therapy, education level of the parents and the effect of cancer on family budget. It's found that when the income level decreases, the approaches of seeking support, helplessness and submissive are increasing.
Conclusion: According to these results, it's evaluated that providing social support by health care team and being informed about their child's illness and treatment options can help parents to cope with anxiety in childhood cancers. Planning the health care programme will also eliminate the negative attitudes and social support systems will be developed.;

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NURSING INTERVENTION FOR FATIGUE IN CHILDREN WITH CANCER LITERATURE REVIEW

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Background/Objectives: Purpose: Cancer-related fatigue (CRF) is one of the most frequent symptoms experienced by children with cancer, and several previous studies reported that fatigue is considered as the most distressing symptom that is related to cancer treatment by children and adolescents patients with cancer. There are some guidelines regarding pharmacological interventions in CRF, however, nursing intervention is still under investigation. Therefore, the aim of this study is to review nonpharmacological intervention and obtain clues to the implementation of nursing intervention that will improve QoL of children with cancer.
Design/Methods: Methods: We searched literature by PubMed by the key words "intervention" "cancer" "children" and "fatigue".
Results: Thirty-one studies were found through the search. We excluded 17 studies which were review articles or investigated survivors fatigue. We examined rest 14 studies. Of 14 studies, 3 were study protocol and these studies aimed to present rationale and design of the clinical research program or evaluated the efficacy of the programs for fatigue in pediatric cancer patients. 2 studies were developed self-reported scales for fatigue in children or adolescents, and 5 were descriptive studies (e.g. frequency of fatigue between children and adolescents was compared). Other 4 studies were randomized prospective intervention studies or case control studies. The aims of randomized prospective intervention studies and care control studies were to examine feasibility and efficacy of the interventions, and a home-based aerobic exercise, a bicycle-type exercise, and a complementary energy therapy were examined its efficacies.
Conclusion: A few interventions to examined to relieve and decrease fatigue in children with caner, and all of the examined interventions were exercises. Further investigations are necessary to establish the standard nursing intervention for fatigue in children with cancer.

P-411

THE IMPACT OF CANCER AND ITS TREATMENT ON PHYSICAL ACTIVITY LEVELS AND QUALITY OF LIFE AMONG YOUNG HONG KONG CHINESE CANCER PATIENTS

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Background/Objectives: Despite the evidence that regular physical activity can have beneficial effects on the physical and psychological well-being of cancer patients, a review of the literature reveals that a majority of young cancer patients fail to attain the same levels of physical activity that they had before contracting the disease. This study is to examine the impact of cancer and its treatment on the physical activity levels and quality of life of young Hong Kong Chinese cancer patients.
Design/Methods: A cross-sectional study was conducted, with 76 young cancer patients admitted for treatment to a pediatric oncology unit, and another similar age group of 148 healthy counterparts from the two integrated child and youth service centers were invited to join the study.
Results: The study found that the current physical activity levels of young cancer patients were markedly reduced when compared with their pre-morbid situation. Moreover, they were significantly less active in performing physical exercise, and reported lower levels of self-efficacy and quality of life than their healthy counterparts. The results of the hierarchical multiple regression analysis showed that physical activity is an important indicator of quality of life among young cancer patients.
Conclusion: The results provide further evidence that cancer and its treatment have negative effects on physical and psychological well-being and quality of life among young cancer patients. There is an imperative need for healthcare professionals to promote the adoption of regular physical activity among such patients, even during the treatment itself.

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VALIDATION OF 'THE RAINBOW PAIN SCALE'

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Background/Objectives: Self-report, when available, is considered the primary way to assess the intensity and other aspects of pain in children. However, self-report scales are often too complex cognitively for preschool-aged children (2-4 years). The Rainbow Pain Scale (RPS) was developed to provide individualized self-reported pain ratings for preschool-aged children. The psychometric properties of this scale have yet to be evaluated. To ensure validity, our first step was to compare RPS scores to a well-validated scale in older children who were able to self-report their pain. Assess the concurrent validity of the RPS in children aged 5 to 10 years as proof of principle.
Design/Methods: We compared ratings of 49 children's pain using the RPS with those on the Faces Pain Scale –Revised (FPS-R). Participants suffering from pain related to cancer were recruited to complete both scales at 3 time points, during both inpatient and out-patient clinic visits. Pearson's r and Cohen's kappa were used to evaluate the level of association between the scales.
Results: The association between RFC and The FPS-R was greater than 0.7 at all three visits; r = 0.96 between the scales at the first clinic visit, 0.97 at the second visit and 0.93 at the third visit. Cohen's kappa between scales was 1.0 at the first clinic visit, 0.95 at the second visit and 0.87 at the third visit.
Conclusion: The RPS shows excellent concurrent validity with the FPS-R in school-aged children. The next step will be to examine the psychometric properties of the RPS in pre-school aged children. We are currently recruiting 100 children from the oncology population age 30 months to 59 months. Convergent validity is being assessed by evaluating the agreement between the RPS and their parents' assessment of their pain on the FPS-R using a Bland and Altman plot.

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RETROSPECTIVE ANALYSIS OF REPORTED DRUG ERRORS IN A PEDIATRIC HEMATO-ONCOLOGY WARD

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Background/Objectives: Working on a Pediatric Hemato-Oncology ward (PHO) involves complex medication regimens. Clear procedures with regard to prescribing and administering medications are important. The hospital uses a reporting system to register (near) incidents and to define corrective and preventive actions, without penalizing consequences for the reporter/culprit.
Design/Methods: We retrospectively analyzed the drug errors reported over a period of 4,5 years (September 2010 - February 2015) and studied the difference in drug errors reported before and after the introduction of an electronic medication program (EMP) in October 2014. Incidents are classified according to the point of time in the medication process. Main stages are: prescription, preparation/distribution and administration of medication.
Results: Before the introduction of EMP the mean number of incidents reported was 2.4/month. Drug errors that occurred during prescription (17%, 20/117) were mostly related to prescribing a wrong dose, concentration or frequency.Most drug errors (69%, 81/117) occurred during the administration to the patient and concerned wrong dose/concentration or frequency (30%, 24/81), wrong drug (15%, 12/81) or an omitted dose (25%, 20/81). There was a decrease in the reporting of errors after the introduction of EMP (0.8/month), 75 % of them were errors in the administration to the patient and none during the prescription.

Conclusion: The most frequent reason for drug errors at the PHO-ward is wrong prescription, and more frequently, wrong administration to the patient. During and after the implementation of EMP many 'growing pains' were observed and there was a decrease in reported errors. We suppose a strong underreporting, probably due to lack of time, as the EMP is more time consuming for prescribers and administrators of medication. It remains important, even during changing processes, that all incidents are reported especially to optimize the use of EMP. In this respect it is extremely important to encourage nurses and physicians to report each incident.

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EXPERIENCES OF PARENTS OF CHILDREN WITH CANCER STAYING AT A MOTHERS' HOSTEL AT THE KORLE BU TEACHING HOSPITAL, ACCRA, GHANA

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Background/Objectives: The majority of children receiving treatment for cancer at Korle Bu Hospital are referred from outside Accra. With their parents, they are accommodated at a hospital hostel. This study seeks to explore the experiences of parents of children with cancer in Ghana staying at the Mothers' Hostel.
Design/Methods: A qualitative study was undertaken with parents of children with cancer staying at the Mothers' Hostel of the Korle Bu Hospital. Using open-ended questions, their experiences were explored.
Results: Twenty parents were interviewed. Most (80%) of parents were between 20 – 40 years of age with the same percentage being females. Eighty percent had other children, 80% had stayed at the hostel for more than four months. Thirty percent had not had any visitors since coming to Accra. Sixty percent had difficulty feeding themselves as one stated "I have to go hungry to be able to feed my child". Sixty-two percent of them relied on grandparents and relatives other than spouses to take care of their other children. Only 30% felt comfortable, the rest complained of a lack of privacy and congestion. Of concern was the fact that 80% expressed feelings of wanting to abandon treatment due to financial difficulties. One person stated "I pray God will have mercy on me and cure my child's disease". Other concerns expressed were worries about the children left at home and their work. Surprisingly, only 30% felt their marriages had been affected. Emotional stress was expressed by 70% of them. There was an expression of "I feel helpless and dejected".
Conclusion: Despite free accommodation being provided for parents and children with cancer for the duration of treatment, they still face major psychosocial challenges and potential treatment abandonment. Paediatric oncology staff in developing countries should be aware of this and strategies put in place to address this.

P-415

FOOTSTEPS AND CHALLENGES OF PAEDIATRIC ONCOLOGY NURSING CARE THROUGH ILLNESS AND BEYOND: A UNIT EXPERIENCE

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Background/Objectives: Paediatric cancer nursing in South Africa is enormously challenging as it compromises of medical, physical, psychological, cultural and social problems and issues. These need a nurse who is highly motivated with an inherent drive to move towards self actualization and creative thinking by pursuing knowledge and to give to the oncology community. South Africa is still considered as a developing country where skills and resources are still out of reach. To highlight how challenges, lack of skills and setbacks can lead to de-motivation or perseverance.To promote the culture of caring, commitment and flexibility for those directly or indirectly involved oncology care. To encourage peers to acquire skills, knowledge, do research and case management in spite of all these challenges.
Design/Methods: A prospective observational and cross sectional survey of from 2001-2014: Staff quota on: experience, training/development opportunities and needs, staff retainment and resignations; Analysis thereof is: expert vs. novice is 1:8, carrier opportunities is 1:15, employment vs. resignations is 2:4Client turnover/satisfaction: 400 – 600 a year, survival 70%- 80%Records on disease profile and research: Cancer mutations and presentation are diverse. Media analysis: 'The Star'newspaper, out of 458,933 deaths in the country in 2013, 8.3% were caused by neoplasm and 'The Star' 3/12/2014, pg4.
Results: Limited skills development: 57%, resignations/transfers/ retirements 45%: and patient turn over 75%.
Conclusion: An oncology nurse serves many roles depending on her experience, insight and education on how to handle changes and challenges facing her profession, client and family.The philosophy of caring demands professional growth and development, but with the ongoing challenge of human and material shortages, care will always be compromised.

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BEABOOK: PATIENT-ORIENTED EDUCATIONAL BOOKLET

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Background/Objectives: The child with cancer feels the need to know what is going on, even when the family tries to hide the diagnosis. To inform the child about the disease increases their cooperation and reduces passivity, also increasing their control over the situation. But the majority of the available information isn't adequate for this. It's necessary to establish patterns able to homogenize the meaning of words, phrases and symbols, contributing to minimize the barriers of understanding, providing an efficient and reliable means for the information exchange. For this purpose, we based ourselves on Information Architecture, which consists of design of shared information environments, seeking to ensure comfort first and secondly technology, and Information Design, which equates the syntactic, semantic and pragmatic aspects for the audience.
Design/Methods: To compile all necessary and relevant information for patients and their families, The Beabook was born, an educational booklet consisting of oncologic words and terms. The method used to develop the material includes categorization, labeling, taxonomy, perspective, knowledge management and lexivisual interface. For each stage of the production process - creation, production, validation and approval - the target audience had an effective participation.
Results: The Beabook is being implemented and it's in the process of collecting data of theoretical approaches. Qualitative analysis of the product has been above expectations and has opened the way for patients and families contribution.
Conclusion: To provide good quality information isn't enough. It's necessary that it will be available and appropriate to the target audience, which has reflective thinking about knowledge and skills related to the subject of investigation, or the consequences will be contrary to the proposed objectives. The crisis of contemporary society reflects the difficulty of transforming data into information and this into knowledge. It's necessary to consider Architecture and Design Information disciplines, in addition to effective consumer participation in the creative and production process.

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DEVELOPMENT OF POST ANAESTHESIA RECOVERY SKILLS, KNOWLEDGE AND COMPETENCE, FOR PAEDIATRIC ONCOLODY NURSES WORKING WITHIN A DAY CARE UNIT IN A PRIMARY TREATMENT CENTRE (PTC)

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Background/Objectives: Numbers of children and young people (CYP) with an oncology diagnosis receiving anaesthesia for lumbar punctures (LP), intrathecal agents and bone marrow aspirates (BMA) are increasing due to the implementation of the UKALL 2013 protocol. However, the number of nurses within the day-care (DC) setting competent to recover CYP post anaesthesia does not represent the increasing patient numbers. A standardised development pathway and competency document to support the training of paediatric recovery nurses within the DC setting of PTC is required.
Design/Methods: Data was collated from other PTC's and organisations/associations on competency documents and pathway available for recovery nurse development within the oncology DC setting. This included exploration of external courses/simulation days available for recovery nurses.
Results: It was established that no national or local competencies or role development pathways specifically for paediatric oncology recovery nurses within a DC setting were available. External courses/simulation days were found to be costly and not meeting the requirements of the role within DC.
Conclusion: With support from the anaesthetic team, a competency document was produced and ratified by the Trust. The document confirms key skills and knowledge required for the recovery of CYP within the oncology DC setting. It is to be completed alongside annual compliance in the completion of Paediatric Intermediate Life Support and study days on stabilisation of the deteriorating child. This is all achieved at a local level saving time, finances and meeting operational demands. The continuing role development of the oncology DC nurse was shown to aid job satisfaction by the increased opportunities and varied role, resulting in greater nurse retention.
Development of this innovative document has also ensured patients and their families receive a personalised holistic oncology journey, with care provided within one clinical unit by multi-skilled nurses who know the specific needs and care requirements for the CYP.

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HEALTH BEHAVIORS OF CHILDHOOD CANCER SURVIVORS (CCSS) IN YOUNG ADULTS

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Background/Objectives: This study aimed to find health behaviors of CCSs in Young Adults.
Design/Methods: Participants are survivors aged 18-39 years, ≧5 years after completion of cancer treatment. The original questionnaire was mailed to survivors.
Results: The participants (n=37:M13/F24, mean age 26.6) are survivors of leukemia (n=28, 75.7%), malignant lymphoma (n=4, 10.9%), and solid tumor (n=3, 8.1%) included 10 hematopoietic stem cell transplantation.*LTFU*:28(75.7%) have been seeing doctors on a regular basis. The frequency is ; once a year (12),once a few months - 6 months(12),every month (4). 20 CCSs (54.1%) visit the clinic for late effects from cancer treatment.*Current state*: full time worker(20), part time worker(6), student(3), self-employed(4), unemployed (1) and going community workshop(1). 21(56.8%) survivors lead a well-regulated life style on weekdays and have lunch and dinner every day but 9 (24.3%) are on no breakfast or almost every day no breakfast. *Drinking*: 26 are habitual and 11 are not habitual, Smoking: 29 are nonsmokers, 5 are current smokers and 3 are ex-smokers. Exercise: 23(62.4%) with no regular physical activities.Mean Body Mass Index (BMI) for men is 22.4 and for female is 20.9 which are slightly lower than healthy people.16 have no experience to go on a diet, 15 have, and 6 are on a diet.More than 80 % survivors interested in "health", "things which regulate life rhythm", "exercise" and "meal and ingredients".But there were several CCSs who answered "No time". And 8 including 2 with BMT experience don't pay attention to effect of sunlight.
Conclusion: About half of CCSs have been seeing doctors or such as late effects. The physique tends to be thin but health behaviors are generally good. It is significant to let CCSs who don't exercise regularly understand the importance of physical activities.

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PARENTAL UNCERTAINTY AND HEALTH-RELATED QUALITY OF LIFE [HRQOL] IN CHILDREN WITH CANCER

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Background/Objectives: Research suggests that parents of children with cancer are prone to feelings of anxiety and depression because they are uncertain if their children will live or if the treatment will work. Due to this vulnerability, they may perceive that their child is experiencing poor HRQOL, which in turn could affect the child's treatment outcomes. The Roy Adaptation Model and Mishel's Uncertainty in Illness Theory are the guiding theoretical framework for this study.
Design/Methods: This study will utilize a longitudinal, exploratory design.
One-hundred newly diagnosed children with cancer ages 2 to 17 years receiving care at Boston Children's Hospital will be recruited. The aims are to: 1) Describe the child's HRQOL at time of diagnosis, 2 months and 6 months after diagnosis; 2) Describe the relationship between parental uncertainty and HRQOL in children with cancer, and if this relationship changes over time; 3) Determine the degree of concordance between child self-report and parental proxy report of HRQOL; and 4) Determine if perceived social support, trait anxiety and depression function as moderators between parental uncertainty and HRQOL in children with cancer. Parents will complete the Beck Depression Inventory, the Multidimensional Scale of Perceived Social Support, and the State-Trait Anxiety Inventory for Adults at baseline. Children and parents will complete the Pediatric Quality of Life Inventory 3.0 Cancer Module Scale and the parents will complete the Parents' Perception of Uncertainty in Illness Scale within the first two weeks of diagnosis, 2 months, and 6 months after diagnosis.
Results: The study is ongoing. However, baseline assessment data will be presented.
Conclusion: Once the relationship between parental uncertainty and children's HRQOL is understood, interventions can be developed to help these families with the long-term goal of improving the children's HRQOL.

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YOU'VE ONLY GOT ONE CHANCE TO GET IT RIGHT" CHILDREN'S CANCER NURSES' EXPERIENCES OF PROVIDING PALLIATIVE CARE IN THE ACUTE HOSPITAL SETTING

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Background/Objectives: Palliative care for children with cancer is rarely hospital centred and predominately care is provided in the community or hospice setting. Vast research has looked at the experiences of children's nurses providing palliative care within the child's home environment or the hospice. This research has suggested that nurses need adequate support to avoid stress and burnout. Parental views focus on the nurses attributes as opposed to the clinical skills which are required. This research study wanted to ascertain whether specific educational preparation or support is needed to prepare children's cancer nurses in providing palliative care in the acute hospital setting.
Design/Methods: The research study used a qualitative approach with semi-structured in depth interviews across three primary treatment centres within the United Kingdom that provide cancer care to children.Data was collected and analysed using a phenomenological approach. Data was collected between October 2011 and February 2012. Interviews took place in the participants preferred location and lasted between forty five and sixty minutes. Data was analysed using the Strauss and Corbin method.
Results: Five themes emerged which were 'lack of a plan', 'managing the symptoms', 'family' and 'experience'. Categories within these themes were devised from participant narratives.
Conclusion: The findings of this research study suggest nurses need specific palliative care education not only at pre-registration level but also continuing professional development.

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THE IMPLEMENTATION OF CENTRAL LINE MAINTENANCE CARE BUNDLE IN REDUCING CATHETER RELATED BLOOD STREAM INFECTION (CRBSI) IN THE PAEDIATRIC ONCOLOGY SETTING OF A TERTIARY HOSPITAL

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Background/Objectives: The study aims to evaluate the effectiveness of a central line maintenance care bundle in reducing the rate of CRBSI in the paediatric oncology setting.
Design/Methods: A prospective, descriptive, quantitative study was carried out to monitor the rate of CRBSI for port a-cath and Hickman line before and after the implementation of a central line maintenance care bundle. The components of central line maintenance care bundle were derived from the recommendation by Communicable Disease Centre (USA) which includes hand hygiene, maximal barrier precaution upon line insertion, Chlorhexidine skin antisepsis, training and education. With multidisciplinary approach, interventions were put in place to improve compliance with each component. Hand hygiene audit was done to ensure 100% compliance. All patients undergoing central line insertion were to have Chlorhexidine shower twice prior operation. Chlorhexidine usage for central line related procedures was revised, emphasizing on duration of cleansing and drying. Central line training were organized 3 monthly for both nursing and medical personel. A total of 57 nurses and 54 doctors were trained from Jan 2013 till Jun 2014. Both regular (6 monthly) and ad hoc audits were carried out to ensure compliance. CRBSI rate and epidemiological data were collected 12 months before and 18 months after the implementation of the bundle in January 2013.
Results: Results showed substantial decrease in the rate of CRBSI per 1000 catheter days for both port-a-cath and Hickman line which are lower than the international benchmark set at 1.45 per 1000 catheter days for port a-cath and 4.65 per 1000 catheter days for Hickman line.
Conclusion: The implemented central line maintenance care bundle is effective in reducing the rate of CRBSI in paediatric oncology. Continued vigilant monitoring and strict compliance to standard practices are essential to further minimise and prevent CRBSI.

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CHILDREN AND ADOLESCENT EXPERIENCE OF HAVING A SIBLING WITH A LIFE THREATENING DISEASE - AN EXAM ASSIGNMENT FROM A NATIONAL PEDIATRIC ONCOLOGY EDUCATION IN SWEDEN

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Background/Objectives: Since 2005 there is a 2 years, part time, national pediatric oncology education in Sweden for registered nurses at Karolinska Institute, founded by the Swedish Childhood Cancer Foundation. All participants were supposed to do an examination assignment preferably based on their clinical experiences and needs. In this particular assignment we focused on siblings as we have noticed that the entire family is affected when a child suffers from a life-threatening illness. The aim of this exam was therefore to explore siblings' experiences of having a brother or sister with a life threatening disease.
Design/Methods: A literature review was conducted of eight articles focusing on siblings in the age of 5-30 years, with a brother or sister with a life threatening disease.
Results: The siblings expressed anxiety regarding if, when and how their ill brother or sister should die. They felt anxiety about their parents' wellbeing, but also regarding themselves if they would become ill as well. They described that family life and routines

were changed, the parents were absent and the siblings took much greater responsibility at home. At the same time they described the family got a better cohesion. The siblings had difficulty in school with concentration and homework. They wanted to participate in the care of the brother/sister and needed better medical information from diagnosis and onward. The siblings also expressed that they needed own support from extended family members, friends as well as other adults.
Conclusion: The pediatric oncology nurses have a key role in including siblings in the care and provide age-appropriate information from diagnosis and onward. It was a valuable exam assignment for clinical nurses in order to increase knowledge about clinical related problems, such as - in this case - siblings' experiences, search for literature, compile the new knowledge and use it in practice.

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BALANCING ADVOCACY AND PATERNALISM; RESEARCH NURSES' EXPERIENCES OF WORKING WITH FAMILIES WITHIN THE PEDIATRIC ONCOLOGY CARE

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Background/Objectives: Pediatric oncology care is a research intense environment where most of the families participate in several research studies. By law, it is required that the family gives their informed consent prior to participation. This often means that the informed consent is obtained in close connection to the disclosure of the diagnosis. It is within this complex situation that the research nurse carries out her work.
Design/Methods: Aim: To describe the research nurse's experience of working with families who have been asked to participate in clinical trials at the pediatric oncology ward.Method: This qualitative study used a Grounded Theory (GT) method. Six research nurses and two consultant nurses were interviewed via internet based Communication.
Results: In the research integrated care environment, the nurses' main concern was that the family should have the opportunity to participate in studies that the nurses believed would be beneficial for the child and the family. When obtaining the informed consent, the nurses balanced advocacy and paternalism. The nurses used a number of strategies in order to make sure that the informed consent was obtained. These included: adapting the information, gently introducing the research and selling the research.
Conclusion: If there are language barriers or psychological barriers that impact the family's ability to give their informed consent, then there is an immediate risk that the nurse will give more weight to paternalism when balancing between it and advocacy. Furthermore, there are problems in meeting the child's right to be able to give their consent to participate in research studies.

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PEDIATRIC ONCOLOGY NURSING RELATED KNOWLEDGE ASSESSMENT FOR NURSES OF 17 HOSPITALS IN CHINA

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Background/Objectives: The objective was to know pediatric oncology nursing related knowledge level of nurses caring for children with cancer in China.
Design/Methods: Five hundred and thirty two nurses caring for children with cancer from 17 nationwide hospitals were sampled conveniently and investigated by multiple choice questionnaires on pediatric oncology nursing related knowledge (142 scores) including 5 domains of disease (34 scores), treatment (36 scores), symptom management (33 scores), critical care (18 scores) and technique (21 scores). Variances were analyzed on hospital, hospital-related region, age, education degree, clinical ladder, working duration, specialty, specialty working duration and post.
Results: Mean score knowledge was 62.95±12.05, showing significant difference among variances (hospital: F=13.18, P=0.00; region: F=6.81, P=0.00; age: F=6.96, P=0.00; education degree: F=16.30, P=0.00; clinical ladder: F=11.22, P=0.00; working duration: F=5.57, P=0.00; specialty: F=15.50, P=0.00; specialty working duration: F=6.23, P=0.00; post: F=3.07, P=0.01). Among 5 regions of China, the lowest score (59.19±10.82) existed in the midland. The score of nurses with diploma (58.83±11.65), or working in general hematology unit (52.25±8.14), or working as basic primary nurse (62.63±12.18) ranked the lowest level as predicted, meanwhile, nurses with 4～5 years working experience or 4～5 years specialty working experience showed the lowest score unexpectedly (59.64±13.36; 59.83±13.04). Five domains among education degrees or specialties, four domains, except technique, among ages, (specialty) working durations or clinical ladders, and the domains of treatment and critical care among posts demonstrated significant difference ($P<0.05$).
Conclusion: Nurses caring for children with cancer in the hospitals of China did not have enough specialty-related knowledge which would influence the clinical competence and quality of care. Related knowledge level displayed significant difference among regions, hospitals or specialties, which hinted the necessity of homogeneous education. Nurses among demographic characteristics or working experiences also demonstrated significant difference on knowledge, which indicated the requirement of targeted education.

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EVIDENCE BASED PRACTICE MEETING FOR NURSES IN A NEW PEDIATRIC ONCOLOGY CENTER

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Background/Objectives: The Princess Maxima Center (PMC) for pediatric Oncology (Utrecht, the Netherlands) has opened in October 2014. In the near future, when the care for all pediatric oncology patients in the Netherlands is centralized in the PMC, it will become the largest center of Europe.In this centralization process, nursing staff from all academic hospitals (7) merged into a new, motivated team. The team was challenged by a large variety of care, such as how to withdraw blood from a central line and how to flush it afterwards. This variety is caused by different experience and approach from the academic hospitals. We aim to harmonize the protocols and to work uniform.Therefore, the purpose of this project is to (1) define important differences in care, (2) reinforce conformity and (3) to develop evidence-based protocols for highly variable practices.
Design/Methods: Weekly evidence-based practice (EBP) meetings will be held. Two nurses with EBP experience and training will chair this meeting, supported by experienced clinical researchers. Based on structured discussions, the nursing team will define important differences in care. Thereafter, uncertainties will be prioritized and Patient-Intervention-Comparison-Outcome (PICO) will be made. For each PICO, one nurse will subsequently review all available evidence and prepare a Critically Appraised Topic (CAT). Depending on the results of the CAT, this will lead to new evidence-based care protocols.
Results: Since January 2015 we defined a large variety in care in our EBP meeting. Further results will be presented at the conference: Examples of remarkable differences in care between the 7 academic hospitalsThe priority PICO's of the EBP meetingsExamples of changes in care.
Conclusion: This project will show a way to solve differences in care protocols in a new, large pediatric oncology center. This will improve conformity and ensure high quality and up-to-date protocols.

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SIOP PODC NURSING WORKING GROUP BASELINE STANDARDS ASSESSMENT IN BOTSWANA

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Background/Objectives: The overall survival rate of children with cancer is 80% in high income countries but often less than 25% in low and middle income countries (LMICs) where 80% of children live. Quality nursing care is essential in paediatric cancer care. The International Society of Paediatric Oncology (SIOP) Paediatric Oncology in Developing Countries (PODC) Nursing Working Group developed six baseline standards for paediatric oncology nursing in LMICs.
Design/Methods: Nursing practices of the Paediatric Oncology Ward (POW) of Princess Marina Hospital (PMH) were analyzed by PMH paediatric nurses and compared to the SIOP-PODC standards. PMH is the only hospital in Botswana managing children with cancer. A score of 0-2 (0 - does not meet at all, 1 -occasionally meets, 2 - meets on a regular basis) was applied to each standard.
Results: The POW of PMH did not meet any of the six standards on a regular basis (score of 2). There is neither orientation for POW nurses nor nursing policies and procedures located on the POW (score of 0). The POW occasionally met the nurse:patient ratio of 1:5; although these nurses were not always oncology trained (score of 1). Some continuing education was available but not 10 hours annually as prescribed by the standard (score of 1). Nurses are included as part of the multidisciplinary team; however, there are no dedicated paediatric oncology nurses (score of 1). Although some improvements have been made including hand sanitation, environmental ward deficiencies remain including limited personal protective equipment and isolation facilities (score of 1).
Conclusion: Based on the SIOP-PODC criteria, PMH does not currently meet the standards for paediatric oncology nursing. The availability of oncology training curricula, a dedicated paediatric oncology unit, mentorship through a twinning partnership and paediatric-trained nurses will make reaching these standards a reality.

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PAEDIATRIC NURSES` PAIN ASSESSMENT AND MANAGEMENT SURVEY IN BOTSWANA

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Background/Objectives: Pain in children can be debilitating. Princess Marina Hospital (PMH) in Gaborone, Botswana is the site of the country's only paediatric haematology-oncology program. A survey of nurses in the paediatric medical and surgical wards of PMH was administered to assess general knowledge of paediatric pain management and familiarity with the 2011 Ministry of Health (MOH) paediatric pain policy.
Design/Methods: Paediatric nurses were given a ten question survey on paediatric pain management and five self-assessment queries assessing nurses' confidence managing paediatric pain. One question assessed awareness of the MOH policy.
Results: The survey was completed by 84% (32/38) of paediatric nurses of which 60.7% were female, 75% were Diploma graduates, 21.9% had a Bachelor's Degree and 3.1% had other training. General nursing experience <10 years was reported by 62.5% while 37.5% had > 10 years' experience. A minority (41.9%) of the nurses reported awareness of the MOH paediatric pain policy. Years of experience impacted knowledge of the policy: 0% of nurses with 10-15 years' experience were aware of the policy compared to 42.9% with 0-5 years, 80% with 6-9 years and 60% with >15 years (p=0.03). Pain management knowledge gaps included understanding opioid routes of administration (70% answered incorrectly), childrens' ability to report pain (62.5% incorrect) and opioid oral:intravenous conversion (75% incorrect). There were no knowledge differences based on gender, education level or years of experience. With regard to their confidence in appropriately assessing pain in children, 81.8% of males responded "agree" or "strongly agree" (4-5 on a 1-5 scale) compared to 23.5% for females (p= <0.01).
Conclusion: Based on the survey results, knowledge gaps exist for paediatric nurses regarding the assessment and management of pain in children as well as awareness of the paediatric pain policy. Interventions including mentoring and in-service training will be instituted to narrow this knowledge gap.

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NATIONAL PAEDIATRIC CANCER RECOGNITION TRAINING PROGRAM IN BOTSWANA

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Background/Objectives: The majority of the world's children who develop cancer live in low and middle income countries (LMIC), and most do not have access to diagnosis and treatment of cancer. Thus, while survival of paediatric cancer in high income countries is 80%, survival is often <25% in LMICs. One major barrier to survival is delayed recognition of cancer leading to death before diagnosis or presentation with advanced disease. To improve timely diagnosis of paediatric cancer in Botswana, we conducted a national training of health care workers (HCW) on the recognition of common signs of paediatric cancer.
Design/Methods: A paediatric haematologist-oncologist based at Princess Marina Hospital (PMH), the only hospital treating childhood cancer in Botswana, visited twelve hospitals throughout Botswana. All HCW attending these sessions were instructed on common presenting signs of childhood cancers and the referral process to PMH.
Results: At twelve hospitals throughout Botswana, 297 HCW [137 nurses (46.1%), 102 physicians (34.3%), 58 others/not identified (19.5%)] attended the training. Of the 297 attendees, 222 (74.7%) completed a pre-test, post-test, self-assessment and evaluation. Formal paediatric oncology training (clinical rotation/workshop) was indicated by 7.8% of HCW and 26.7% had paediatric oncology exposure (clinical experience/lectures/readings) during their training program. Awareness of the global burden of pediatric cancers increased by 55% and knowledge of survival rates by 128.3%. Acquaintance with the pediatric oncology referral process in Botswana increased by 133.3%. Respondents found the training helpful (96.6% responded 4-5 on 1-5 scale) with 89.6% saying it would change their practice.
Conclusion: Missed or delayed diagnosis of paediatric cancer negatively impacts survival. The majority of HCW in Botswana indicated they received no training in paediatric oncology. We demonstrated that a brief training session improves health care workers' knowledge of paediatric cancer and understanding of how to refer children with suspected cancer to sub-specialty care.

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HUMAN FACTORS TEAM-TRAINING LEADS TO IMPROVED PATIENT OUTCOMES AT THE BEDSIDE FOR THE PAEDIATRIC ONCOLOGY CHILD

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Background/Objectives: Much has been published about the positive effects of team-training simulation in the healthcare setting. When healthcare teams communicate efficiently we can expect improved team processes leading to better patient outcomes and decreased adverse events. At the SIOP 2011 conference held in Auckland delegates where given the opportunity to take part in a trial human factors team-training simulation session designed specifically for the paediatric oncology environment. Interest amongst delegates was high with the majority stating that they increasingly wanted active learning opportunities at the bedside.
Design/Methods: The findings from the trial session run at the SIOP conference lead us to develop a permanent paediatric oncology programme. Building on the foundations already laid by the Starship Simulation Team we were able to take what had worked in other areas of the hospital and tailor it to our specific needs. In taking in-situ human factors team-training to the bedside it allowed us to meld together a combination of different learning styles that enabled us to demonstrate improved patient management at the bedside.
Results: By applying the principles of crisis resource management it has been noted that responses to and management of the deteriorating child have improved greatly. By standardising our teaching model we have been able to create a standard approach to care. There is now also evidence of improved communication within our team, leading to quicker identification and management of the deteriorating child.
Conclusion: Within one year we have built an in-situ human factors simulation programme for the paediatric oncology environment. Where previously there was uncertainty and fear around simulation there is now a willingness to embrace not only in-situ simulation but a variety of different education techniques.

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TRANSITIONS THROUGH SURVIVORSHIP: MODEL OF CARE AFTER CHILDHOOD CANCER TREATMENT

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Background/Objectives: The issue of transition is a central theme and repeated experience in survivorship following childhood cancer treatment. In many cases this involves transition from active treatment to surveillance, to long term follow up/supported self management as well as transition across paediatric, teenage and adult services. The final transition differs from other childhood diseases, as cancer itself is no longer a problem. However, the potential complexity of outcome can create dependence on the paediatric oncology setting and may delay the transition process to late adolescence or early adulthood. Staff working in a single paediatric oncology centre in the UK reflected that these multiple transitions, dependence and meeting the ongoing needs as adulthood progressed could be smoother, more proactive and user focused.
Design/Methods: Building on previous work undertaken in national survivorship programme a revised model of care was designed and implemented. This programme: Educates children on their cancer diagnosis, potential and actual consequences of treatment; Encourages and supports incremental participation in self management; Prepares for transition to the teenage survivorship clinic; Increases teenager's autonomy in their care and holistic needs through ownership of their treatment summary, care plan and holistic needs; Prepares teenagers for discharge to supported self-management in the community or; Transition to an adult survivorship clinic at a new centre with expertise in sub specialities required for adulthood.
Results: This programme has allowed a more cohesive, planned and user focused model of care. A model that allows survivorship to reflect the bi-psychosocial model of development of childhood, adolescence and adulthood. Staff work with those who use the service on an individual pathway of care and have collaborated with colleagues across services and providers to allow managed transition to adulthood.
Conclusion: This poster describes the ethos, design, challenges, collaboration and implementation to develop a survivorship programme creatively and within finite resources.

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DEVELOPING A NURSE-LED CLINIC FOR PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKAEMIA DURING MAINTENANCE THERAPY

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Background/Objectives: Children on maintenance therapy attend clinic once a month for review and administration of bolus vincristine (VCR). The child is reviewed by the Consultant, Leukaemia Advanced Nurse Practitioner (ANP) or a Specialist Registrar. A clinic nurse then inserts a cannula and administers the vincristine which is checked by a second nurse. Both of these steps can incur a long period of waiting for the patient and family during a busy treatment clinic. A nurse-led clinic has been set up to improve the patient pathway and to ease the congestion in consultant-led clinics.
Design/Methods: Following initial written consultant referral, children are booked into a 30 minute appointment every 4 weeks. The child is reviewed by the ANP and the VCR given immediately after the consultation, with the ANP acting as the second checker to the cannulating nurse. Children eligible for the clinic receive 100% doses of VCR and dexamethasone. Those patients with significant toxicity or who are not receiving 100% doses remain in the consultant-led clinic. During the clinic's first 10 weeks families were offered the opportunity to complete the hospital friends and family survey and data was collected to ascertain the length of time each patient spent in clinic. This was also collected from patients attending the consultant-led clinics to enable data comparison.
Results: With 51 clinic attendances the average time spent in the nurse-led clinic was 50 minutes compared to 2 hours and 20 minutes in the consultant-led clinic. Patients were seen on average within 10 minutes of their appointment time compared to 50 minutes in the consultant clinics.100% of parents who completed the hospital friends and family survey said that they are extremely likely to recommend the service to others.
Conclusion: The data collected demonstrates that the nurse-led clinic provides a more time efficient service without compromising patient and family satisfaction.

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SURVEY OF PEDIATRIC ONCOLOGY NURSING EDUCATION IN SIXTEEN COUNTRIES

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Background/Objectives: In response to the lack of specialized pediatric oncology nursing education and training at St. Jude Children's Research Hospital international partner sites, the Latin American Center for Pediatric Oncology Nursing Education was founded in 2007. The center provides culturally sensitive and language appropriate training and ongoing mentoring of pediatric oncology nurse educators, a role pioneered in Latin America through this program.
Design/Methods: In efforts to assess nurse educator roles and programs at International Outreach Program partner sites, including those outside of Latin America, the International Outreach Nursing Program conducted an audit through a web-based survey. The survey assessed orientation program and continuing education content; the nurse educator role, responsibilities, and satisfaction, and nurse patient ratios. Thirty-two nurse educators and/or administrators from twenty-five hospitals in nineteen countries were invited to participate in the survey.
Results: Responses were received from twenty nurses representing sixteen countries, six from lower-middle income countries, thirteen from upper-middle income countries, and one from a high income country. Of those, fourteen reported having a pediatric oncology nursing orientation program in addition to a hospital-based orientation program. For this survey, orientation was defined as two weeks of pediatric oncology education in addition to hospital orientation. Of the fourteen, two met the criteria; however, supportive documentation was not provided. Eleven out of twenty reported having a full-time pediatric oncology nurse educator. Part-time educator positions involved staffing or supervisory responsibilities and a limited amount of time for nursing education. The average nurse-to-patient ratio was 1:6, ranging from 1:3-16, with nine hospitals' nurse patient ration $\geq$1:6.
Conclusion: Pediatric oncology nurses in low, middle, and upper-middle income countries continue to have less than optimal support and education. This is a major impediment and contributes to the disparity in survival rates between high and low income countries.
Acknowledgements: Thank you to the American Lebanese Syrian Associated Charities (ALSAC).

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COMMUNITY OUTREACH: EDUCATING THE WELL CHILD AND EASING TRANSITION AFTER TREATMENT FOR THE ONCOLOGY PATIENT

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Background/Objectives: Community outreach is the responsibility of oncology nurses worldwide. Cancer prevention for lung, skin and cervical cancers must begin at a young age. Research shows a link between sunburns in youth and an increased risk of skin cancer; the known cause in 95% of cervical cancer is Human Papilloma Virus; one-third of young smokers will die prematurely from a smoking-related disease.
Design/Methods: Recognizing that the complex care of the pediatric oncology patient does not cease upon discharge the Dana-Farber/ Boston Children's Cancer and Blood Disorders Center created the Pediatric Oncology Community Outreach Program. This hospital-based program consists of a home visit to facilitate the coordination of care between the hospital, home and community for a newly diagnosed patient. The goal of the visit is to reinforce and review discharge instructions, medication reconciliation and plan of care with community agencies. The Pediatric Community Cancer Prevention Initiative uses a mobile health van delivers an evidenced-based prevention curriculum to schools, health fairs, and beaches. This program is based on the assessment of children's literacy, learning styles, knowledgebase and cultural concerns.
Results: Ongoing monitoring of this program has revealed that 57 percent of patients required an intervention in the transition from hospital to home by the pediatric oncology nurse. The most common interventions include medication management; central line care and issues related to home care supplies. The Pediatric Community Cancer Prevention Initiative educates approximately 500 children and families each year in the community. Using validated tools to measure effectiveness, the Harvard School of Public Health will study the impact of this program on behavior, prevention and outcomes.
Conclusion: Community outreach programs are aimed at teaching well children healthy behaviors and cancer prevention strategies. Equally as important are nurse designed community outreach programs that target patient education needs when transitioning from hospital to home.

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IMPACT OF THE IMPLEMENTATION OF A NUTRITION THERAPY PROTOCOL ON UNDERNUTRITION IN CHILDREN AND ADOLESCENTS WITH CANCER

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Background/Objectives: Despite advances in Paediatric Oncology, undernutrition is still a major concern among these patients all around the world. However, Nutrition therapy is often neglected, regardless of studies demonstrating that undernutrition is strongly associated with poorer outcomes and remediation of poor nutritional status results in survival comparable to that of children with optimal nutritional status. The use of Nutrition protocols is essential to standardise nutritional care and follow up. The aim of this study was to investigate whether the implementation of a Nutrition therapy protocol at a tertiary Paediatric Oncology hospital in Sao Paulo, Brazil had an impact on undernutrition.
Design/Methods: A database containing nutritional assessments of children and adolescents with cancer from April/2007 to December/2014 was analysed. The data was divided in before and after the implementation of a Nutrition therapy protocol (January/2012) and the percentage of patients classified as undernourished by mid upper arm circumference (below 5th percentile according to Frisancho, 1999) was compared. The chi-square test was used to verify the statistical significance of the difference between the frequencies.
Results: A total of 4502 nutritional assessments of oncologic patients from 1 to 18.9 years were analysed, 1588 before (42.6% female; mean age 8.9 years) and 2914 after (42.7% female; mean age 9.7 years) the implementation of the protocol. The frequency of undernourished patients dropped from 34.6% to 26.9% ($p < 0.05$).
Conclusion: The implementation of a Nutrition therapy protocol decreased the frequency of undernutrition in this group of paediatric oncology patients, as measured by MUAC.

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THE DIETARY RESTRICTIONS AT HOME BETWEEN CYCLES OF CHEMOTHERAPY

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Background/Objectives: During the period patients experience chemotherapy induced myelosuppression, dietary restrictions are used to prevent infection. However experience shows the details of dietary restrictions vary widely between establishments. This study aims to determine how widely dietary restriction criteria, including the commencement and cessation of dietary restrictions and the specific foods restricted, vary with each institution. The results showed that for patients at home between cycles of chemotherapy, some establishments instated similar restrictions to neutropenia patients while others had no restrictions at all. The objective of this study was to determine what foods were restricted at home between cycles of chemotherapy.

Design/Methods: Mailed survey. The anonymous questionnaire was sent to one nurse working at each of the institutions registered with JPLSG (145 institutions). The study period was between February and March 2013.
Results: Thirty-seven (25.5%) nursing administrators agreed to participate in the survey. Twenty-eight surveys were returned (collection rate 75.7%). Of the institutions that responded, 11(39.3%) wrote about dietary restrictions during that time. Two (18.2%) establishments had no dietary restrictions. Two institutions used the same restrictions as for a period of neutropenia, and seven establishments used laxer dietary restrictions than for neutropenia. The most commonly restricted foods were raw meat and raw seafood (nine institutions each; 81.8%) and raw eggs (seven; 63.6). Followed by natto, honey, natural cheese and raw cream (three; 27.3%), then Japanese pickles, fresh vegetables and fruits, unroasted nuts and sushi (two; 18.2%).
Conclusion: During at home periods between chemotherapy treatments there are institutions implementing dietary restrictions and others that don't. Among institutions implementing dietary restrictions there was a wide range of restrictions from those implementing the same restrictions as for neutropenia and others limiting nothing but raw fish, meat and eggs.

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IMPLEMENTATION OF A NURSE-LED CLINIC FOR CHILDREN WITH A BRAIN TUMOR ON THE PEDIATRIC HEMATOLOGY WARD : FIRST INSIGHTS

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Background/Objectives: In 2013 a nurse-led clinic for patients with solid tumors was introduced on our ward. Initially we focused on children diagnosed with brain tumors. They often receive a combination of surgery, chemotherapy and/or radiotherapy. Inevitably, they have contact with a wide range of professionals. Our goal is to improve patient care by introducing a nurse as case manager during this complex pathway.In the nurse-led clinic, the consultations take place on well described time points as well as on demand of the patient and his parents. These consultations are free of charge.
Design/Methods: We analyzed 6 months records from the newly established solid tumor clinic. We compared expected number of visits based on the time points with the reality and looked at reasons for consultation.
Results: Thirty patients were diagnosed with and/or treated for a brain tumor and included in this study. 230 consultations took place. The average number of visits for each patient was 7. During these visits different topics were discussed (n=588): information about treatment itself (n=100), follow up (n=115), and this often in combination with emotional support for patients and their parents (n=235), are most common discussed items. Considering the key-time points (at diagnosis, before surgery, before start chemotherapy, at the end of treatment,..), we expected 114 visits. The patients or their parents asked for 116 extra visits while hospitalized, by e-mail or by telephone.
Conclusion: Despite the short period of implementation, we experienced that patients and their parents find their way to the nurse-led clinic, not only at key-time points. The nursing consultant is accessible when needed to provide more information .Our main goals for the future are to inform all health care providers involved in the care for these children about the nurse-led clinic and to anchor it in a clinical pathway for children with a brain tumor.

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TO ASSESS THE LEVEL OF SATISFACTION AMONG PARENTS OF CHILDREN WITH CANCER REGARDING NURSING CARE IN TMH

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Background/Objectives: Patient satisfaction has become an important indicator to measure the quality of care rendered to the patients while in hospital. Patient satisfaction surveys can help identify ways of improving nursing and health care services. The pilot study was planned to assess the parent satisfaction with nursing care in selected hospital. To identify level of parent satisfaction in various aspects of nursing care and thereby improve the quality of care and approach. Set Up: Pediatric Ward of TMH.
Design/Methods: Design: Descriptive Exploratory study. Methodology & Data Collection: The study tool was a questionnaire which had four aspects of nursing care: *communication, physical, psychological and socio-economical* and assessment biographic data of the parents.
Results: The overall rating scale was 4.6 on an average (on a Likert scale of 1-5 where 1 was poor rating and 5-excellent). The mean score was 93.1. Highest scores (109) was for infection control practices communicated well and timely reinforcement given. Lowest scores (79) was given for explanation during orientation phase and diagnosis, physiology of disease, treatment and prognosis of the child. There was a trend seen with the patients admitted first time were more satisfied than those admitted more than once. The nurse scored 3.7 mean score (out of 5) for reference given to social help given by hospital and various NGOs.
Conclusion: Nurses are pivotal in communicating and counseling about all aspects of nursing care. Hence this could help to reduce the fear, anxiety and uncertainty among parents and children.

Posters: Psychosocial (PPO)

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TO ASSESS THE CONTINUED IMPACT OF HOLISTIC CARE PROVIDED AT ST. JUDE INDIA CHILDCARE CENTRES (SJICCC) TO PEDIATRIC CANCER PATIENTS, THEIR FAMILIES AND COMMUNITIES

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Background/Objectives: SJICCC has provided a 'home away from home', for 5087 children since 2006. An earlier study undertaken with ALL patients from Tata Memorial Hospital and presented at SIOP 2012 in Auckland showed that the holistic care provided to these children did favorably impact both morbidity and mortality. The purpose of this study is to understand the impact St Jude's has had on the quality of life of patient-families and communities when they return home after treatment. To use these findings to further support the families, as well as improve our model.
Design/Methods: A pilot study was conducted with 30 families at the centre to establish the parameters of the study. A random selection of 37 families who have returned home and who agreed to participate in the study and home visits were interviewed. Their homes were photographed and a checklist of items observed was maintained. Before returning home 24 families were counselled how to handle the readjustment. Three of the older children also participated voluntarily. All were contacted to follow up and their feedback is recorded.
Results: There is an observed change for the better for the entire family when the daily, routine, cleanliness of the home and eating habits improve. More than 70% of the families have managed to keep their homes clean. Children learn these good habits and pass them on to others. Thirteen(or 34.21%) of the families have relocated for better homes and schools. The 24 families counselled prior to returning home found the sessions valuable. They appreciated the ongoing support. All found the information regarding water purification, maintaining harmonious relations with family members and responding to medical emergencies particularly useful.
Conclusion: The study shows the impact of holistic care has been long lasting and has a ripple effect on the extended families and communities.

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DEVELOPMENT OF A CHILD EXPERIENCE MEASURE FOR CHILDREN WITH CANCER

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Background/Objectives: Little is known about young children's views of hospital care and whether services meet their needs. Most measures are aimed at children older than seven years and rely on parents as proxies for the younger age group. There is a lack of validated measures for children with cancer. A multi-professional working group undertook to develop a measure for children with cancer, ages four to twelve to report their experience of being in hospital.
Design/Methods: The group employed a rigorous development process drawing on the principles of service evaluation. A literature review was first undertaken to identify the domains and questions around which the measure would be structured. A creative process between the group and an artist followed to identify the format and images for the measure. Input from other professionals, stakeholders and parents in the development of the measure were obtained by means of an expert advisory forum. The measure was then shared with children with cancer and their families at a one-day interactive workshop, including design and testing activities. Feedback was utilised to revise the measure and inform development of a digital version.
Results: The key domains identified from the review were: overall experience; physical environment; social environment; interactions; treatment and procedures, and feelings. The measure consists of a series of cards with positive/negative images on opposite sides that explore each domain. A list of questions accompanies each image, and acts as an additional prompt.

Conclusion: A collaborative approach involving children, families, professionals, stakeholders and an artist enabled the working group to develop a measure designed specifically for children with cancer. The measure builds on existing knowledge and highlights the importance of consulting with children in the creation and early testing of a prototype. The development process will be presented followed by a demonstration of the digital version.

P-440

THE DEVELOPMENT AND IMPLEMENTATION OF A HOLISTIC NEEDS ASSESSMENT TOOL FOR CHILDREN WITH CANCER AND THEIR FAMILIES

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Background/Objectives: Cancer in childhood has social, practical and emotional consequences in addition to the effects on the child's physical health. In the UK, national guidelines state that keyworkers (who are usually Specialist Nurses) need to assess and document these needs, and address them through multi-disciplinary working and signposting. Patients' key concerns can be assessed through a Holistic Needs Assessment (HNA). To date, the HNA tools in the cancer literature are adult-focused and tailored to individuals. There is a need to design a child-focused tool that recognises that the wellbeing of the child with cancer is dependent on his or her whole family being supported. A pilot project is being undertaken at Great Ormond Street Hospital to address this gap.
Design/Methods: A Holistic Needs Assessment tool that is suitable for children and families was developed. Specialist cancer nurses were given a tailor-made 2-day training course to introduce them to the tool, enhance their communication skills, and practice using the tool in semi-structured interviews with actors. They then piloted the use of the tool with recently diagnosed children and their families.
Results: The effectiveness of the HNA tool will be assessed by evaluating families' and nurses' and feedback about Holistic Needs Assessments, as well as an analysis of the time this takes for nurses. Specific case examples will be shared. The question of how this work complements the work of the wider multi-disciplinary team, including social workers and psychologists, will also be addressed.
Conclusion: Training specialist nurses to carry out Holistic Needs Assessments can equip the service to better identify and meet the emotional and social needs of children with cancer and their families. Some of the challenges in the process of developing and introducing a new tool for use by specialist nurses will be discussed.

P-441

BEHAVIORAL CHANGES IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA TREATED WITH BFM-95 PROTOCOL

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Background/Objectives: CNS prophylactic treatment has reduced the risk of CNS relapse and thereby resulted in a remarkable increase in survival rates. However, improved survival rates have not been achieved without neuropsychological sequelae. Therefore, this study aimed to examine the impact BFM-95 protocol on behavioral problems of children diagnosed with ALL.
Design/Methods: All children (n=25) diagnosed with ALL who received CRT and HD-MTX as part of their treatment protocol were included. Child Behaviour Check list for ages 6-18 was used to assessing the behavioural problems (anxious/depressed, withdrawn/depressed, social, somatic complaints, attention, thought, rule breaking). Five assessments were done during induction, end of re-induction, end of re-induction II, commencement of maintenance, and end of maintenance. ALL children were compared to a group of healthy children (n=55). Baseline and post assessment completed for healthy children while baseline and post assessment were done for ALL children. Parents completed the behaviour check list questionnaire across those five phases.
Results: Behavioral problems of somatic complaints, rule breaking, and aggressive behavior differed significantly among five assessments. When comparing the first, second, third and fourth assessment mean scores, ALL children's scores decreased on somatic complaints and aggressive behaviour by the fifth assessment after the completion of the CNS prophylactic treatment.There was no significant difference between treated ALL and healthy children with respect to behavioral problems on anxiety/depressed, withdrawn/ depressed and aggressive behavior in the baseline assessment. Although, there was a significant difference observed between treated ALL children and healthy children on anxious/depressed, withdrawn/depressed social problems, thought problems, attention problems and aggressive behavior at the post assessment.
Conclusion: Behavioural problems of somatic complaints, aggressive behaviour and rule-breaking behaviour were of more concern after diagnosis and during the intensive phase of treatment. It was found to gradually reduce to the baseline scores and normal behaviour was evident after completion of the treatment.

P-442

IN WHATEVER LANGUAGE 'CANCER' IS UNDERSTOOD: EXPERIENCES OF LIMITED ENGLISH PROFICIENT HISPANIC FAMILIES RECEIVING CARE FOR PEDIATRIC CANCER

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Background/Objectives: The diagnosis of cancer in a child is always stressful but more so for families who do not speak the native language of the country where they are receiving care. The objective of this study was to explore the perspectives of Hispanic families with limited English proficiency receiving care for their child's cancer. The aim of the study was program development that would best meet the needs of these families.
Design/Methods: Parents were recruited at a tertiary care pediatric care institution in the Midwest to participate in a qualitative focus group conducted in Spanish. A total of 10 parents from 6 families participated. The focus group was digitally recorded, transcribed verbatim in Spanish, translated to English, double checked for accuracy by a certified bi-lingual translator, and then analyzed for themes pertinent to the experience of families.
Results: Three main themes emerged from the focus groups: 1) Interpreter errors and miscommunication and the burden of siblings or the patient interpreting for family; 2) Language is the key to building relationships and trust through the cancer experience; 3) the sharing of socio-cultural experiences is cornerstones to provider-patient trust.
Conclusion: This study demonstrated the importance of access to bilingual providers who can speak directly to patients of any language to avoid challenges with interpretation, form direct and meaningful relationships, and provide socio-culturally competent care. We now have a Spanish-speaking clinic with a dedicated bilingual provider for oncology care. It is important to identify bilingual providers who can provide equal care to families with limited English proficiency regardless of their primary language, particularly when they are dealing with a long-term, life-threatening illness.

P-443

COMPLEMENTARY AND ALTERNATIVE (CAM) PRACTICES, TRADITIONAL HEALING (TH) PRACTICES, AND CULTURAL COMPETENCY IN PEDIATRIC ONCOLOGY IN HAWAII

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Background/Objectives: Hawai'i is an ethnically diverse island state with a high rate of both Traditional Healing (TH) and Complementary and Alternative Medicine (CAM) use. The aim of this study is to assess the rates of use of TH and CAM within the pediatric oncology population, as well as glean any insights into delivering culturally competent care to these families.
Design/Methods: A 9 item anonymous survey is being distributed to every pediatric oncology patient in the inpatient and outpatient setting at Kapi'olani Medical Center for Women and Children for a 3 month period starting March 2015, hoping to capture all children in active treatment (estimated 25-30 patients) as well as long term follow ups (between 60-90 patients). The survey inquires about patient and family ethnicity, traditional healing practices used in the home and hospital, and CAM practices used in the home and hospital. It also inquires about their perception of culturally competent care received in the medical center.
Results: Results from the survey will provide data on a more refined ethnic breakdown of the patient population, what percentage of each ethnicity uses TH/CAM, and what types of TH/CAM are being utilized. Free form comments regarding culturally competent care will also be included and analyzed for any common themes.
Conclusion: Results from the survey will be analyzed reported prior to SIOP meeting, adding to the body of knowledge on the rates of use of TH and CAM in the pediatric oncology population in Hawaii, an ethnically diverse island state. This knowledge could be used to improve the delivery of culturally competent care to this patient population.

P-444

ASSESSMENT OF SLEEP IN PEDIATRIC PATIENTS WITH CANCER

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Background/Objectives: The aim of this study was to characterize sleep disorders of children with cancer.
Design/Methods: Participants included children (5 – 12 years old). There were 135 children with cancer and 190 healthy controls eligible for evaluation. The patient group

consisted of 104 (77%) children with lymphoproliferative cancer (acute lymphoblastic leukemia (ALL) n: 76, lymphoma n:28), and 31 (23%) with diagnosis of solid tumor. Oncologic treatment was completed in 100 patients with cancer (Group1: survivors), treatment is continuing in 35 patients (Group2). Healthy children matched for age, sex, economic status, parental education and family structure constituted the control group (Group3). Sleep was evaluated by using the validated Turkish version of the Children's Sleep Habits Questionnaire (CSHQ). Clinical characteristics and the treatment details of the patients were recorded from medical records. No significant differences was found between parents of patients and controls with respect to age, gender and educational level.
Results: Sleep problems were detected in half of our patients with cancer. There were no statistically significant differences in total sleep score and subscale scores between patients and healthy controls. No significant differences for average bedtime, length of wakings and total sleep duration existed between the groups. Solely the waketime was found significantly different between patients and controls. We couldn't demonstrate significant difference in sleep scores and sleep characteristics of patients who did or did not receive intratechal chemotheraphy, HD methotrexate, HD cytarabine, craniospinal radiotherapy.
Conclusion: Although our results indicated that neither childhood cancer survivors nor patients with cancer during treatment period had no more sleep problems than their healthy peers, sleep problems were not uncommon in whole study group. Sleep problems were identified in about half of of children with cancer and also healthy controls. This study underlines the need to screen, assess and manage sleep problems in children with diagnosis of cancer.

P-445

EVALUATION OF HEALTH RELATED QUALITY OF LIFE IN CHILDREN WITH CANCER AND IN THEIR MOTHERS

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Background/Objectives: To evaluate quality of life of children with cancer both child's and mother's perspectives. Also to evaluate quality of life of their mothers.
Design/Methods: Children who diagnosed with cancer and has been treated at least 6 months in our center and their mothers are included to study. Quality of life (QoL) is evaluated by quality of life questionnaire (KINDL®). Quality of life of mothers was evaluated by WHO Quality of Life -BREF scale (WHOQOL-BREF). Ethical committe approval was taken.
Results: The median age of patients was 9 years, and M/F ratio was 0.65. The mean age of mothers was 34 years. The total QoL score and chronic disease QoL score of patients were 71 and 55, respectively. The total QoL score and chronic disease QoL score of patients with the mother perspective were 69, and 53, respectively. The QoL scores of patients with both the patient and the parent perspective was found correlated. The maximum and minmum scores of patients were in family well-being subscale (79), and in physical well-being subscale (63), respectively. There was no gender difference in total scores of QoL. The QoL scores of mothers were 14.11±2,9 in physical field, 11,55±3,4 in physicological field, 13,69±3,4 in social field, and 11,9±2,6 in environmental field. The self esteem scores of patients and environmental field scores of mothers was found correlated.
Conclusion: Children with cancer show lower QoL scores compared to the general population that published in the literature. In patients especially chronic disease QoL scores, and in mothers QoL scores of physicological and environmental fields were effected. It has been thought that environmental factors including economic status, financial resources, physical security and reachability of health care, effect the self esteem of children with cancer. Further studies are needed in this field.

P-446

THEY WANT THE TRUTH WHILE STILL BEING ALLOWED TO HOPE – AN INTERVIEW STUDY WITH SEVERELY ILL CHILDREN ON RECEIVING BAD NEWS

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Background/Objectives: It remains a great challenge when and how to inform a severely ill child about Bad News, e.g. that no more treatment is available and the disease will lead to death. Studies focusing on the child's own perspective on how they wish to receive Bad News are few. In the present study we interviewed children with malignancies regarding their own preferences on how they wish to receive Bad News.
Design/Methods: We conducted individual interviews with ten children, aged between 7 and 17 years, under treatment for a malignancy at a single pediatric oncology unit in central Sweden. Interviews were audiotaped and analyzed with qualitative methodology using systematic text condensation.
Results: The children expressed that they wanted truthful information, and they did not want to be excluded from Bad News regarding their own illness. However, even though they expressed a wish for truthful information they also wanted Bad News to be given in as positive wordings as possible, allowing them to keep hope. In addition, the children wanted to receive Bad News at the same time as their parents and in words they could understand.
Conclusion: All children in our study expressed a strong wish to receive truthful information even in the case of Bad News. Importantly, they wished Bad News to be delivered in a sensitive way allowing for a glimpse of hope to remain. Our findings may assist physicians struggling with how to inform severely ill children about a poor prognosis.

P-447

ACCESS TO CARE AND PSYCHOLOGICAL WELL-BEING IN PEDIATRIC ONCOLOGY

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Background/Objectives: Research indicates that demographic and community factors such as patient age at diagnosis, number of local primary care providers, and community socioeconomic status may be related to patient access to specialized oncology care and patient medical outcomes. These variables have yet to be examined as they relate to psychological outcomes. The aim of this study was to examine demographic, family, and community factors as they relate to access to care and psychological well-being in children with cancer and their caregiver.
Design/Methods: Participants were 223 caregivers (89% mothers; 54% married) of children diagnosed with cancer ($M = 11.1$ years; 44% female; 47% White, 48% African American; *Med* time since diagnosis = 2.2 years). 30.1% children were diagnosed with ALL/AML, 26.9% brain tumor, 14.3% solid tumor, and 28.7% another type of cancer. Caregivers completed demographic information and the Family Symptom Inventory, a measure of child and caregiver depression/anxiety symptoms. State records provided local number of pediatricians and median community income. Distance from the single specialty pediatric oncology center was calculated using GoogleMaps. Analyses were conducted in SPSS 22.0.
Results: Child demographic variables (age at diagnosis, gender, ethnicity) were not independently related to child or caregiver depression/anxiety (p's > 0.05). Number of local pediatricians, median community income, and distance from specialty oncology care were also not related to child or caregiver depression/anxiety (p's > 0.05). However, caregiver financial difficulty was associated with both child ($t = 2.41$, $p = 0.02$) and caregiver ($t = 4.40$, $p < 0.01$) depression/anxiety symptoms. More African American caregivers reported financial difficulty than White caregivers ($\chi^2 = 5.5$, $p = 0.02$).
Conclusion: Access to local medical care and specialty oncology care were not associated with psychological outcomes in this pediatric oncology sample. However, psychological health disparities appear to exist for African American families due to more frequent financial difficulties.

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FIRST SUMMER SCHOOL FOR CHILDREN WITH CANCER IN ISTANBUL

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Background/Objectives: Summer school / camp programs are wonderful experience for kids with cancer and their families. Although these programs are available in USA and West Europe, they are not common in developing countries.
Design/Methods: "The summer school for kids with cancer and their families" project, the first of its kind in Istanbul, Turkey, was planned and coordinated by Izzet Kebudi, a senior in high school who had previous training/experience of a summer school program for children in a limited-resource area in Turkey. The summer school was free of charge. Volunteers of the Childhood Cancer Love and Support Society (COKSEV) supported the project. A short survey at the end of the summer school was done to get feed back for promoting the project for coming years.
Results: 40 children with cancer, their siblings and parents joined the program. Half were coming from other cities or neighboring countries. Most families had poor socioeconomic resources. The major theme was "To learn about our environment". A one-week program was done, continued with once weekly tours during the summer. Each day education in English for beginners, painting/music, outdoor excursions in Istanbul were done. These included, historical tour of Istanbul, Miniaturk (an openair museum), a Bosphorus boat tour, Classic Car Museum, Aquarium, Turkish Airlines Flight Simulation School, Helicopter Ride over Istanbul. Every day breakfast and a full

lunch was served to all children and families. The kids and families were very happy to join such a program and expressed their wish to join further programs.
Conclusion: The Summer School Project was very succesful and gave the patients, siblings and parents a chance to be together, have fun and to open up. They expressed that during the psychological burden of cancer, it may them better cope with cancer and their treatment process.

P-449

SECONDARY TRAUMA FACED BY HEALTH PROFESSIONALS PROVIDING END OF LIFE CARE TO CHILDREN WITH CANCER

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Background/Objectives: Health professionals who deal with end of life care, have the job of breaking bad news and taking the patient through the treatment process with a child with cancer also undergo secondary trauma which affects their quality of life.
Design/Methods: Twenty-four health professionals were interviewed using a semi structured questionnaire and these included mental health professionals, nurses and doctors who were working with children with cancer in Children Cancer Unit, Indus Hospital.
Results: Qualitative analysis of data gathered from interviews revealed themes such as feelings of helplessness, repression of their emotions and an aversion to noise and crowds. Some turned to family and friends for comfort and reassurance. Quality of life and emotional well being were factors that were adversely affected as health professionals carried the aftermath of the effect of end of life care into their personal lives and interpersonal relationships.
Conclusion: Health professionals' need for venting and training in stress reduction and self awareness activities are possible ways so as to help them in overcoming secondary trauma.

P-450

DEPRESSIVE TRENDS IN CHILDREN AND ADOLESCENTS SUFFERING FROM BETA-THALASSEMIA

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Background/Objectives: Thalassemia is a chronic disease affecting 10,000 people in 60 countries (Alavi.A 2007). Many studies show that prolonged medical conditions cause depression (Patten, 1999; Gagnon & Patten, 2002; Katon.2003, Patten, 2005). Due to the invasive procedures and suffering, Beta-Thalassemia cause great psychological distress to both children and their caregivers (Klein, 1998). Study shows 14-24% prevalence of psychiatric problems in Thalassemic patients (Hoseini SH et al, 2007).Our current study aims to determine the risk factors and frequency of depressive trends in children and adolescents suffering from Beta-Thalassemia.
Design/Methods: Sample consisted of 195 registered patients of A.M.T.F (Female=95 and Male=100). Based on age range the sample was divided into two groups, Group A = children (4-9 years) and Group B = adolescent (10-16 years). Detailed interview with a self-made screening measure was administered on parents to find out the level of depression in patients.
Results: Chi-square and t-test was applied in order to analyze the data. Results show high prevalence of depression, depression n= 131(66.83%), no depression n=65(33.16%). Analyses reflect that age influences the level of depression Adolescent (71.05%) and Children (64.16%). Analysis also shows difference in level of depression between both genders. ($t=2.975$, $p<.05$).
Conclusion: There is a high possibility of developing depressive trend in children affected with Beta Thalassemia; especially females. Therefore, there is a dire need of psychological screening and appropriate treatment in order to improve physical; as well as mental health.

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QUALITY OF LIFE AND ADAPTIVE BEHAVIOR OF CHILDHOOD BRAIN TUMORS SURVIVORS - COMPARATIVE ANALYSIS, PRACTICAL APPLICATIONS

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Background/Objectives: Difficulties with operationalization of the quality of life (QoL) concept, the reliability measurement problem, and discrepancies between the health related QoL and personal satisfaction from life, tend to look for new approach to late effects of childhood brain tumors. The new way seems to be assessment of adaptive behavior defined as the performance (not only ability) of daily activities required for personal and social sufficiency, and measured by Vineland-II.
Design/Methods: Psychological repeated testing and long-term observation was performed in 350 childhood brain tumor survivors (various types and localizations of tumor) to determine psychosocial late effects and QoL. Age at psychological diagnosis ranged from 6 to 26 years. The patients were examined using battery of neuropsychological methods and psychological interview. Analysis of medical history was also performed. From this group randomly selected 30 patients to assessment by the Vineland Adaptive Behavior Scales – expanded form (Vineland-II).
Results: In our sample patients present low scores in the all domains: communication, daily living skills, socialization, motor skills, with significantly low level of social contacts. Typical problems in this area: difficulties in appropriate expression of emotions, inadequate mimic and body language, problems with establish and maintain peers relationships, low tolerance of frustration, trouble with postpone of gratifications. An interesting problem emerging from research and requires a deeper exploration are the differences between the declarations of the patients or their parents expressed during the psychological interview and the real level of adaptive behavior.
Conclusion: The results of our study suggest that adaptive behavior concept well describes and explains the problems of this group of patients. Vineland-II is a useful and reliable tool to assess psychosocial late effects survivors of cancer as a group as well as a method to individual assessment. It also allows prepare an individual psychological interventions and rehabilitative program for particular patient.

P-452

COMPARISON OF BODILY MEMORY IN TWO GROUPS OF PEDIATRIC CANCER SURVIVORS DIFFERING IN AGE OF DISEASE ONSET

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Background/Objectives: Studies of pediatric cancer survivors show that most have an impressive ability to cope with their cancer experience and adequate psychosocial adjustment in their life subsequently. It is also known that there are early childhood memories that are manifested as bodily memory, which may store impressions not available consciously.To compare bodily memories in two groups of pediatric cancer survivors differing in age of disease onset.
Design/Methods: The participants were 50 young adult cancer survivors, 16 to 24 years old, divided into two study groups, in line with the age of disease onset: (a) 0-3 years and (b) 8-11 years. The number of subjects was 24 (16 men, 8 women) in group (a) and 26 (17 men, 9 women) in group (b). The clinical diagnoses were: solid tumors, 17; lymphoma-leukemia, 24; brain tumors, 9. After receiving the IRB permit (RMC 540-14) the subjects were contacted by one of the investigators who conducted with each individually a telephone interview according to a prearranged list of questions, with predetermined response options, referring to four themes: Behavioral indices; Bodily sensations; Organ sensitivity; and Nightmares.
Results: When all questions were considered together, a significant difference was found (chi-square, P=0.001) between the two groups. The "behavioral indices" questions did not differ significantly between the two groups, while "bodily sensation" (P=0.002), "organ sensitivity" (P=0.02) and "nightmares" (P=0.04) demonstrated a significant difference in terms of chi-square between the two groups, whereby the first group scored higher than the second.
Conclusion: The results demonstrated that the group with earlier disease onset (0-3 yrs) has more bodily memories than the group with later disease onset. The explanation could be either that earlier disease onset is related to stronger emotional impact or that cognitive elaboration and language development that promote coping and acceptance is less develop during the early ages.

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COMPARING "FREQUENCY" AND "INTENSITY" BASED PERCEIVED COGNITIVE FUNCTION REPORTED BY PARENTS AND CHILDREN

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Background/Objectives: Cognitive dysfunction is a common concern for children with brain tumors and those who received neuro-toxic treatment. Child- and parent-perceived cognitive function (PCF) could be used for repeated assessment given their ease of administration, low cost and relevance to patients' daily lives. The purpose of this analysis was to evaluate whether agreement between parent- and child-reported PCF was associated with rating scale type (frequency vs intensity) and whether the level of agreement differed between children with versus without cancer.
Design/Methods: Data from 1,409 children (mean age=12 yrs) drawn from the US general population and their parents and 515 children with cancer (53% brain tumor; mean age=14 yrs) were analyzed. For cancer sample, 34% received radiation therapy,

72% chemotherapy, 71% surgery and mean years since last treatment = 3.3. All completed two versions of a newly developed pediatric perceived cognitive function short-form (pedsPCF-SF). Both had the same 13 item stems but with different rating scales: 1) "frequency" (from "none of the time" to "all of the time" and 2) "intensity" (from "not at all" to "very much"). Weighted Kappa was used to evaluate agreement at individual item level between parent- and child-reported pedsPCF-SF. Intra-class correlation (ICC) was used to evaluate agreement at the scale level.
Results: For cancer sample, weighted kappas between children and parents were 0.27-0.39 for both intensity and frequency. For general population, weighted kappas were 0.53-0.67 and 0.64-0.70 for intensity and frequency, respectively. At the scale level, higher agreement was found on general population sample (ICC=0.77 and 0.81 for intensity and frequency, respectively) than cancer sample (ICC=0.46 and 0.38, respectively).
Conclusion: This study showed higher agreement between children and their parents without cancer compared to those with cancer. Results from this study can be applied to improving assessment in future cancer studies.

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RESILIENCE IN PARENTS OF A CHILD WITH CANCER

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Background/Objectives: Due to improved survival rates in pediatric oncology more attention is given to psychosocial factors. There is growing evidence that resilience is one of these important factors. Resilience implies an ability to withstand stress, but the literature is confounded by a lack of a consensus definition. There are several different conceptualizations: 1) preexisting trait that allows persons to thrive in the face of adversity, 2) dynamic process of positive adaptation and 3) a final outcome. The aim of the present study is to investigate resilience over time in parents of a child with cancer.
Design/Methods: Between June 2010 and December 2012 all parents (n=334) of a child with a new diagnosis of cancer were invited to participate. Eventually, 64 parent couples gave consent to participate. The resilience-Scale-NL was assessed four times: at diagnosis (n=64), 6 months (n=38), 1 year (n=28) and 2 year (n=14) after diagnosis. The total score of the mother and father was compared at each time point with age and gender norms.
Results: No significant differences were found on any time point for the resilience score of couples compared with the average norm scores. However, a significant difference was found after diagnosis for the total group of participants, but the score was still within normal limits (t-score 47.87). 20-22% of the parents obtained a clinical deviant score (t-score <40) at all time points.
Conclusion: Our longitudinal study demonstrated that in the majority of parents resilience was not negatively affected by the diagnosis of cancer and treatment of their child. However, more than 20% of the parents obtained a clinical deviant score. Additional, our study provided some preliminary evidence of the stability of resilience. More research is needed to investigate the group of parents with low resilience scores, in order to find strategies to support better this potential vulnerable group.

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BEREAVED SIBLINGS' ADVICE TO HEALTH CARE PROFESSIONALS WORKING WITH CHILDREN WITH CANCER AND THEIR FAMILIES

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Background/Objectives: Even if healthy siblings go through several challenges throughout the cancer-trajectory they often stand outside the spotlight of attention. Therefore, this study explored siblings' advice to health care professionals (HCPs) working with children with cancer and their families.
Design/Methods: In this nationwide study, performed in Sweden 2009, 174/240 bereaved siblings (73%) participated, and 108 answered an open-ended question about what advice they would like to give to HCPs working with children with cancer and their families. Data were analyzed with content analysis.
Results: Most of all siblings' advice was related to support. They wished to be included, either to get support themselves or because they wanted to be involved in the brother's/sister's care; they wanted better medical information, to be more practically involved and suggested that HCPs should give parents guidance on how to involve siblings. Other advice was related to the ill child's care, e.g. listen to how the ill child wanted to be cared for, or siblings wish for HCPs to mediate hope, but also realism.
Conclusion: Siblings' advice focused on inclusion from diagnosis until bereavement in order to facilitate siblings' psychosocial needs not only in the health care setting but also within the family.

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COPING STRATEGIES FOR GRIEF AMONG SIBLINGS WHO HAVE LOST A BROTHER OR SISTER TO CANCER

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Background/Objectives: Cancer-bereaved siblings report several distressing problems such as sleeping difficulties and unresolved grief years after the loss. The aim of this study was to identify coping-strategies for grief among cancer-bereaved siblings.
Design/Methods: This study was based on an open-ended question from a nationwide survey, conducted 2009 in Sweden, among cancer-bereaved siblings who have lost a brother/sister during 2000-2007 (N=174, response-rate 73%). The open-ended question "What has helped you in your grief after the death of your brother or sister?" was analyzed with content analysis.
Results: Many of the siblings' strategies were either related to different ways of distracting themselves from distressing thoughts/feelings in relation to grieving or to think of, feel and express their grief in different ways. Strategies for distraction were related to keep themselves busy with work and hobbies, and to return to everyday routines. To think of, feel and express themselves in relation to the grieving included e.g. talking to others, crying, and writing, but also talking to their dead brother/sister. The siblings also evoked positive memories (the good times together), and negative memories, e.g. their brother's/sisters' suffering. To think/feel and express thoughts and feelings in relation to the grieving versus distracting themselves from distressing feelings/thoughts did not always compete; some individuals reported strategies related to both these aspects. Family, friends and pets often assisted the sibling to express their feelings/thoughts but also distraction. Other strategies were associated with religious beliefs, e.g. that siblings will meet again. Waiting for time to pass was also mentioned as a strategy; since some siblings were convinced that time would heal some of their grief.
Conclusion: Siblings reported a wide range of different strategies to cope with their grief. Most coping-strategies found are accessible and may be valuable for health care professionals in order to support future bereaved siblings.

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CANKIDS CHILD LIFE PROJECT INDIA: A CHILD LIFE MODEL FOR A RESOURCE LIMITED SETTING

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Background/Objectives: The cancer diagnosis is an immediate crisis for the family and psychological support is a vital component of treatment. Child life is a field dedicated to providing psychosocial support to children and families facing difficult circumstances in the healthcare setting. Although child life is a new concept within the Indian healthcare setting, the Pediatric Psycho-Oncology program uses child life principals and philosophies. We value the rights of the child to play and have a stimulating, enriching, safe and clean healthcare environment to promote optimal development. The CanKids Child Life Project objective is to improve the quality of life for children with cancer in India.
Design/Methods: CanKids has initiated a Child Life Project, which serves as a low cost model for other cancer institutions and organizations. This initiative outlines advocating and implementing the "Child Friendly Ward Project" and child life interventions to make the hospital environment the best possible place for children. We start by educating and sensitizing the hospitals of the importance of psychosocial care of and then partnering with them.
Results: The implementation of the Child Life Project across India provides optimum healthcare experiences for children and families facing cancer. This project brings in breakfast game tables, art display boards, shoe racks, toy and book libraries in addition to implementing child life interventions. These resources promote health, psychological well-being and encourage continuation of proper development throughout the healthcare process.
Conclusion: Our goal is to spread awareness about the child's right to have a safe stimulating environment and partner with hospitals to effectuate child friendly wards, individual counseling, group counseling, and play therapy. In implementing this project, the amount of stress experienced by children and families facing cancer is reduced and healthcare providers are empowered to be more effective when working with the child and family.

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TREATMENT-RELATED LOCUS OF CONTROL AND LIKELY CORRELATIONS WITH COPING IN CHILDREN SUFFERING FROM ALL: A MULTICENTRIC STUDY

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Background/Objectives: The study examines the variable of locus of control - either external or internal - in children with ALL at treatment phase, because, despite its significance in the psychosocial adjustment process as an evolutional resource, it has been rarely investigated. When facing the critical events, children's own sense of self-efficacy can guide them towards active behaviour - *monitoring coping* - or towards passive one, such as avoiding responsibility - *blunting coping*. The possible relationship between attribution styles and coping has been investigated.
Design/Methods: Participants: an experimental group of 40 children with ALL at treatment regimen phase (average age=10.8, SD=2.5), recruited from two Italian Oncology and Haematology centres (Monza; Palermo); a control group of 30 healthy children.Tools: Locus of Control Scale for Children (Nowicki Strickland, 1973); Child Behavioral Style Scale (Miller, 1987).A multivariate analysis of variance was calculated to compare the scores obtained by each group. The paired t-test was utilized to compare the mean of the scores of the scales of locus and those of coping. Pearson's *r* coefficient was calculated to measure the correlation between locus and coping.
Results: The internal locus of control score obtained by the experimental group is higher than the score of the external locus ($t=11.7$; $df=39$; $p<.001$), and it is much higher in the control group ($F_{(2,69)}=5.53$; $p<.05$). The experimental group also shows a statistically significant correlation between external locus and monitoring coping ($r=400$; $p<.05$), in spite of the fact that the monitoring is the prevailing coping style adopted by both groups ($t=3.09$; $df=39$; $p<.005$).
Conclusion: The predominance of internal locus of control coupled with the monitoring coping is a resource for children with ALL useful to consciously cope the treatment phase. The correlation between external locus and monitoring coping displays children's preference to react actively.

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MENTAL AND PHYSICAL OF CO-ORDINATES OF OPPOSITIONAL DEFIANCE DISORDER IN BETA-THALASSEMIC ADOLESCENTS & PRE-ADOLESCENTS

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Background/Objectives: Thalassemia continues to be the most common form of Hemolytic anemia (Dubey, Parakh, & Dublish, 2008), which is 5.3% prevalent in Pakistani Population (Ahmed, 1998). It results in poor physical and mental health among patients (Azarkeivan et. al., 2009). Moreover it causes substantial disturbances in every aspect of life and well-being.Since depression & anxiety continue to be the major ailments associated with thalassemia (Mednick et al., 2010, Kiskek, Krim, Turhan&Turan., 2013) not much attention has been given to the behavioral deficits co-morbid with Thalassemia .Beratis (1993) found high frequency of Oppositional defiance disorder in thalassemic children along with high ferritin rates in them. Our study brings into light prevalence of these behavioral abnormalities in Thalassemic children and associative medical factors that constitute the diagnosis of ODD.
Design/Methods: Our study population comprised of 197 registered Beta-Thalasemic patients of A.M.T.F, the gender ratio composed of (Females= 95, Males= 100). Sample was classified into 2 age based groups (Group 1: Preadolescent 4-9 years; Group 2: Adolescent 10-16 years). Sample was screened through a self-structured questionnaire measuring the level of ODD, along with a detailed clinical interview.
Results: Data was analyzed through non parametric test, chi-square and independent sample t-test. Result values indicate high incidence of oppositional defiance disorder in Thalassemic children ODD: n=141 (71.93%). Analysis also reflect that age impacts the level of ODD in children (Group 1: Preadolescent=70%& Group 2: Adolescent = 75%).However no significant gender difference was observed ($t= 1.15$, $p > 0.05$).
Conclusion: Beta-Thalassemia inadvertently causes many emotional and behavioral disturbances, the impact of which is detrimental to the physical health of child.The multidimensional treatment approach employed at Afzaal Memorial Thalassemia Foundation, makes it possible to identify psychological issues comorbid with Thalassemia[. Psychological Screening and diagnostic procedures utilized at A.M.T.F appear to be a valid tool to enhance compliance of transfusion dependent child towards treatment.

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THE STIGMA OF CANCER IN DEVELOPING COUNTRIES

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Background/Objectives: The diagnosis of cancer is seldom disclosed to children or discussed with them in developing countries after completion of chemotherapy. We present data on the extent and patterns of social stigma associated with the diagnosis of childhood cancer in middle income families in India after completion of therapy.
Design/Methods: This a retrospective oral questionnaire done on parents of children treated in India over a ten year period between 2002 and 2012. The children who were less than 7 years old during therapy and were in remission over 3 years were chosen as our study population. The parents were questioned on 3 parameters – discussion of the treatment of cancer with the child, attitude towards follow up care and fear regarding long term side effects of the treatment.
Results: A total of 59 parents were interviewed for the study. The diagnosis was Leukaemia in 37 children, Hodgkins lymphoma in 5 and NHL in 10 children. Only two parents had discussed the diagnosis of cancer with their child (3.4%). Follow up was not offered for fear of sensitive questions from the children in 83% of children and only 10 children have been coming for regular annual follow up since discharge. All parents - 100% expressed fears about delayed side effects from the chemotherapy especially on pubertal growth and fertility but did not wish to discuss this issue with the child. Separate appointments were made to perform a chart review in 12% patients by the parents to address this issue of late side effects.
Conclusion: The social stigma of cancer chemotherapy in our society has resulted in a huge loss of data on the psychosocial aspects of cancer and its impact on the family. More COPE programs – creating opportunities for parent empowerment are required to overcome these barriers and help support these families long term.

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DEVELOPMENT OF A NOVEL WEB-BASED RESOURCE TOOL FOR PATIENTS & FAMILES OF CHILDREN WITH LIVER TUMORS : THE SIOPEL PATIENT / FAMILY FORUM

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Background/Objectives: Hepatoblastoma and hepatocellular carcinomas are the most common primary malignant liver neoplasms in pediatric patients under the age of 18 years. Due to the rarity of these tumors, when confronted with these diagnoses, patients, survivors, and their families, are challenged in identifying support networks that permit them to share information and experiences. In an effort to facilitate communication, clinicians, survivors, and parents have cooperated to develop a novel web-based virtual support network.
Design/Methods: Funded by a grant from ENCCA (the European Network for Cancer Research in Children and Adolescents), hysician representatives from SIOPEL, in collaboration with pediatric liver tumor survivors and their parents, developed a web-based service, the Patient/Family Forum. Membership requires registration with a secure username and password. Once registered, clients may utilize this forum to share their experiences, solicit advice, and benefit from the experiences of others. This secure web-based platform is hosted by the Italian Supercomputing facility, Cineca. The interface language may be customized by clients to their own and exchanges between users may take the form of public group or private messaging. The forum is supervised by two moderators (one pediatric liver cancer survivor and one parent). Questions regarding medical concerns such as diagnosis, prognosis, and treatment, are referred by the forum moderators to recognized experts in the field for coordinated review and response.
Results: This Patients/Family forum was developed and launched in July, 2014.
Conclusion: Such a forum serves as a potential model for the development and cultivation of international support communities for patients, parents, and survivors of other rare paediatric rare malignancies. The research leading to these results. This effort has received funding from the European Union's Seventh Framework Programme (FP7/2007-2013) under the project ENCCA, grant agreement n° 261474The authors have no financial interests to declare.

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PREVALENCE OF SYMPTOMATIC ANXIETY IN PRE-ADOLESCENT AND ADOLESCENTS SUFFERING FROM BETA-THALASSEMIA: A LONGITUDINAL STUDY

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Background/Objectives: Thalassemia is a lifelong condition-requiring adherence to a cumbersome medical procedure. The course of disorder affects not only the physical condition of the child but also impedes his/her mental health. (Mednick, 2010). Anxiety disorders are considered to be the most common type of psychopathologies affecting Child and adolescent with a ratio of about 10-20 %. (Bersntein GA et al., 1996, Moreno MA et al., 2010). Many researches have been conducted in the western society to investigate the prevalence of anxiety in Beta-Thalassemia patients. However there is a dearth of research data in Pakistan calculating this risk factor. This research paper brings into light the prevalence and incidence of symptomatic anxiety in pre-adolescent and adolescents suffering from Transfusion dependant Beta-Thalassemia.
Design/Methods: The sample population comprised of 196 beta-thalassemia patients, registered in Afzaal Memorial Thalassemia Foundation. The inclusion criteria encompassed an age range of 4-16 years, whereby 2 categories (i) pre-adolescent (age range 4-9 years) and (ii) adolescent (age range 10-16 years) were made. A self-made screening questionnaire was administered on the caregivers along with in depth history and clinical observation of child during psychotherapy sessions.
Results: The result findings indicate high incidence of anxiety in children suffering from Beta-Thalassemia. Chi-square values show Anxiety: n=128(65.30%). It was found that Anxiety was significantly higher in pre-adolescent (65%) as compared to adolescent (60%).There was no significant difference in level of anxiety among both genders ($t=1.74, p>0.05$).
Conclusion: The study indicated that children suffering from Beta-Thalassemia are at a higher risk for developing anxiety disorders. There is a strong need of adjunct psychotherapeutic sessions with medical treatment to alleviate their quality of life and mental health.

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PHYSICIANS AND NURSES BURN OUT IN PEDIATRIC ONCOLOGY DEPARTMENTS IN ISRAEL

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Background/Objectives: Burn out is a term used to explain the decrease job performance and commitment as well as the stress and dissatisfaction of health workers. There are three characteristics of burn out - depersonalization, low personal accomplishment and emotional exhaustion. The health care experiences psychological and physical stress increasing along the years and negatively affecting the quality of life and the quality of care of the medical teams.
Design/Methods: We used a questionnaire consisting of three components: Demographic variables, Burnout Questionnaire –MBI and Coping Strategies Questionnaire –COPE.The questionnaire posted to all the physicians members of the Israel Society of Pediatric Hematology Oncology and to the nursing staff of the main pediatric Hematology Oncology departments in Israel.
Results: 119 subjects filled the questionnaire, 41 medical staff and 78 nursing staff. Regarding the question: "Do you feel burnt out", on a scale from 0-6 (6- more burnt out), the nursing team answered on average 3.6 ± 1.6 as opposed to the medical team 2.3 ± 1.6 ($p=0.003$) as this single question correlate with the statistical analysis of the sub-questionnaires that demonstrated differences between the groups in emotional fatigue, depersonalization and emotion focused coping and the nurses reported on higher burn out feelings. A significant correlation was found between the nursing staff's age groups and their emotional fatigue- the higher the average age, the higher the feeling of emotional fatigue ($p=0.03$).
Conclusion: In this study, we found that there are differences between the nursing team and the medical teams both in the level of burnout as well as in the level of coping. These findings consider the basic differences between the nurses and the physicians and can be explained especially by the support received outside of the workplace.

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TO HEAL A STUDENT, NOT JUST HIS DISEASE

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Background/Objectives: The importance of hospital schools has been rising during the last decades. They have gained a lot of influence in the lives of children and teenagers under treatment for different diseases. Those in paediatric hematology/oncology units are not an exception. Though the hospital schools are nowadays capable of synchronize their work with the patients regular schools, the purpose of this project is to present and describe a case report which underlines de role of the hospital schools as themselves, as a teaching tool which is useful in the goal of educating its students in a global and comprehensive way.
Design/Methods: It presents the case of a 16 years old boy who was merely a patient (with a localized osteosarcoma that required preoperative and post-operative chemotherapy, high complexity surgery and inmunotherapy) without any kind of learning activity. Its approach is necessarily cross-disciplinary, but the present report has an educational perspective and it stresses the function, possibilities, advantages and disadvantages of hospital schools within paediatric oncology units and their coordination with the rest of the staff. It does it by putting the patient in the middle of its scope, trough a humanist vision that emphasizes the real meaning of education. Its methodology is qualitative.
Results: The patient had finished the obligatory educational stage and wasn't enrolled in any school. He was apathetic and he had had a negative experience in a former hospital schoo. Through the Montepríncipe Hospital School in the Paediatric Hematology/Oncology Unit (HM Montepríncipe Hospital) became a curious and motivated student.
Conclusion: Though it does not have a single conclusion, this project concludes that hospital schools are not just a way of linking the patients with their regular schools, but a powerful tool to help healing process, since cancer has both physical and psychic effects and consequences.

Posters: Radiation Oncology (PROS)

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18-FDG PET-MRI IN PEDIATRIC ONCOLOGY. A NEW DIAGNOSTIC AND TREATMENT PLANNING TOOL

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Background/Objectives: It is shown that PET-CT with 18-FDG, has a high sensitivity and specificity in studies of whole body in evaluating pediatric malignancies. However the of exposure to ionizing radiation, has led us to search new diagnostic tools such as PET-MRI. PET-MRI is a very novel technique worldwide, and is part of the so-called integrated image studies in which a single test is used to improve not only the diagnosis of the patient's illness and its treatment effect, but to improve the cost-effectiveness.
Design/Methods: A descriptive analysis of the technical characteristics and pathologies of the studies is conducted. Nine pediatric studies have been done from November 2014 to March 2015. Our equipment is a Siemens Biograph MMR formed by the PET and 3T MRI with simultaneous acquisition of both techniques. 6MBq are injected 18-FDG in studies of full body and a fixed dose of 111 MBq in brain studies. We have used different protocols depending on the pathology of the patient. In all the studies we acquired specific sequences of post-contrast MRI with gadolinium.
Results: A total of 9 patients were studied. Indications for PET-MRI were: radiation therapy planning (2 DIPG,1 relapsed STS, 1 anaplastic ependimoma and 1 disseminated pinealoblastoma), end of treatment evaluation (1 hodgkin disease) and re-staging (1 relapsed medulloblastoma and 1 relapsed neuroblastoma).
Conclusion: The 18-FDG PET-MRI is a technique of integrated images, with high sensitivity and specificity in the diagnosis of pediatric tumors, and a significant decrease in the rate of exposure to ionizing radiation in children compared to other diagnostic techniques.

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RAPID-LEARINING SYSTEM FOR PAEDIATRIC RADIOTHERAPY - IMPLEMANTATION OF A NATIONWIDE WEB-BASED QUALITY ASSURENCE PLATFORM AND REGISTER IN PAEDIATRIC RADIATION ONCOLOGY IN AUSTRIA

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Background/Objectives: In Austria each year only a small amount of children receive radiation at five different centres. Due to the limited amount of cases and the inhomogeneous group of tumours an expert level is difficult to achieve. Up to now the collaboration among these centres is based on communication via telephone, e-mail and postal services. Objective is the development of a centralized web-based platform to evaluate the standard of nationwide pediatric radiotherapy and subsequently build up a nationwide register.
Design/Methods: All children receiving radiotherapy will be registered before start of treatment at the web-based quality assurance platform. The patients´ histories, all relevant diagnostic reports and radiological images will be uploaded and pseudonymized. Thereafter the patient cases will be discussed among the pediatric radiation oncologist group. The defined target volume and treatment plan will be

evaluated with respect to dose distribution to the tumour and organs at risk.The implementation will roll out in four stages to simplify and unify the actual process of data aggregation and data representation, to grantee an easy data access for all collaborating centres.Stage 1: First use of digital DICOM-archive Stage 2: Enabling a secure digital data transfer and data access to the archive via stand-alone client softwareStage 3: The stand-alone client software is replaced by a web-based online viewerStage 4: Completing the fully accessible web application by adding upload features and automatized processes. Apart from the web front end, which allows the user to interact and to exchange data, another crucial part of the platform is the back end that is responsible for data management and data archiving of medical multimedia data.
Results: The first results will be presented at the congress.
Conclusion: A national quality assurance platform and register of pediatric radiation oncology will be built up for further research and advanced training.

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IMPLEMENTATION OF PROTON THERAPY FOR PEDIATRIC TUMORS AT THE NEW PROTON FACILITY IN TRENTO

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Background/Objectives: Although both photon and proton radiation techniques permit similar target volume coverage, the physical properties of protons allow a better sparing of normal tissues with the consequent reduction of acute and late toxicities.
Design/Methods: The Trento facility is equipped with active beam delivery based on spot scanning. A cyclotron provides beams of variable energy (70-226 MeV at isocentre) and spot size (σ 3-7mm in air at isocentre). Each treatment room is equipped with a gantry which allows 360° rotation of the beam line, 6 degrees of freedom robotic treatment table, two orthogonal X-ray devices, a CT on-rails in one room and a cone-beam CT in the other. Two horizontal beam lines are placed in a third room. The center is equipped also with a dedicated CT and 1.5T MRI and an anesthesia area. In October 2014 the facility started clinical activity on adult patients; the plan is to accept pediatric patients around six months later.
Results: We evaluated 25 pediatric cases (21 national and 4 international) referred by physicians, parents and family members. The mean age was 9 year (range, 1-20) and the histology was: rhabdomyosarcoma (2), high-risk medulloblastoma (4), diffuse intrinsic pons glioma (2), meningioma (2), primitive neuroectodermal tumor (3), choroid plexus carcinoma (1), Ewing sarcoma (2), low-grade glioma (3), chordoma (1), atypical teratoid rhabdoid tumor (1), pituitary germinoma (2), osteosarcoma (1), malignant schwannoma (1). Nineteen patients were evaluated eligible to receive proton radiation although the radiation timing was not always correctly set. Six patients were declined due to metastatic progression of disease or because already treated with high doses of radiation.
Conclusion: At Trento Proton Center, we expect to treat in a very near future pediatric patients and to contribute to the limited but growing body of literature demonstrating effectiveness and safety of protons for pediatric tumors.

Posters: Rare Tumours

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RUPTURED SOLID PSEUDOPAPILLARY NEOPLASM OF PANCREAS (SPT) MANAGED BY CHEMOTHERAPY AND LIMITED SURGERY

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Background/Objectives: To report a case of SPT of pancreas highlighting that chemotherapy may be used as an adjunct to surgery in management of such tumors to avoid morbid surgical resection.
Design/Methods: We report here, a case of SPT managed successfully using low dose chemotherapy followed by limited surgery.
Results: An 11 yr old female presented with severe abdominal pain, bilious projectile vomiting and signs of shock. A firm abdominal mass was palpable in the epigastric region. USG abdomen revealed a large heterogeneous mass in lesser sac. CECT showed a large ruptured necrotic hemorrhagic mass in relation to the body and tail of pancreas. An exploratory laparotomy was planned and major debulking of ruptured pancreatic tumor was done. Biopsy was s/o a Solid pseudopapillary neoplasm of pancreas Tumor cells stained positive for Synaptophysin, CD 10 and beta catenin and negative for chromogranin. However she developed recurrence of symptoms after 2 months. CECT abdomen showed evidence of large mass in relation to the tail of pancreas s/o residual tumor. It was opined that a surgical resection at this point of time would mean complete pancreatectomy, splenectomy, bowel resection and a temporary colostomy. In consultation with the gastrosurgical team it was decided to give her 4 Cycles of VAC chemotherapy and reassess for surgery later. She showed some decrease in the size of the mass .It was then planned to take her for surgery. Only a distal pancreatectomy with splenectomy was done. The resected margin was free of tumor and all 12 regional lymph nodes were tumor free. Three months after the surgery she is asymptomatic and has no evidence of recurrence.
Conclusion: SPT of Pancreas is a rare tumor with a little literature on management guidelines. We successfully combined chemotherapy with surgery in this young girl to avoid morbid surgical outcome.

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MEDIASTINAL CYSTIC TERATOMA WITH RIGHT SIDED EXTRA RENAL WILMS TUMOR-A RARE CASE REPORT

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Background/Objectives: Wilms' tumour is one of the most common tumours of childhood, majority of these tumours arise from the kidney .Very few cases, only about 100 documented cases of Extrarenal Wilms' tumour had reported. Mediastinal teratoma also seen in children but association of these two is rare. We failed to find any case report. So we decided to report it.
Design/Methods: A 26 months old boy presented with fever, chest pain, respiratory distress & abdominal distention for 8 months. His respiratory distress was not relieved by medication. He used to scream with pain. He had anorexia & weight loss. With these complains, in last 8 months, he got admitted 9 times in 6 different hospitals and investigated with CXR 16 times, USG of abdomen 4 times, CT Scan of Chest two times and undergone minor chest surgery 5 times and major surgery once (mini thoracotomy & open drainage). On examination he was irritable, ill-looking, dyspnoeic, mildly anaemic & no lymphadenopathy was found.Respiratory system examination suggestive of left sided pleural effusion with scar marks & a sinus with purulent discharge on left side. Right kidney was palpable, ballotable & non-tender.
Results: Several investigation like x-ray chest revealed trachea shifted to rt side and left lung totally opaque and comment was left sided pleural effusion. CT scan report was in favour of left sided renal mass and metastatic lesion at left lung. Thoracotomy was done and found cystic teratoma, confirmed by histology. Laparotomy was done to remove the mass.The mass was free from kidney. Histology report in favour of extra renal wilms tumour. Pathology slide was reviewed and expert panel board confirmed the case of extra renal wilms tumor.
Conclusion: With meticulous history, clinical examination, proper investigation and appropriate surgical approach may identify the rare cases.

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MANDIBULAR DESMOID FIBROMATOSIS: BALANCING AGGRESSION OF CARE FOR A BENIGN DISEASE

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Background/Objectives: Desmoid fibromatosis is a rare benign tumour which grows rapidly and destroys local tissue. Mandibular predilection may cause impingement on the airway and surrounding neurovascular structures. A high risk of recurrence needs to be weighed against the risks of mutilating surgery and chemotherapy for a tumour which does not metastasize, but its rarity precludes a strong evidence-base for care.
Design/Methods: We retrospectively reviewed our management and outcome of cases of mandibular desmoid fibromatosis presenting over 5 years at Tygerberg Academic Hospital, Cape Town.
Results: Three patients presented with unilateral mandibular swellings of 2 months' median duration at a median age of 29 months. Mean tumour volume on magnetic resonance imaging (MRI) was 129cm^3. No syndromic features or significant family history was found. Core needle biopsy confirmed diagnosis in each case. Patient A (a 41 month-old male with 67cm^3 left-sided lesion) had a primary excision with hemi-mandibulectomy and concurrent osteomyocutaneous free fibular flap repair, with clear resection margins. Patient B (a 29 month-old female with 211cm^3 left-sided lesion and nocturnal stridor from airway compression) had the same procedure performed after two courses of vincristine, adriamycin and cyclophosphamide (VAC). Neoadjuvant chemotherapy achieved 17% tumour volume reduction, but microscopic excision margins were positive. Patient C (a 16 month-old malewith 107cm^3 right-sided lesion with parotid involvement, airway compression radiologically, facial nerve palsy and previous exomphalos repair) had tumour progression on VAC chemotherapy. Gross tumour debulking was followed by 8 cycles of methotrexate with vinblastine and a 1.8cm^3 residual lesion on subsequent MRI did not progress. All patients had good functional outcome at 46 months average follow-up (range 30-55).

Conclusion: Individualized management that aims to control local disease but preserves function and cosmesis requires a multidisciplinary team in aggressive fibromatosis of the jaw not amenable to simple wide local resection. Long-term multicentre cohorts should clarify care choices.

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MALIGNANT TRITON TUMOR AND NEUROFIBROMATOSIS. A RARE CASE REPORT AND LITERATURE REVIEW

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Background/Objectives: Malignant peripheral nerve sheath tumors (MPNST) constitute a rare variety of soft tissue sarcomas. Malignant triton tumor (MTT), a very rare, highly aggressive soft tissue tumor, is a subgroup of MPNST coexisting with malignant rhabdomyoblasts. Only case reports and small seriers of patients have been published.
Design/Methods: We present a case report of a 6 year old boy with NF-1 and MTT. A review of the literature was done.
Results: We report a sporadic case of MTT in a 6 year old boy. We present the clinical course, pathological findings and image findings. Immunohistochemistry confirmed the neurogenic origin with S-100 expression and the rhabdomyoblastic differentiation with desmin and vimentin positivity. Parcial surgical excision was done and preoperative chemotherapy was given.
Conclusion: MTT are a rare form of peripheral nerve sheath tumors that follows a particularly aggressive course. Given its rarity, only case reports and small series of patients have been published. Early diagnosis and referral to multidisciplinary team are important in ensuring the best diagnosis and optimal therapy in this young age. Complete surgical resection and adjuvant radiotherapy should be the cornerstones of treatment for MTT, but preoperative chemotherapy can be given.

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CLINICAL FEATURES AND TREATMENT RESULTS OF PATIENTS WITH HEMANGIOMA

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Background/Objectives: Hemangioma is a disease with high incidence of spontaneous recovery. It is not usually evident at birth. But, rapid growth after birth, stabilization of lesion between 1 and 2 years of age and involution after 2 years of age are some clinical features of hemangioma. Vascular malformations in the opposite situation should be considered. Hemangioma is the most common benign vascular tumors of childhood.
Design/Methods: Forty-nine patients with hemangioma who admitted between 2001-2015 were evaluated retrospectively.
Results: The median age of onset and age at admission were 0 (0-156, mean 8.4) and 7 (0.25-192, with a mean of 19.9) months. The localization of lesions were 57.2% (n = 28) on head region, 16.3% (n = 8) on trunk, 16.3% (n=8) on limb, and 10.2% (n = 5) on neck region. 17 patients (34.7%) were treated with propranolol alone in 12 (24.5%) patients, steroid alone in 2 (4.1%) patients, prednisone and propranolol in 2 (4.1%) patients, propranolol and surgery 1 (2%) patients were used. Regression was observed 81.6% of patients (n = 40). The number of hemangioma (>1) ($p = 0.026$, HR = 9.5, 95% CI 1.3-69.2) and treatment except observation ($p = 0.008$, HR = 10.5, 95% CI 1.8-59.1) were found significant in the univariate analysis, and treatment except observation was found effective on clinical response ($p = 0.014$, HR = 9.8, 95% CI 1.5-90.9).
Conclusion: Despite very small at birth, hemangioma can grow rapidly in the first year of life. Treatment indications are ulceration, infection, bleeding, and some special location such as laryngeal, tongue, eyelid, ear canal. Treatment options include observation (90%) and treatment modalities such as steroid, propranolol, interferon, chemotherapy, interventional radiological lesion embolization, surgical resection and laser which are applied to prevent organ dysfunction. Number of hemangioma and underwent to treatment except observation are significant on treatment response.

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EUROPEAN SURVEY ON THE EXISTENCE AND ACTIVITY OF COOPERATIVE GROUPS DEDICATED TO CHILDREN AND ADOLESCENTS WITH VERY RARE TUMORS. AN EXPO-R-NET/EXPERT INITIATIVE

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Background/Objectives: Very rare tumors (VRT) in children are an orphan disease in terms of lack of clinical and biological knowledge, dedicated studies, economic interest. VRT are heterogeneous: some are characteristic of childhood (pneumoblastoma, pancreatoblastoma, …), others are frequent in adults but rare in children (carcinomas, melanoma, …), where they show distinct characteristics. For this reason, VRT have been included in EXPO-r-NeT, a EU funded project that aims to reduce inequalities in childhood cancer survival and healthcare capabilities in different member states. A major objective is to improve access to high quality care for children with VRT that may require specialized resources or expertise not available in every center.
Design/Methods: The chairs of each European pediatric oncology society and, where existing, the coordinator of the national VRT cooperative group have been invited to respond to an online survey.
Results: 36 countries (including Turkey and Israel) responded: a VRT cooperative group exists in Italy, Germany/Austria, Poland, France, Spain, the Netherlands. A registry is active in the UK/Ireland and Hungary. In 2015, VRT groups have been formed in Croatia and Israel. Thus, structured activities dedicated to children with VRT exist in only 30% of European countries. This translates in a "coverage" of approximately 60% of the European population. The absence of activity was justified by low clinical and scientific priority and/or lack of trained staff. "Small" countries declared that the limited number of children with VRT does not justify dedicated resources.
Conclusion: in many European countries, VRT management is not at the same level of other more frequent pediatric cancers. The establishment of an international network, based on the EXPeRT experience, would be important to establish standards of care, allow consultation, facilitate access to expert centers. *ExPO-r-Net project is funded by The European Union in the framework of the Health Programme (2008-2013), grant 201312 07.*

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MALIGNANT PANCREATIC TUMORS IN CHILDREN: EXPERIENCE IN INSTITUTO NACIONAL DE PEDIATRIA IN 9 YEARS

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Background/Objectives: The Pancreatic tumors are very rare in pediatric age. It is occur in 1 per 18000 cases during childhood and it's the cause of 0.2% of the pediatric cancer death worldwide. This issue, leading to apply the same approach performed in Adults patients. The aim of this study is relate our experience in management of the malignant pancreatic tumor in children in our institution during the period between 2006-2015.
Design/Methods: We developed an ambispective study when we observed the cardinal symptom, the diagnostic method, the surgical technique used, the pathology results and the evolutions of each case.
Results: We treated nine cases with pancreatic tumors in age between 0-17 years. The cardinal symptom was abdominal pain in seven patients, follow by vomits in five patients and abdominal distension by mass in three. The average age was 7.5 years with a range between 2-12 years. The pathology evaluation report four Solid Pseudopapillary tumor (SPPT), two pancreatoblastoma, one Teratoma, one Pnet and one Islets Cells Carcinoma + Pheochromocytoma. Location of the lesion was head in 5 cases. We take to the OR all the cases and performed Whipple procedure in 5 cases and distal Pancreatectomy in four, (one of these cases was a distal pancreatectomy + Splenectomy). Complications occur in 5 cases (one bleeding, one pancreatic fistulae+ intrabdominal abscess, one intrabdominal abscess, one pancreatic insufficiency, one progression of the disease).
Conclusion: We establish a method to approach to malignant pancreatic tumors in our institution. Otherwise, we suggest a worldwide multicentric study to define a standard approach method.

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NASOPHARYNGEAL CARCINOMA IN CHILDREN AND ADOLESCENT; EXPERIENCE OF EGE UNIVERSITY FROM TURKEY

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Background/Objectives: The incidence of nasopharyngeal carcinomas (NPCs) among children and adolescents varies widely among different regions and races. The aim of our retrospective study was to evaluate the clinical features, histophathology, treatment results, and late toxicities of patients with NPCs.
Design/Methods: Between 1988 and 2014, 31 patients younger than 20 years old were treated and followed up in Ege University, Department of Pediatric Oncology and 2 other state hospitals in İzmir.
Results: The mean age of 31 patients was 13 (8-17,5) years. Male to female ratio was 1.6/1. Neck mass (cervical lymphadenomegaly) (67.7%), headache (16.1 %), hearing loss and nasal obstruction (12,9%) were the most common complaints. Twenty–five (80,6%) patients had undifferentiated carcinoma (type III), 6 (%13,4) patients had other non-keratinizing carcinoma histopathologically. There were 29 (93.5 %) patients in stage III (locally advanced disease) and in stage IV. EBV serology/ DNA was investigated in 16 patients and was found positive. Before RT, German POG protocol (Cisplatin, 5- FU and MTX) was applied. However, 5 (48.4%) patients did not receive MTX. All patients received local radiotherapy (60 Gy). After that they received IFN –beta for 6 months. Follow- up mean time was 6, 5 years (1.- 14.9 years). Three patients relapsed in mean time 7.8 monhts. In all patients 7- year relapse free survival (RFS) rate was 87.1%, and overall survival (OS) rate was 92.9 %. Late toxisities seen in patients were neck fibrosis (51.6%), hypothyroidism (35.4%) and hearing loss (12.9%).
Conclusion: Most children and adolescent patients with NPC are local –regional advanced diseases at first diagnosis and the outcomes are generally better than adults. But late toxisities due to RT are significantly high. Also, response-adapted RT is worth for further evaluation to minimize late toxicities.

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CONGENITAL GIANT MELANOMA - A PARTICULAR BIOLOGICAL ENTITY

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Background/Objectives: Melanomas in infants are a rare and heterogeneous disease. Initial presentation, clinical course, genetic background and prognosis may be different than in older chrildren or adults.
Design/Methods: We report on a female infant, born after uneventful pregnancy that presented with a large subcutaneous tumor at the occiput, about 5 cm in lenth, and 1.4 cm thick. Primarily, an excision biopsy was performed.
Results: Histopathology revealed the diagnosis of a malignant melanoma of epitheloid type, with tumor-infiltrated margins. Two subsequent resections were performed, finally leading to tumor-free margins. Genetic analysis of the tumor performed by CGH revealed an unspecific aberration on chr. 1 and a copy number loss on chr. 17 that is not typically seen in adult melanomas. Staging showed no lymph node enlargement or signs of metastasis; however, no sentinal node biopsy was done. The mother was free of melanoma, thus excluding diaplacentar transmission, and there was no family history of malignancy or syndromous disorders. In the infant, no further therapy was performed. The child is now 4 years old with normal development and no sign of relapse.
Conclusion: We conclude that even large melanomas in small infants may have a good prognosis with surgical therapy alone. The genetic basis of melanomas may be different in infants as compared to older children or adult patients.

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NASOPHARYNGEAL CARCINOMA IN CHILDREN AND ADOLESCENTS: A SINGLE INSTITUTION EXPERIENCE OF 64 PATIENTS

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Background/Objectives: The aim of our study is to investigate the epidemiological, clinical, radiological, therapeutic particularities of the nasopharyngeal carcinoma (NPC) in children, and to determine prognostic factors correlated with outcome and features of a series of 64 cases collected in the Pediatric Hematology Oncology Center of Rabat.
Design/Methods: A total of 64 newly diagnosed NPC patients younger than 21 year old in the Pediatric Hematology and Oncology Center of Rabat, from 2001 to 2010 were retrospectively analyzed. Overall survival (OS) rate estimates and Kaplan–Meier survival curves were calculated.
Results: Most patients were male (77%). Median age was 12 years. The main presenting symptoms were neck mass (83%), tinnitus/hearing loss (61%), bloody nasal discharge (50%), headache (53%), and nasal obstruction (36%). Stage I, II, III, IVA, IVB and IVC patients accounted for 0%, 1%, 42%, 25%, 28%, 1% and 3%, respectively. All patients were treated by neoadjuvant chemotherapy either. The complete response rate to chemotherapy was 78%. All patients were treated by radiotherapy: 70 Gy to primary tumors, 50 Gy to cervical lymph nodes and 70 Gy to lymphadenopathy. Locoregional relapses were observed in 5 patients, with a median delay of 45 months from the end of treatment (14-82 months). Local control was 92%. The 2-, 5- and 10- year overall survival (OS) rates were 90%, 84% and 76%, respectively. Relapse-free survival (RFS) was 94%, 84% at 5 and 10 years respectively. The main long-term complications of therapy were trismus (59%), hearing loss (52%), xerostomia (50%) and neck fibrosis (37%).
Conclusion: The majority of patients were diagnosed at the advanced stage. Children and adolescents with NPC had excellent survival except metastatic disease. The TNM stage was the most relevant prognostic factor.

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A RARE CASE OF CRIBRIFORM FLORID HYPERPLASIA IN MALE PATIENT WITH BILATERAL GYNECOMASTIA: A MIMICKER OF FEMLAE CRIBRIFORM IN SITU CARCINOMA?

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Background/Objectives: Bilateral gynecomastia is an uncommon condition that affects male patients at puberty. Most of these cases are related to obesity and precocious puberty which gynecomastia reverts only with clinical therapy or observation. Surgical mastectomy is only indicated for aesthetic purpose or when malignancy is suspected by radiologic findings. Bilateral breast in situ carcinoma is extremely rare in patients with bilateral gynecomastia and few reports were recovered from scientific publications.
Design/Methods: We present a case of bilateral gynecomastia without previous diseases or endocrinology abnormalities but treated obesity.
Results: A 16-years-old male patient was treated with surgical bilateral mastectomy because of progressive bilateral breast augmentation since 6 years old and diagnosed as bilateral cribriform low grade in situ carcinoma. He was admitted for second opinion and additional adjuvant therapy. No remarkable clinical, androgenic and female hormones as well as whole body computadorized tomography alterations were detected. After pathological and immunohistochemistry evaluation, the final diagnosis was bilateral florid cribriform ductal hyperplasia.
Conclusion: Despite bilateral in situ carcinoma in gynecomastia is uncommon; this condition is far more commonly reported in literature than our case of cribriform florid hyperplasia which there was only one case reported in literature. This reality imposes an additional challenge for the diagnosis due to lack of histopathological criteria or solely based on experience in female breast diseases. However, the bilaterallity, cribriform pattern and cytokeratin 5/6 expression in young male patient favors benign condition with favorable outcome.

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UNDIFFERENTIATED NASOPHARYNGEAL CARCINOMA IN CHILDREN: A RETROSPECTIVE STUDY IN THE CENTER OF TUNISIA

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Background/Objectives: Nasopharyngeal carcinoma (NPC) occurs very rarely in childhood. Children and adolescents are more likely to have advanced disease with particularly lymph nodes metastasis but they have a significantly better chance of survival. The risk of long-term treatment-related toxicity also may be a more important issue in younger individuals.
Design/Methods: This is a retrospective study of 17 pediatric patients who were diagnosed with undifferentiated nasopharyngeal carcinoma and treated at Farhat Hached hospital from 1994 to 2013.
Results: The mean age at diagnosis was 13 years (10-17 years). The male to female ratio was 1.4. The most common presenting symptom was neck swelling (82%). The mean duration of symptoms before diagnosis was 3 months (1-9 months). Eight patients had stage III disease (47%), 9 patients had stage IV disease (53%). All patients were treated by chemotherapy (88% received neo adjuvant chemotherapy containing cisplatin, 12%

palliative chemotherapy). Eighty two% of the patients were treated by radiotherapy at a median dose of 67G (*range from44Gy to 128Gy*). The complete response rate was 53%. On follow-up, 11 patients (64.7%) were still alive at last clinical contact. Five patients (33%) developed distant metastasis; 4 were lost to follow-up and 02 died (12%). The median overall survival was 40 months. The main long-term complications of therapy were neck fibrosis (23.5%), xerostomia (100%) and growth retardation (23.5%).
Conclusion: The outcome of children with undifferentiated carcinoma improved over the past 4 decades with the use of cisplatin-based chemotherapy and higher RT doses. However, many survivors had long-term treatment-related morbidities.

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SUCCESSFUL LONG-TERM USE OF SORAFENIB IN PROGRESSIVE PULMONARY METASTASES IN PEDIATRIC PAPILLARY THYROID CARCINOMA

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Background/Objectives: Sorafenib has been studied in adult patients with advanced thyroid cancer and prolonged their progressive-free survival. Reports on the use of this substance in the pediatric population are scarce.Our objective is to present a young girl with progressive metastases due to RAI-resistant PTC who achieved stable disease with few side-effects with long-term use (4 years so far) of Sorafenib in adult dose.
Design/Methods: A twelve year old girl had been diagnosed with PTC 6 years previously (TNM 2002) pT3N1bpM1 (pul). She underwent thyreoidectomy, neck dissection, and eight courses of radioactive iodine, the final three courses after retinoids. But pulmonary metastases progressed, thyreoglobulin increased and signs of pulmonary insufficiency developed. Off-label use of Sorafenib was initiated in 5/2011, 200 mg once daily and step-wise increased to twice 400 mg after 6 months. Hematologic side-effects were minimal, also cutaneous side-effects were mild (grade 1 hand / foot syndrome). Due to cramping, diarrhea and weight loss, therapy was decreased to once daily 400 mg after a year and increased again to the full dose after 5 months. Thereafter minor reductions of the dose were necessary for a further few months, but for two years now the patient has tolerated the full dose of 2 * 400 mg with hardly any side-effects. Thyrotropin-suppressive therapy, calcium and calcitriol therapy were continued as before.
Results: One month after initiation of Sorafenib the extensive pulmonary metastases showed a mild reduction, thereafter we observed stable disease with MRI / CT. Thyreoglobulin levels and thyreoglobulin antibodies have remained elevated without significant decrease due to fluctuating values (thyreoglobulin 200 ng/ml - 75 ng/ml).
Conclusion: In a case of pediatric PTC with progressive pulmonary metastases and no further RAI option Sorafenib con help to stabilize the disease with the adult dosage of 2 * 400 mg without severe side-effects.

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CASE REPORT: PERIVASCULAR EPITELIOID TUMOR UTERUS OF CHILDREN 5 YEAR OLD

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Background/Objectives: Perivascular epitelioid tumor (PEComa), a recently defined tumor, is a very rare disease. These tumors have primitive mesenchymal tissue origin. It is characterized by the presence of a peculiar population of myomelanotic marker-positive perivascular epithelioid cells. They don't have a specific visualization of radiological diagnosis. Diagnosis is possible after the immunohistochemical analisis. Tumor is commonly detected in the uterus. Tumor classified into the structure of a typical pitch benign and malignant. The differential diagnosis is carried out with epithelioid leiomyoma and leiomyosarcoma and endometrial stromal sarcoma with. All the world maximum observation 161 cases of malignant uterus PEComas, 6 cases described in children. Extremely unfavorable prognosis, with a median survival of less that 2 years. Only surgical treatment for common cases possible to use radiotherapy, whose don't have been proven. No sensitivity to chemotherapy.
Design/Methods: From 2000 to the present in Federal State Scientific Institution "Russian Cancer Research Center named. Blokhin " were 2 women with this diagnosis. They received surgical treatment. On December in 2014, a 5-year-old girl with abdominal pain and vaginal spotting was diagnosis with PEComa of the uterus with metastasis in iliac lymphatic node. The girl underwent surgical treatment – hysterectomy with appendages right to pre-embolization of vessels.
Results: After this treatment, there was no evidence of recurrence or further metastasis. Conducted dynamic monitoring.
Conclusion: Surgery is the only effective treatment for perivascular epitelioid tumor.

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PROPRANOLOL AS A FIRST-LINE TREATMENT OF HEMANGIOMA: SINGLE CENTER EXPERIENCE

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Background/Objectives: Infantile hemangiomas (IHs) are the most common benign vascular tumors in infancy. Spontaneous regression is expected in majority of IHs, so watchful waiting is the best management. Currently propranolol has taken the place of corticosteroids for the treatment of risky IHs. Herein we aimed to analyze our patients with IHs treated with propranolol.
Design/Methods: There were 180 patients with diagnosis of IH, treatment was indicated in 10.8% (n:19) of them, and these 19 patients received propranolol as a first-line treatment between January 2012 - June 2014. Medical records of these 19 patients were analized retrospectively. Clinical characteristics, physical examination findings, treatment indications, treatment details, responses and side effects of propranolol were analized retrospectively.
Results: The median age at diagnosis was 4.5months (1–15), and F/M ratio was 5.33. The most common hemangioma localization was skin and head-neck region in 63% of patients. Treatment indications were local complications (haemorrhage, ulceration, infection) (42%), life threating organ dysfunction (37.6%) and relative indications (26.3%). The median follow-up period was 19.5months (3-41). Pallor and partially regression in hemangiomas were observed between the fourth and sixth weeks in all patients. Complete remission occured in 13 patients, treatment is going on with partial remission in remaining 6 cases. There was no observed side effects of propranolol.
Conclusion: Propranolol is a well-tolerated, efficacious, and safe drug for treatment of IHs. It can be initiated and administered in the outpatient setting. Treatment indications of IHs may become more flexible taking into account of the safety profile of propranolol.

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A TERTIARY HOSPITAL EXPERIENCE OF CHEST WALL LESIONS IN CHILDREN

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Background/Objectives: Primary chest wall tumours originate from different constructions of thoracic wall such as soft tissues, the bony thorax, or extra-pleural region. These tumours are rare and the management of these lesions is challenging and often controversial. We report our multidisciplinary experience in the management of primary chest wall tumours.
Design/Methods: All patients, 16 years and under, who received treatment for chest wall lesions were evaluated. The study period extended over 15 years from 2000-2014. Data was obtained for demography, presentation, management, surgical technique and outcomes.
Results: Primary chest wall tumours were noted in ten patients. There were seven female and three male patients. The most common presentation was a mass. The pathology included rhabdomyosarcoma, osteochondroma, lipoblastoma and ewing's tumour. In only three patients (30%) was the lesion benign. The most common site of distant metastasis was lung (40%).Treatment included surgery alone (40%) and surgery with neo-adjuvant/adjuvant treatment (60%). Reconstructive surgery was undertaken in two patients. The postoperative recovery was mostly uneventful. One patient had a small pneumothorax and two patients had muscle paresis, all of which were successfully treated conservatively. The median hospital stay was 4 days (range 3-7). Disease free survival was noted in eight patients (80%) to date. Two patients were not amenable to curative surgery as they presented at a late stage with locally advanced disease and were given palliative treatment leading to a mortality of 20%.
Conclusion: Chest wall tumours are rare and majority are amenable to surgical resection. The morbidity associated with surgical resection is low. Delayed presentation has a significant impact on the outcome.

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SIROLIMUS IN THE TREATMENT OF CHILDREN WITH DIFFERENT COMPLICATED VASCULAR ANOMALIES

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Background/Objectives: Vascular anomalies comprise a heterogeneous group of disorders that are categorized as vascular tumors (e.g. hemangiomas or hemangioendotheliomas) or vascular malformations. Treatment options include interventions such as resection, embolization, laser therapy and sclerotherapy or medical treatment such as propranolol, steroids, interferon and cytostatic chemotherapy. Mammalian target of rapamycin (mTOR) seems to play a key role in the signal pathway of angiogenesis and subsequently in the development of various vascular anomalies. The successful use of the mTOR inhibitor sirolimus has been reported recently in children with lymphatic malformations and Kaposiform hemangioendotheliomas.
Design/Methods: Six patients (4 males, 2 females) with different vascular anomalies (Kaposiform hemangioendothelioma n=2, combined lymphatico-venous malformation n=2, diffuse microcystic lymphatic malformation with pleural effusions n=1, and orbital lymphatic malformation n=1 were treated with sirolimus in a dose of 0.1 mg/kg/day perorally. Diagnosis was established at birth in 4/6 children and at the age of 10 or 13 months, respectively. Three of the children initially had a Kasabach-Merrit phenomenon (KMP).
Results: Median duration of treatment with sirolimus was 10 months (range 3 to 53 months), 2 children are still treated. Three children achieved complete remission, KMP resolved within 2 months in all patients. Partial remission was seen in 3 children, in one of them complete surgical resection of an orbital lymphatic malformation was successfully performed after a 6- month pretreatment with sirolimus. Treatment with sirolimus was tolerated well, only mild reversible leukopenia was observed.
Conclusion: Sirolimus proved to be effective in 6 children with complicated lymphatic or lymphatico-venous malformations as well as in children with Kaposiform hemangioendothelioma and KMP. Treatment was tolerated well with acceptable side effects. More clinical data are needed to evaluate the optimum length of treatmen t and possible long-term side effects.

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HEMAGIOPERICYTOMA AN UNUSUAL PRESENTATION AS NECK MASS IN A NEW BORN CHILD CAUSING RESPIRATORY DISTRESS

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Background/Objectives: Cervical neoplasm in the child giving rise to obstectric emergency is a rare entity. More commonly cervical teretoma nasopharyngeal tertomas, dermoids the congenital goitres and cystic hygroma are the diagnosis. We operated a new born child with neck swelling presenting with respiratory distress. Histopathological diagnosis of the swelling was hemangiopericytoma. This is a very rare entity.
Design/Methods: Primigravida was referred to our obstectric department with fetal distress at full term. Caesarean section was done to deliver a male infant. The new born showed signs of severe respiratory distress with neck swelling. He was incubated and resuscitated, CT scan showed a large homogenous mass compressing the trachea and oesophagus. Chest X-ray showed pulmonary edema. All other parameters were within normal range. On exploration a well defined homogenous mass was completely excised. Post operative recovery was uneven full. HPR showed haemangiopericytoma. The child is on regular follow up.
Results: Respiratory insufficiency in immediate new born is an emergency requiring multidisciplinary action prompt intervention by the neonatologist is life saving. In our patient C-section immediate incubation correction of acidosis and fluid resuscitation gave the infant the fighting chance. Hemangiopericytoma is very rare and often multicentric vascular tumour most commonly found at retrophyranx, distal index finger and buttocks. In all around 224 cases have been discussed in literature. It is believed to be potentially malignant though the growth rate is slow. The recurrence is 80% when involving central nervous system as compared to 41% to other organ systems. Surgical excision is the treatment of choice with radiotherapy showing promise.
Conclusion: This case is unusual because of site and presentation of the disease.

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ANGIOMATOID FIBROUS HISTIOCYTOMA: A CASE OF LOCAL RECURRENCE AND METASTASES THAT RESPONDED TO CHEMOTHERAPY

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Background/Objectives: Angiomatoid Fibrous Histiocytosis (AFH) is a rare soft tissue tumour of intermediate malignant potential that most commonly occurs in the dermis or subcutaneous tissues in children and young adults. AFH is usually successfully treated with wide local excision. Local recurrence is unusual (~10 % cases) and very rarely (<2%) distant metastases can occur. There is only one previous report of response to chemotherapy. We report a child with AFH who relapsed both locally and with lymph node metastases who showed a good response to chemotherapy.
Design/Methods: A 3-year-old boy presented with a painless firm lump within the flexor surface of the right forearm, MRI scanning demonstrating a 1.9×1.5×1.5cm subcutaneous mass. Complete surgical excision was performed with a histological diagnosis of AFH, positive for EWS-CREB1 fusion gene.
Results: 18 months later, he developed a right axillary lymph node mass. Axillary clearance was performed with nodes showing AFH metastases. MRI demonstrated four lymph nodes in the upper arm and two nodes at the elbow. Within the forearm there were signs of local recurrence with two masses with a maximal diameter of 12 and 15 mm respectively.Surgery was felt to carry a high risk of morbidity. He was thus treated with chemotherapy, receiving six cycles of ifosfamide and Doxorubicin according to the EpSSG non-RMS Study. MRI following four cycles of chemotherapy showed a clear response of the two areas of local recurrence and also of all of the affected nodes. An MRI after six courses showed further response. He received three additional courses of single agent ifosfamide and will now be observed closely with frequent scans.
Conclusion: This case confirms that children with AFH may rarely develop lymph node metastases. Furthermore, we report that metastatic AFH may respond to chemotherapy, and this modality should be considered in the treatment of metastatic or unresectable cases.

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CARDIOPULMONARY BYPASS SURGERY OF COMPLICATED GIANT TUMORS OF THE ABDOMEN AND RETROPERITONEUM IN CHILDHOOD

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Background/Objectives: Surgical treatment is one of the main stages of the combined treatment in children with solid tumors that directly prognosis the good long-term results.
Design/Methods: Were made 8 of surgical interventions for children with solid tumors with the use of cardiopulmonary bypass. The selection of patients for surgery with the use heart-lung machine was performed on the inclusion criteria: the presence of a complicated giant tumors of the abdomen and retroperitoneum with a high risk of fatal bleeding; a thrombus in the inferior vena cava and/or right atrium; the presence of concomitant heart disease requiring surgical correction.
Results: Radical nephrectomy was performed four patients with nephroblastoma in conditions of artificial circulation: in one of them simultaneous operation is performed with the removal of tumor thrombus fixed right atrium and another one - with the removal of floating thrombus of the inferior vena cava and right atrium, in another patient due to tumor invasion into the splenic artery and vein was performed radical nephrectomy with splenectomy. One patient was performed with left lateral segment liver resection with a complex two-stage correction of complex congenital heart defect; one patient with malignant paraganglioma performed a left adrenalectomy with simultaneous operation for removal of tumor thrombus of the inferior vena cava and right atrium and one patient underwent removal of a giant malignant neurosarcoma in the retroperitoneal space and pelvis. Long-term results of treatment: 3 patients have died due to disease progression, 2 of them patients with Wilms tumor, other one patient with a malignant paraganglioma.
Conclusion: The use of cardiopulmonary bypass surgery complications giant solid tumors in children allows to perform most difficult surgical procedures with which were considered earlier, unresectable tumors achieving good long-term result of the combination treatment.

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PEDIATRIC GASTRIC CANCER PRESENTING WITH MASSIVE ASCITES

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Background/Objectives: Gastric adenocarcinoma is rare cancer case in children, so a few cases had been reported with the complete clinical procedure in Taiwan.
Design/Methods: In this case, a16-year-old boy felt abdominal fullness with a poor appetite for 7 days. We used the Sonography, Computed tomography (CT) imaging to discover the gastric mucosa thickness with omentum caking and diagnosed his gastric adenocarcinoma by endoscopic biopsy.
Results: Gastric adenocarcinoma was proven on a 16 yr young boy and the finding is rare in the pediatric population.
Conclusion: Even the incidence of gastric adenocarcinoma is very rare in pediatric patients. Based on the change of modern diet habits, we should pay more attention focus on the possibility on gastric cancer when a child presents the symptoms of distended abdomen and massive ascites.

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DESMOID TUMORS IN CHILDREN

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Background/Objectives: Desmoid tumors (DT) are locally aggressive tumors with no known potential for metastasis. However, tumor invasion into vital structures can result in substantial morbidity and may be even fatal. DT are account for about 0.03 percent of all neoplasms and less than 3 percent of all soft tissue tumors. Clinical behavior and recommended treatments are often dictated by anatomic site.
Design/Methods: Long-term results of treatment in Pediatric DT patients (pt) were evaluated in the Republic of Belarus from 1996 to 2013. A total of 40 children (boys-23, girls-17) with median age of 7,7 years (range 1-16) were treated and 39 of them underwent tumor excision and 1 -tumor biopsy. Tumor sites were: pelvic area- in 18 pt, lower extremity (ex)-8, upper ex-2, abdomen-5, head & neck-3 and others-4. Radiotherapy was given in 14 patients including 6, who received radiotherapy with local electromagnetic hyperthermia. Chemotherapy (usually vinblastin+metotrexate) was administrated in 10 cases, 6 of them additionally received tamoxifen. Tamoxifen without chemotherapy was given in 4 patients as well.
Results: In 14 pts tumor relapsed, particularly in 5 pts two and more times during 12 months after wide excision. Conservative treatment curried out in 10 pts with non operable relapsed tumors. PR registered in 1 pt, SD- 8 and PD-1 with Gardner syndrome who died. 39 pts are alive. Ten years overall and relapse-free survival rate were 94 % and 49% respectively (follow up 74 months).
Conclusion: Our results based on considerable number of patients suggest that radical surgical excision is the method of choice in the treatment of DT patients. Additional chemo, radio as well as hormone therapy could be used in locally advanced and recurrent forms of disease.

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A CASE REPORT: ANGIOMATOID FIBROUS HISTIOCYTOMA IN A 5-YEAR-OLD GIRL AND REVIEW OF THE LITERATURE

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Background/Objectives: Angiomatoid fibrous histiocytoma (AFH) is a rare disease that is often misdiagnosed initially, accounting for approximately 0.3% of all soft tissue tumors. Although predominantly occurring in children and and young adults, the age distribution is wide. There is a slight female predilection. The tumor usually presents as a slowly growing mass within the deep dermis and subcutis, although deep-seated lesions have been described. It most often arises within the extremities but can also occur on the trunk or neck. Surgery remains the mainstay of management, and can effectively control local recurrences and metastases. Herein we describe a case report of a 5-year-old girl whose presentation was concerning for lypoma. Subsequently we review of the relevant literature.
Design/Methods: An 5 year-old girl presented with a painless mass in her right arm for 2 months without constitutional symptoms. Physical exam demonstrated a mobile, nontender, palpable mass along the lateral aspect of the right arm without erythema or soft tissue swelling. The patient underwent en bloc surgical excision, whose biopsy reported AFH. The patient had local recurrence 9 months after the operation. Tumor excision biopsy (wide resection) was performed which reported AFH with disease-free margins. Two months after the operation presents new local relapse, so we decided to meet Radiotherapy (currently serving treatment).
Results: AFH is a rare soft tissue tumor most commonly occurring in children, adolescents, and young adults. Surgery alone with a wide local excision can be utilized to establish local control; however, in cases where a marginal excision is planned, radiation therapy should be utilized to maximize control.
Conclusion: AFH is a rare disease that is often misdiagnosed initially. The diagnosis of AFH is made based on histopathology and immunohistology Radiotherapy may be utilized when wide excision margins are not feasible. AFH does have low potential for metastasis.

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GESTATIONAL TROPHOBLASTIC NEOPLASIA WITH RESIDUAL LUNG MASSES AFTER CHEMOTHERAPY

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Background/Objectives: Clinical Details.
Design/Methods: A sixteen year old girl presented with cough, abdominal pain and vaginal bleeding. She had a spontaneous abortion 3 months before. Examination was significant for pallor and abdominal masses. Blood investigations revealed a haemoglobin of 4g/dl and a B-HCG of 424 846 IU/L. An abdominal ultrasound showed a bulky uterus with no foetus and a large left adnexal mass. Chest X-ray showed cannon-ball lesions. Splenic lesions were seen on CT-scan. A diagnosis of Gestational trophoblastic neoplasia, high risk, was made – FIGO stage IV, prognostic score 8. She developed uncontrolled vaginal bleeding which necessitated surgery. A fungating mass was found, extending through the myometrium into the left adnexa. The tumour was confirmed as a gestational choriocarcinoma. She was treated with chemotherapy until the BHCG normalised and for 6 weeks thereafter. Post-treatment CT scan was significant for residual lung masses. She was in marker remission with a BHCG of 1. She was followed up clinically without removal of the lung masses. Four months post treatment she remains in marker remission and the lung lesions are unchanged in size.
Results: Discussion.
Conclusion: Gestational trophoblastic disease (GTD) refers to a range of pregnancy-related disorders with abnormal trophoblast proliferations. Benign GTD's include complete and partial hydatidiform moles and malignant GTD's include invasive moles, choriocarcinoma and placental site trophoblastic tumour. The diagnosis of GTD is made on combined clinical and radiological findings in the setting of a rising or plateauing level of BHCG post pregnancy as biopsy is deemed too dangerous owing to the vascularity of the tumours. The FIGO prognostic scoring system separates low risk patients (0-6) from high-risk patients (≥7). High risk patients, including all choriocarcinomas, are treated with multiagent chemotherapy. Five-year OS vary between 75-90%. Residual masses post-treatment in patients with marker remission likely represent non-viable tissue and should not be removed.

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PLEOMORPHIC LIPOMA NECK IN A 10 MONTH OLD CHILD : A RARE CLINICAL ENTITY

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Background/Objectives: Neck masses are not uncommon in children and commonly include congenital lesions and their complications. Other masses include lymphadenopathy, vascular, inflammatory, infectious and malignant lesions. Lipomas are rare in children. We report the first case of Pleomorphic Lipoma in the paediatric population in world literature.
Design/Methods: Ten month old male child presented with a lump on the right side of the neck noticed for 3 -4 days. No constitutional symptoms were present. On examination a 5×4 cm lump noted in the right lower cervical region which was non tender, firm in consistency, slight mobile in lateral directions and the overlying skin was normal. Contrast Enhanced Computed Tomography (CECT) neck showed a well defined heterogeneously enhancing mass measuring 4.3×4.5×2.7cm (CC x AP x TR) in the right posterior triangle of the neck with few hypodense areas within it. Fine needle aspiration cytology was inconclusive.
Results: Complete excision of mass under general anaesthesia was done. Histopathology showed lipomatous tumor with spindle cells. The higher magnification showed multinucleated floret cells and bizarre cells. The tumor cells were positive for CD 34 immunohistochemically. At one year follow up the patient is doing well with no recurrence.
Conclusion: Pleomorphic lipoma is a disease of older men not previously reported in children. The treatment includes complete excision of the mass with regular follow up. It may be considered as a differential in large insidious neck masses.

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STEPS TOWARDS AN EUROPEAN VIRTUAL TUMOR BOARD FOR VERY RARE TUMORS— REPORT FROM THE EUROPEAN COOPERATIVE STUDY GROUP ON PEDIATRIC RARE TUMORS AND EXPO-R-NET PROJECT

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Background/Objectives: EXPO-r-NeT is an international EU-funded project. Among other activities, EXPO-r-NeT aims to improve access to qualified care for children with very rare tumors (VRT) by intensified networking between pediatric oncology centers and national study groups. Based on the activities of the recently founded EXPeRT, a tumor board structure shall be developed. Here, we report on the national and international consultation activities of EXPeRT and its national partners.
Design/Methods: The EXPeRT group has developed a structure for consultation activities. International consultations regarding particularly rare or complicated cases are centrally coordinated (expert-advice@klinikumdo.de), using a specific consultation request form. Between October 2014 and February 2015, the national coordinators reported all national and international consultations to EXPeRT.
Results: In this 5-month period, the national VRT boards and the EXPeRT board responded to 143 consultation requests. 48 requests were international, either within the EU (n=24) or from pediatric oncologists outside of the EU (n=24). Between the national groups, the panel of diagnoses varied according to the scientific focus of the group, with a high proportion of very rare sarcomas in France or Italy, and non-germ-cell gonadal tumors in Germany. 24 patients have been discussed within the complete EXPeRT panel and/or with associated experts for specific entities.
Conclusion: There is a continuous demand of consultation regarding pediatric VRTs. With the increasing visibility of the EXPeRT group, increasingly more requests from EU and non-EU states are seen. Approximately, 80% of consultation requests can be solved at the national level. For particularly rare and difficult cases, an IT-based consultation platform is currently established, which will allow a thorough discussion of the patients. In addition, recommendations for diagnosis and treatment are currently consented to assist pediatric oncologists in clinical management. *ExPO-r-Net is funded by the European Union in the framework of the Health Programme (2008-2013), grant 201312 07.*

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THYMUS TUMORS IN CHILDREN: A REPORT FROM THE EUROPEAN COOPERATIVE STUDY GROUP FOR PEDIATRIC RARE TUMORS (EXPeRT)

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Background/Objectives: Background: Thymomas and thymic carcinomas are extremely rare in children in which no therapeutic guidelines has been established.
Design/Methods: Methods: Retrospective analysis of clinical data and therapeutic characteristics of pediatric patients till 18 year with thymus tumors treated in years 2000-2012 and registered in the EXPeRT database of the cooperating national rare pediatric tumors working groups from France, Italy, Germany, and Poland.
Results: Sixteen children with thymoma (median age 11 y) and 20 patients with thymic carcinoma (median age 14 y) were included into study. At diagnosis R0- in 11 patients with thymoma and one with thymic carcinoma; R1- in 3 cases and R2- in 4 patients. Chemotherapy was administered to 22 children (17-neoadjuvant chemotherapy). Eight patients with thymic carcinoma received additional radiotherapy. 17 patients died (15-thymic carcinoma, 2 -thymoma). Five-year OS for patients with thymic carcinoma is 21.0±10.0%.
Conclusion: Thymoma is the tumor with good prognosis but thymic carcinoma has very poor prognosis independent of multimodal management. Multidisciplinary, multicenter approach and collaboration with adults' physician are necessary in order to propose homogenous guidelines.

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MALIGNANT MELANOMA IN CHILDREN: ETIOLOGY, TREATMENT, AND PROGNOSIS

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Background/Objectives: To evaluate the etiology, treatment and prognosis of the malignant melanoma in children.
Design/Methods: Twentyone patients who had been diagnosed with malignant melanoma between 1972 and 2015 were retrospectively analyzed. Age range was 0.5-14 years (median: 8), male/female ratio was 13/8. Staging was done according to AJCC. High dose interferon, or CDDP based regimens have been used.
Results: We could define the etiologic factors in only 5 (23.8%) patients. In three patients malignant melanoma occurred within the area of Giant hairy cell nevus, one melanoma patient previously had bone marrow transplantation due to Gricelli syndrome, one patient also had Xeroderma pigmentosum.Tumors were located in head and neck (7), trunk (5), ocular (2), upper extremity (2), lower extremity (2), and intracranial (1). Tumor location was not detected in two patients. Stage distributions were 0 (1), I (1), II (5), III (6), and IV (6). The stage was not defined in two patients. Six patients did not require treatment due to low stages. High dose interferon was given to 9 patients. Three patients were treated with cisplatin based protocols, and three with other chemotherapeutic regimens. Five patients died with disease progression. Overall survival was 75%, whereas event-free survival rate was 70%. Prognostic factors on survival were treatment with interferon (p=0.001) and metastatic disease (p=0.01).
Conclusion: Malignant melanoma is rare tumor in childhood period. Metastasis is the worst prognostic factor. Melanoma patients were treated successfully with high dose interferon in our series.

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CARCINOID TUMORS IN CHILDREN: HACETTEPE EXPERIENCE

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Background/Objectives: Carcinoid tumors (CT) are rare in children. We aimed to review our institutional experience to document their distribution, clinical presentation, treatment and follow-up data.
Design/Methods: Among 10000 children with cancer diagnosed between 1972-2014, we identified 20 CT cases (0.2%). Data regarding age and sex, initial symptoms, physical examination findings, radiologic and other laboratory data, surgeries, treatment approaches and outcomes were noted.
Results: Median age of 20 children was 13.5 years (7-16; male/female: 8/12). Primary tumors were located in appendix in 16 cases, in main bronchi (n=2), in left lower lung (n=1), in ileum (n=1). All 16 cases with appendiceal CT presented with abdominal pain, 4 had fever, 3 had vomiting; preoperative diagnoses were acute appendicitis in 15 and ovarian mass in 1. Histopathological examination of surgical specimens revealed invasion of submucosa in 7, tunica muscularis in 7, serosa in 6 cases; median tumor size was 0.8 cm (0.2-2 cm). Fourteen cases had no evidence of recurrence at a median follow-up of 8 years, 2 cases were lost to follow-up. A 7-year-old boy had a CT of the ileum with abdominal dissemination, ileocolectomy was performed, but he died with progressive disease despite chemotherapy. Two cases with CT of main bronchi were admitted due to cough, hemoptizis, fever and pneumonia, both tumors were resected. The boy who had a positive lymph node received chemotherapy, both cases are disease-free for 13 and 14 years. The adolescent boy with a pulmonary CT and Cushing syndrome findings underwent tumor resection. None of the cases had carcinoid syndrome symptoms.
Conclusion: No clinical or laboratory findings suggestive of CT were evident in children with appendiceal CTs pre- or postoperatively; none necessitated further intervention or treatment. Localized CTs in children were mostly curative with surgical resection.

Prognosis is poor for patients with metastatic disease, who might need novel therapeutic strategies.

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USEFULNESS OF LONG TERM FOLLOW-UP FOR THE CHILDHOOD CANCER SURVIVOR - A CASE OF PEDIATRIC THYROID CARCINOMA FOLLOWING THE TREATMENT OF NEUROBLASTOMA

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Background/Objectives: Neuroblastoma(NBL) is one of the most frequent solid tumor and mass screening had used to be performed at six months in Japanese children. Recently, lomg term follow-up(LTFU) is very important for heavily treated childhood cancer survivor(CCS) because of late complications such as endocrine disorder, metabolic disease, second cancer and so on.
Design/Methods: We present a case of pediatric thyroid carcinoma diagnosed 12 years after the treatment for infantile NBL.
Results: The patient is a 12-year-old girl with a history of infantile NBL with Horner's syndrome diagnosed in 6 months of age. She had no family history of thyroid disorders and underwent chemotherapy, surgical resection and autologous bone marrow transplant (aBMT) with high dose chemotherapy at 10 months of age. After aBMT, she achieved VGPR because of residual tumor with no signs of tumor marker elevation. LTFU was started in January 2012 between two departments of Pediatrics. Two years later at 12 years of age, a large mass was noted in the left thyroid. Since other laboratory findings were within normal, she underwent thyroid tumor resection. Pathological diagnosis revealed papillary carcinoma of thyroid with metastatic lymph node. After the operation, she is receiving l-thyroxin for hypothyroidism and is well doing.
Conclusion: There are no adequate studies to draw conclusions about treatment for children with thyroid cancer. We emphasize the importance of LTFU in cooperation with at least the two specialized department in CCS.

Posters: Renal Tumours

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PROFILE AND OUTCOME OF WILMS' TUMOR PATIENTS AT THE UNIVERSITY OF THE PHILIPPINES-PHILIPPINE GENERAL HOSPITAL (UP-PGH): A RETROSPECTIVE STUDY (2008 - 2014)

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Background/Objectives: Wilms' tumor (WT) is highly curable with appropriate multimodality treatment. At Philippine General Hospital, the country's national referral center, radiation, surgery and chemotherapy are available but survival rates for solid tumors remain low. We reviewed our WT experience and outcomes.
Design/Methods: Medical records of newly-diagnosed patients with WT from January 2008 to December 2014 were reviewed. Treatment outcome was determined at study endpoint, February 2015.
Results: Thirty-nine children with WT were seen, ages 0.3-9 years (mean 3.1). M:F ratio 1.05:1. All were unilateral. Twenty-four (61.5%) treated with NWTS V and upfront nephrectomy. Five had lymph node sampling (LNS) and 2 tumor spillage. Post-surgical staging: stage I (n=2), stage II (n=1), stage III (n=2), stage IV (n=1) and no LNS (n=18). Pathology: favorable (n=14), unfavorable (n=1), unspecified (n=8) and blastemal (n=1). Four (16.7%) received radiation. Fifteen patients (38.5%) underwent neo-adjuvant chemotherapy due to unresectable tumor (n=8) and as per SIOP regimen (n=7), adopted in March 2014. Thirteen (86.7%) had nephrectomy after 5-22 weeks of chemotherapy (mean 9.9), 1 abandoned and 1 unresectable. Six had LNS and 1 tumor spillage. Post-surgical staging: stage I (n=2), stage II (n=0), stage III (n=6), stage IV (n=4) and no LNS (n=2). Pathology: favorable (n=3), unspecified (n=3), necrosis (n=3), blastemal (n=4) and mixed type (n=1). Five (38%) received radiation. At study endpoint, 20 (51.3%) completed treatment: 13 in remission, 6 lost to follow-up and 1 relapsed. Eight (20.5%) abandoned treatment. Eight (20.5%) died due to disease (n=7) and toxic death (n=1). Two (5.1%) have progressive disease. One (2.6%) on-going treatment. The overall survival (OS) rate at 63 months is 71.4% and 54.7% with abandonment as an event.
Conclusion: Abandonment of treatment, incomplete staging and therapy contribute to poor WT outcome. Knowledge of the treatment protocol and close coordination between subspecialties will help improve survival.

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HEPATIC SINUSOIDAL OBSTRUCTION SYNDROME IN SOUTH AFRICAN CHILDREN TREATED FOR WILMS TUMOUR: PREVALENCE, RISK FACTORS AND OUTCOMES

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Background/Objectives: Wilms Tumour (WT) is one of the commonest tumours in children. Hepatic Sinusoidal Obstruction Syndrome (HSOS) is a documented complication following treatment of WT but the role of malnutrition in the development of HSOS has not been studied. Malnutrition reduces tolerance to chemotherapy and increases the risk for toxicity. This study aims to determine the prevalence, predisposing factors and outcomes of HSOS in children with WT.
Design/Methods: Descriptive retrospective analysis of medical records of children treated for WT, who developed HSOS, at the Paediatric Haematology/Oncology Unit, Chris Hani Baragwanath Hospital.
Results: Eighty two patients were evaluated. Utilising the MacDonald's criteria, 19 patients (23%) had 21 episodes of proven HSOS and 13 episodes of suspected HSOS. Irradiation (OR 0.5; 95% C.I. 0.25- 1.98; P= 0.5) and a right-sided WT (OR 0.65; 95% C.I. 0.21- 1.9; P= 0.73) predicted the development of HSOS but were not statistically significant. Serum albumin levels were lower in the affected group (P = 0.02), but these patients were not more malnourished according to Z-scores. Apart from 2 deaths, outcomes were good, with all other patients showing full resolution of symptoms.
Conclusion: A higher prevalence of HSOS was shown than previously reported. Traditional risk factors showed a trend towards significance. Low serum albumin levels may reflect a child's overall nutritional status, however as an acute phase reactant its use as a biochemical marker of malnutrition may have limitations. Further study of the role of nutrition is warranted.

P-500

EXPRESSION OF PODOPLANIN IN PAEDIATRIC RENAL TUMOURS

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Background/Objectives: High stage renal tumours have a worse prognosis as compared to stage I and II tumours, the prognosis being best in stage I. There are studies on lymphatic spread in adults with renal renal cell carcinoma. However metastasis by lymphatics in Wilms tumour and other renal tumours in children has not been adequately studied. In this study we analyzed the lymphatic distribution in these tumours by immunostaining for lymphatic marker D2-40.
Design/Methods: A cross-sectional, observational study was conducted in the department of pathology in a general hospital of east Delhi, India. Immunohistochemistry with D2-40 antibody was performed and lymphatic density was counted (in twenty two cases of paediatric renal tumours) within the tumour, in the renal capsule and sinus area. This was correlated with stage and type of the tumour. The findings were compared to twenty two cases of adult renal tumours.
Results: Using the Mann-Whitney U test significant difference was observed in peritumoural lymphatic density in the capsule (p value=0.009) and sinus (p value=0.024) of kidneys with tumors in adults and children, the values being significantly higher in the adult patients. Spearman's rho for correlation between increasing age and intratumoural lymphatic density was significant (p value=0.042).
Conclusion: The higher peritumoural lymphatic density in adult tumours may either be due to increase in number of lymphatics with age or indicate increased secretion of lymphangiogenic cytokines by adult tumours (renal cell carcinoma) as compared to paediatric renal tumours. The increase in intratumoural lymphatic density with age also reflects on the increased potential for metastasis in older children as reported in literature. However these findings are preliminary and need confirmation on a larger sample.

P-501

MALIGNANT RENAL TUMOURS IN SINGLE INSTITUTION, SINMALIGNANT RENAL TUMOURS IN SINGLE INSTITUTION, SINGAPOREGAPORE

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Background/Objectives: Renal tumours represent 7% of childhood malignancies. This study retrospectively reviewed clinical profile and outcome of patients with malignant renal tumour in KK Women's and Children's hospital (KKH), Singapore.
Design/Methods: The study was approved by Singhealth Centralized Institutional Review Board. We included all patients with malignant renal tumours seen at KKH from 1997 to 2012 (16 years).
Results: We identified a total of 29 patients. There were 15 females and 14 males with median age at diagnosis of 3.5 years (range 0.25 to 11 years). 22 patients (75%) presented with abdominal mass either isolated or along with fever, poor feeding, vomiting, abdominal pain, haematuria or hypertension. Four presented with painless gross haematuria only. Two patients had tumour diagnosed on screening - one had underlying aniridia; the other had hemihypertrophy with umbilical hernia. One child was diagnosed incidentally during workup for diabetic ketoacidosis and fever. The histological diagnoses included: Wilms tumour (21/29, 72.4%), malignant rhabdoid tumour (4/29, 14%), clear cell sarcoma (3/29, 10.3%) and renal cell carcinoma (1/29, 3%). The staging according to NWTS were: 7 (24%) stage I, 8 (28%) stage II, 9 (31%) stage III and 5 (17%) stage IV. All patients received treatment according to NWTSG protocol except one who was treated with SIOP protocol. Median follow up time was 4.7 years. There were two deaths in this series – both had stage IV malignant rhabdoid tumour. One patient with stage III clear cell sarcoma developed disease recurrence. The remaining patients were alive and recurrence-free.
Conclusion: Although the numbers were small, our series demonstrated excellent disease-free outcomes for paediatric renal tumours, especially Wilms tumour.

P-502

SIRT1 PROTEIN EXPRESSION IN WILMS TUMOR

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Background/Objectives: Histone deacetylase Sirtuin 1 (SIRT1) is involved in tumorigenesis and may function either as a tumor promoter or suppressor.The objective of this study was to characterize SIRT1 expression in Wilms tumor (WT) and to determine whether its three components display different expression patterns.
Design/Methods: Histological slides of 58 patients with WT diagnosed between 1998 and 2012 enabled the selection of areas of blastema (n=42), epithelium (n=9) and mesenchyme (n=40). Additionally, non-neoplastic renal parenchyma adjacent to WT (n=23), fetal kidney (n=11), renal dysplasia (n=6) and renal non-WTs (n=16) served as controls. SIRT1 nuclear expression was evaluated by immunohistochemistry and quantified using image analysis (GenASIs Go-Path, ASI). Five random images of selected areas in each slide were evaluated to determine H-score. Non-parametric tests were used for statistical analyses.
Results: WT patients included one adult and 57 children [median age: 48 months (range: 6 months–10 years)]. Median SIRT1 expression was higher in WT [H-score: 153 (range 0.9-295.5)], than in benign tumors [1.95 (1.4-2.1)], fetal kidney [24.1 (0.5-128.2)], adjacent renal parenchyma [39.2 (1.9–79.7)] and dysplasia [19.8 (9.8-44.9)] ($p<0,001$). Among WT components, blastema displayed the highest H-score [269.5 (range: 42.5-294.4)] compared to epithelium [196.6 (137.5-296.1)], although not reaching statistical significance ($p=0.061$). Mesenchyme showed significantly lower expression than blastema or epithelium [46.6 (6.1-190.6)] ($p<0.001$), and the same trend was observed for malignant non-WTs [114.1 (3.4–280,2)].
Conclusion: SIRT1 is overexpressed in WT, mostly in blastema and epithelium, and in other malignant renal tumors. It may serve as WT biomarker as well as a promising therapeutic target.

P-503

WILMS TUMOUR: EXPERIENCE AT A TERTIARY CENTER IN A RESOURCE LIMITED SETTING

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Background/Objectives: Wilms tumour (WT) is the commonest primary malignant renal tumour of childhood. Enormous progress has been made in its treatment, resulting in an outcome exceeding 85% in high income countries. It is however a difficult cancer to treat in developing countries with much lower survival rates. To review the clinical profile and outcome of treatment of children with WT at the University of Port Harcourt Teaching Hospital (UPTH), Nigeria.
Design/Methods: All patients with WT admitted into the Paediatric Oncology unit of the UPTH from January 2011 to December 2014 were reviewed. Their clinical profile, management and outcome were analyzed using SPSS version 20.0.
Results: Out of 105 children with various childhood malignancies, 31(29.5%) had WT: 17 males (54.8%), 14 females (45.2%). All children presented with abdominal mass, 6 (19.4%) had hypertension. All had an abdominal ultrasound, 9(29%) had abdominal CT scan while only 11(35.5%) had histological diagnosis. Twenty-six children (83.8%) had metastatic disease at diagnosis and 4(13%) had bilateral disease. Sixteen (51.6%) received native treatment prior to presentation, 19(61.2%) had chemotherapy, 12(38.7%) had surgery and 3(9.6%) radiotherapy. Twelve patients (38.7%) defaulted with or without commencement of treatment while mortality was recorded in 8(25.8%) cases.
Conclusion: Most children with WT had advanced disease at presentation. Default and mortality rates are high in our environment. Introduction of palliative care from diagnosis as an integral part of management, and free treatment of childhood malignancies are advocated to reduce default rate and improve outcome.

P-504

RESULTS OF PATIENTS CON WILMS TUMOR STAGE 1 (WTS1) TREATED IN A PEDIATRIC ONCOLOGY CENTER

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Background/Objectives: Renal tumors represent 5 % of all malignant tumors in children. Among those, 92 % are WT. Stage is one of the most important prognostic factor. According to the International Society of Pediatric Oncology (SIOP), WTS1 Overall Survival (OS) at 4 years is around 98 % and the Event Free Survival (EFS) reaches 92 %. The purpose is describe patients with WTS1 treated with SIOP protocols at the Hospital de Niños "Ricardo Gutierrez" (HNRG). To analyze the OS and the EFS of these patients.
Design/Methods: Clinical charts of patients diagnosed with WTS1 were retrospectively analyzed between January 1990 and May 2013. The variables evaluated were age, sex, risk according to SIOP Protocols, histological type and treatment received. Kaplan Meier Estimator was used for the survival analysis.
Results: Thirty four patients with WTS1 were included. Male 20 (56 %). Median age 37 months (range 7-146 months). Right kidney 20 (56%). High risk (HR) 3 patients, intermediate risk (IR) 28 patients, low risk (LR) 4. Median follow-up 63 months (range 1 to 163 months). Three patients relapsed: 1 locally and 2 at distance; 2 patients IR (focal anaplasia and mixed type), 1 patient HR (blastemal type); 1 deceased due to disease progression, 2 alive (1 complete remission and 1 in treatment). The 5-year OS was 98 % and the EFS was 91,4 %.
Conclusion: The OS and EFS of these patients was similar to the findings reported by international literature. However, the sample size is not statistically significant to define other adverse prognostic factors for relapse.

P-505

EMERGENCY SURGERY IN CHILDREN WITH NEPHROBLASTOMA

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Background/Objectives: Nephroblastoma - one of the most common solid tumor of childhood (6-7%). Sometimes patients come to the hospital for urgent surgical indications, and it is necessary to perform emergency surgery on the first stage of treatment.
Design/Methods: From 2006 through 2012, at the Institute of Pediatric Oncology were treated 156 children with monolateral nephroblastoma. According to the plan are made surgery in 141 (90.4%) patients. Emergency surgery was performed in 15 (9.6%) patients. The reason for emergency surgery in 11 cases was bleeding (hematuria), do not respond to conservative treatment, and in 4 cases - suspected rupture of the tumor, which was confirmed in only one case. In this group all patients underwent nephrectomy, retroperitoneal lymph node biopsy. For all children, the diagnosis is confirmed morphologically. There were no deaths and threatening surgical complications. Postoperatively, patients were treated with chemotherapy and, if indicated, radiation therapy, according to the accepted protocol.
Results: 14 children are alive more than two years after the end of special treatment. One child subsequently died of tumor progression of the disease.
Conclusion: Implementation of adequate surgical intervention in emergency and urgent situations in children with nephroblastoma, except in cases of tumor rupture, does not lead to a deterioration in survival in this group of children.

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RARE PEDIATRIC MALIGNANT TUMORS: SINGLE CENTER EXPERIENCE

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Background/Objectives: Knowledge of the clinical presentation, management, and long-term outcome of rare pediatric tumors has been based on limited single institution data or studies on adults. Aim of this presentation is to share our experience about rare childhood malignancy from Istanbul University, Istanbul Medical Faculty, Division of Pediatric Hematology/Oncology.
Design/Methods: We retrospectively evaluated records of 13 patients with rare malignant tumors in terms of presentation and outcome.
Results: We have 13 patients; each of whom was diagnosed with rare tumors namely sialoblastoma, intracardiac sarcoma, infantile choriocarcinoma, renal rabdomyosarcoma, breast rabdomyosarcoma, thyroid papillar carcinoma, granulocytic sarcoma of the bladder, signed ring cell carcinoma of the stomach and angiosarcoma except peripheral T cell lymphoma diagnosed in 2 patients and Li- Fraumeni syndome in 2 relative patients. The median age of the patients was 6 years (3 day-16 years), Six of them were male. Five of them were adolescent. Symptoms and signs of the diseases were very heterogeneous and nonspesific: Symptoms of our patients were mass(10), lympadenopathy(4), fever(4), chest pain and palpitation (2), hematuria (2), pericardial, pleural effusion and ascites(2), headache, convulsion, vomiting(1), DIC (1), back pain(2), pathologic fractures(1). Two patients had a family history with cancer and R337P mutation (member of p53 gene family). Pathologic diagnosis was very difficult and need further stain and consultation. The mean time between onset of symptoms and diagnosis was 2 months(15 days-4 monhs). Eleven patients admitted to hospital with advanced stage. Six patients succumbed to death. Four patients alive without disease. Three patients are under treatment.
Conclusion: Due to the broad heterogenity of tumor types and encompassing rare pediatric malign tumors, the limited resources of the different groups, registries and clinics has resulted in disparity within the clinical and molecular genetic study of rare childhood cancer. These problems might be solved by establishing large international cooperative groups.

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OUTCOME OF WILMS TUMOR IN CHILDREN: SINGLE CENTER EXPERIENCE

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Background/Objectives: Wilms tumor (WT) is the most common renal malignancy and accounts for 6-7% of all childhood cancers. Advanced stages associated with worse prognosis. Regional outcome data is secarse. The aim of this study is to determine the demographic and outcome of WT patients in King Faisal Specialist Hospital-Jeddah.
Design/Methods: A retrospective chart review was performed. Laboratory and clinical outcome data for a total of 27 patients with WT diagnosed between 2000 and 2013 were analyzed.
Results: Out of 27 patients 16(59%) were females. The mean age at time of diagnosis was 3.4(+/-3) years. Abdominal mass was the most common presentation (n=15, 56%) followed by hypertension (n=8, 30%). Distribution of the cases according to staging I, II, III, IV and V is 22%, 15%, 26%, 22%) and 15% respectively. Seven (26%) patients had lung metastasis at presentation. Majority of cases had a favorable histology 25(93%). The median time between symptoms and diagnosis was 28(Range: 11-270) days. All patients treated with National Wilms Tumor chemotherapy trial-4 except one. Twenty six (96%) patients got surgical resection, 22 of them had complete and 4 had partial resection. Thirteen patients (48%) received radiation. Relapse was observed in 10(37%), 2 are due to treatment abandonment. All relapse cases were salvaged with chemotherapy. However, 3 of them were expired (11%). The median time of relapse was 5 months. Three patients had lung relapse and 3 had both lung and pelvis relapse. Event free survival (EFS) was 63% and overall survival (OS) was 89% with median follow-up period of 37(Range: 8-78) months.
Conclusion: We observed increased number of relapses in comparison to the published international data. This could be due to delay of starting treatment and/or abandonment treatment. Therefore, regional multicenter study is needed to better understand the epidemiology and outcome of Wilms tumor.

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CHARACTERIZATION OF CYCLIN D1 IMMUNOREACTIVITY AND IDENTIFICATION OF NOVEL TRANSLOCATIONS IN CLEAR CELL SARCOMA OF THE KIDNEY

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Background/Objectives: Pathological diagnosis of clear cell sarcoma of the kidney (CCSK) is challenging because it resembles blastemal Wilms tumour (WT) and other paediatric sarcomas, but lacks a distinctive immunophenotype. Recently, subsets of CCSK have been found to have the YWHAE-FAM22 translocation t(10;17)(q22;p13). This also occurs in high-grade endometrial sarcoma in which it is associated with cyclin D1 overexpression. We sought to determine YWHAE-FAM22 translocation status and cyclin D1 immunoreactivity in a series of CCSKs.
Design/Methods: Immunohistochemical staining staining for Cyclin D1 was performed on 8 CCSKs from 7 patients, and compared with a custom tissue microarray of other renal tumors. YWHAE-FAM22 fusion status was determined by RT-PCR. Conventional cytogenetics and fluorescence in-situ hybridization (FISH) were performed to characterize karyotypes and novel translocations that were identified.
Results: No CCSK in our series had the YWHAE-FAM22 fusion transcript. However, novel karyotypes were identified in 2 cases – t(2;13)(q13;q22) and t(3:17)(q29;p11.2). FISH utilizing break-apart probes flanking the break-points showed a break-apart signal in tumor specimens but not non-neoplastic kidney sections. Seven of seven CCSK (100%) showed diffuse and strong nuclear cyclin D1 staining, excluding one case with poor tissue section antigenicity. In comparison, 3 of 3 congenital mesoblastic nephromas (100%), and 18 of 29 (62%) neuroblastomas showed diffuse and strong positive staining. Six rhabdoid tumors and 1 metanephric adenoma showed patchy and weak staining. Among WTs, stromal and blastemal components were negative, and epithelial components showed 2+ to 3+ staining in 50-75% cells forming morphologically distinctive epithelial structures.
Conclusion: CCSK shows strong and diffuse nuclear cyclin D1 immunoreactivity which helped to distinguish CCSK from blastemal WT, metanephric adenoma and rhabdoid tumours, but not from neuroblastomas and mesoblastic nephromas. Unlike in endometrial stromal sarcomas, Cyclin D1 overexpression in CCSK is not consistently associated with YWHAE-FAM22 translocation. In addition we describe novel somatic translocations t(2;13)(q13;q22) and t(3:17)(q29;p11.2) in two cases.

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PREOPERATIVE RISK FACTORS IDENTIFIED FOR INTRAOPERATIVE EXTENSIVE HEMORRHAGE OF WILMS TUMOR

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Background/Objectives: The role of surgery in the therapy of Wilms tumor is paramount while extensive Intraoperative hemorrhage is a severe complication. Here we present our data on the treatment of Wilm's tumor with an emphasis on finding preoperative risk factors associated with extensive hemorrhage during nephrectomy.
Design/Methods: We retrospectively reviewed all patients diagnosed with Wilms tumor and had undergone radical nephrectomy between January 2005 and January 2013 at Shanghai Xinhua Hospital. Patient characteristics noted include age at surgery, gender, body weight, tumor laterality, tumor histology and administration of preoperative chemotherapy. Preoperative CT parameters recorded include tumor dimensions, and displacement of great vessels. A radiologist will calculate tumor volume and assigning a tumor stage. All of the nephrectomy was performed by five experienced surgeons.
Results: There were 80 patients diagnosed with Wilms tumor (57 males, 23 females) included in this study. There were 38 cases of left side tumor and 43 cases of right side tumor;48 cases classified as stage I \ II tumors and 32 cases classified as stage III \ IV tumors; 10 cases accompanied by great vessel displacement; 19 cases underwent preoperative chemotherapy. Comparison of patients with and without intraoperative extensive hemorrhage (defined as ATLS Class III and IV blood loss) demonstrated no significant differences in age, sex, body weight, tumor laterality, and tumor stage. Significant differences existed on the rate of great vessel displacement, the rate of preoperative chemotherapy and tumor volume ($P < 0.05$). Patients with tumors greater than 600 cm^3 had an increased risk of extensive hemorrhage compared with those less than 600 cm^3.
Conclusion: Patient with wilms tumor volume greater than 600 cm^3 and great vessel displacement is prone to suffer extensive hemorrhage during nephrectomy and should be handled carefully.

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WILMS TUMOR INCIDENCE IN THE KYRGYZ REPUBLIC

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Background/Objectives: To study age-specific, regional and ethnic childhood Wilms tumor incidence in the Kyrgyz Republic.
Design/Methods: Calculated the incidence rate of childhood solid tumor of kidney between 1989 and 2013. Collected a histological and cytological dates, and deaths certificates. Estimated population relative risk (RR) for the Wilms tumor in children at the urban and rural areas, and ethnic groups. Counted crude, age-standardized rates (ASR) per 1 000 000.
Results: There were registered 1009 with a new diagnoses of cancer in children.Total annual childhood cancer incidence was 71.8 per 1 million. The most frequent diagnostic groups were leukaemia's (31.5%, ASR 21.7) and lymphomas (17.4%, ASR 10.4). Wilms tumor was on the 2nd place among solid tumours (7.1%) with ASR 5.1 (124 cases, 72 boys and 52 girls). Male/ female proportion was 1.44. Wilms tumor incidence was significantly higher at the South regions (Osh, Galalabat, Batken) with ASR 7.2 compare with North (Bishkek, Chui, Issyk-Kul, Naryn) areas (4.3). High incidence of Wilms tumor was registered in the rural (RR=1.2, 95% CI 3.0, 7.7) compared with urban regions. High incidence rate of Wilms tumors was registered in the Uzbeks ethnic group (6.1), compare with native Kyrgyzs (3.9) or Russians (4.4).
Conclusion: Childhood Wilms tumor incidence in the Kyrgyz Republic is low and similar to those reported from some Asian developing countries. Our findings suggest an ongoing need for population-based surveillance and etiologic research.

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THE EFFICACY OF THERAPY BY IFOSFAMIDE, CARBOPLATIN AND ETOPOSIDE IN CHILDREN WITH RECURRENT WILMS' TUMOR IN A SINGLE CENTER HOSPITAL STUDY

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Background/Objectives: Different researches reported that hematopoietic stem cell transplantation following high dose chemotherapy will improve the survival rate in patients with recurrent wilms' tumor. In this study the question is about the rate of efficacy of using Ifosfamide, Carboplatin and Etoposide with more courses in mentioned patients without bone marrow transplantation.
Design/Methods: Children less than 15 years old with recurrent wilms tumor during May 2007 to April 2013 implied in this study. The chemotherapy regiment was according to NWTS-5R. The hematopoietic recovery after each cycle and tumor size following four cycles of ICE was evaluated. Finally the data analyzed by SPSS software version 22 and compared with different literature reviews about stem cell transplantation's results.
Results: Seven cases enrolled that 57.1% (n=4) had initial stage II and 85.7% (n=6) had Favorable histology. The median time from diagnosis to relapse was 19 months. The sites of relapse were pulmonary (n=5, 71.4%) and renal (n=2, 28.6%). The median number of days for hematopoietic recovery with G-CSF rescue was 22 days following the ICE cycles. After four cycles of chemotherapy 85.7% of patients showed complete and partial response rate. Five-year survival rate was 68.6% and the median time of disease free survival was 19 months following the end of chemotherapy.
Conclusion: Chemotherapy with more number of ICE cycles in mentioned patients can improve the response rate and overall survival with low toxicity. The suggestion of authors is administration of ICE cycle with more courses whereas there aren't suitable criteria for bone marrow transplantation of the patient.

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NEPHRON-SPARING SURGERY FOR NEPHROBLASTOMA IN CHILDREN AND ITS IMPACT ON SURVIVAL

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Background/Objectives: Today, in pediatric oncology there are two groups of researchers who have exactly the opposite point of view on the use of this type of intervention. One group of researchers believes that nephron-sparing surgery can be applied for the treatment of children with nephroblastoma, the second group is of the opinion that this type of intervention should only be used for bilateral nephroblastoma. The aim of our study was to summarize the experience gained in the pediatric oncology unit of the National Cancer Institute.
Design/Methods: We retrospectively reviewed the database for the time period of 2007-2014. The study involved the Wilms' tumor patients under 18. We evaluated clinical-radiological data.
Results: During 2007–2014, 186 children with nephroblastoma received in-patient care in the pediatric oncology unit. 33 of these underwent nephron-sparing surgery, that makes 17.7% of the cases. 13 children were treated for bilateral nephroblastoma, in 20 cases there was a unilateral nephroblastoma. In patients with unilateral nephroblastoma distribution by stages of disease was as follows: 2 children were operated with st. I (10%), 13 children with st. II (65%), 4 with st. III (20%), 1 with st. IV (5%). At the present moment all children who were under observation after nephron-sparing surgery are alive.
Conclusion: Children with Wilms' tumor quite rarely undergo nephron-sparing surgery. This type of operation was previously used exclusively with bilateral tumors, but recently there appeared a tendency to expand the indications for nephron-sparing surgery. The study showed no difference in survival in children after nephron-sparing surgery and children who have undergone radical nephrectomy. Taking into consideration a number of studies that have shown a high risk of chronic renal failure in patients with one kidney after nephrectomy, the use of nephron-sparing surgery is of higher priority.

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DOES PROLONGED PRE-OPERATIVE CHEMOTHERAPY AFFECT RESECTABILITY AND SURVIVAL OF WILMS TUMOR?

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Background/Objectives: To determine effects of prolonged chemotherapy on resectability of Wilms Tumor. Survival of patients with Wilms tumor has improved significantly owing to development and adherence to comprehensive treatment protocols for the diagnosis, chemotherapy, surgery and radiation in addition to public awareness. Poor healthcare infrastructure, inconsistent referrals, and varied skill level of physicians hinder in following a regimented treatment protocol in developing countries.
Design/Methods: A retrospective study of patients with Wilms tumor (WT) was conducted in a cancer hospital in Pakistan. Patients undergoing > 4 cycles of preoperative chemotherapy were included in the study. Patients following SIOP protocol (4 cycles of preoperative chemotherapy), having surgery outside and bilateral tumours were excluded. Three groups were identified. Group I patients received pre-operative chemotherapy followed by surgery. Group II includes patient where tumour remained inoperable after prolonged chemotherapy. Group III patients presented with a recurrence to our hospital that had upfront surgery elsewhere.
Results: A total of 25 patients with WT were studied. Eleven patients in Group I had 11 patients who underwent surgery after mean 16.4 (range 6 -34) weeks of chemotherapy. Five patients in Group II had inoperable tumors after 19.4 (16 -34) weeks of chemotherapy. Six of 9 patients in group III remained inoperable after 25 (6-42) weeks of chemotherapy, while 3 patients underwent excision of recurrence after 8 cycles of chemotherapy. Treatment response was observed in 11 (68.7%) patients of groups I and II.Neither the resectability improved with prolonged chemotherapy nor size reduction observed in group III patients.
Conclusion: Our review suggests that prolonged pre-operative chemotherapy does not improve resectability of Wilms tumors.

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PARTIAL NEPHRECTOMY VERSUS TUMOR ENCULATION FOR WILMS TUMORS CRITERIA AND OUTCOME: PROSPECTIVE SOUTH EGYPT CANCER INSTITUTE STUDY

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Background/Objectives: Approximately 5 - 10% of children with Wilms tumor present with bilateral disease. The treatment challenge is to achieve a high cure rate while maintaining adequate long-term renal function. In unilateral Wilms' tumor (WT), nephrectomy is the standard surgical approach, whereas partial nephrectomy (PN) is controversially discussed.
Design/Methods: We prospectively evaluated the feasibility of nephron sparing surgery (NSS) in children with unilateral (WT) and bilateral (WT). All patients' receive preoperative chemotherapy for 6 weeks and postoperative chemotherapy. From 2006 to

2014, 9 patients with bilateral (WT) and 6 patients with unilateral (WT) underwent nephron sparing surgery.
Results: Nine patients with synchronous, bilateral (WT) were identified, including 4 patients who underwent successful bilateral tumor enculation procedures. Three patients who underwent successful bilateral (PN) and 2 patient underwent tumor enculation on one side and nephrectomy on the other side where the tumor destroys whole normal renal tissue. Six patients with polar unilateral (WT) were identified and candidate for (PN). Four patients underwent successful (PN). Two patient develops postoperative hematoma and positive margin in postoperative pathology underwent radical nephrectomy. Postoperative complications included postoperative hematoma in 2 patients, wound infection in 2 patients, microscopic residual in 2 patients. Long-term complications included local tumor recurrence in one patient, incision hernia in one patient, Distant relapse in lung in one patient who saved by lung metastatectomy. The overall survival rate was 87% (mean follow-up, 4 years); both patients who died had unfavorable histology.
Conclusion: (PN) eliminate the need for, nephrectomy in polar stage I unilateral or bilateral (WT) however enucleative surgery is a reasonable option and oncologycally safe in bilateral multi-centric or central (WT) after receiving preoperative chemotherapy.

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LONG-TERM OUTCOME OF THE REMNANT KIDNEY IN PATIENTS AFTER NEPHRECTOMY FOR WILMS TUMOR

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Background/Objectives: Wilms tumor (WT) is the second most common abdominal tumor in childhood, with survival rates of 80-95%. Many attempts have been made to assess and reduce the potential long-term complications, including renal dysfunction. The present study sought to evaluate the function and growth rate of the remnant kidney in children after nephrectomy for unilateral WT and to identify risk factors for renal injury.
Design/Methods: Data were retrospectively collected on all patients treated by radical nephrectomy for unilateral "WT" in 1995-2014 at Schneider Children's Medical Center of Israel. Glomerular filtration rate (GFR) was calculated according to the Schwartz formula. Hypertension was defined as systolic blood pressure above the 95th percentile for age, sex, and height. Length of the remnant kidney was expressed in standard deviations (SD) from average for age and size.
Results: Sixty-four children met the inclusion criteria. Median age at presentation was 3.5 years (0.5-14). At presentation, mean GFR was 100ml/min/1.73m^2; 22% of patients had a GFR less than 80ml/min/1.73m^2 and 74% had hypertension. At the last visit mean GFR was 103ml/min/1.73m^2; 18% of children had a GFR less than 80ml/min/1.73m^2, and 25% had hypertension. Albuminuria was found in 22%. There was no correlation of chemotherapy type with decreased GFR or increased blood pressure. Radiotherapy was a significant risk factor for protein secretion (p=0.02). Renal length increased significantly, from 0.9SD at presentation to 2.9SD at the last visit (R<0.01). The maximal growth rate was observed during the first post-nephrectomy year.
Conclusion: Although the overall prognosis of children after nephrectomy for WT is guarded, the present cohort had a 20% rate of impaired renal function in the long term. Radiotherapy increased the risk of proteinuria. Close follow-up of this patient population is necessary to monitor the effect of hyperfiltration on the remnant kidney and determine the need for treatment.

P-516

MANAGEMENT AND OUTCOMES OF NEWLY DIAGNOSED WILMS' TUMOR AT TWO LARGE CENTERS IN EGYPT

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Background/Objectives: A huge progress has been made since the early 1970s in the treatment of Wilms' tumor (WT), resulting in a survival outcome of more than 85%. Our study aimed at evaluating the demographics, disease characteristics and treatment outcomes for unilateral WT patients at the National Cancer Institute and Children Cancer Hospital-Egypt.
Design/Methods: A prospective cohort study included newly diagnosed pediatric patients with nephroblastoma between January 2010 and December 2011. Patients were treated according to an institutional protocol based on current COG protocol and were followed till December 2013.
Results: One-thirty five patients were included in the study. 72 were males (53.3%), mean age was 3.5 years. 35 patients (25.9%) were initially metastatic. Post surgery, 49 patients (36.3%) had stage III tumor, 40 patients (29.6%) had stage I and 11 patients (8.1%) were stage II. Anaplasia was seen in 15 patients (11.1%). The median follow-up was 29.3 months (0.3 - 46.6 months). 3-year OS and EFS in favorable histology patients were 83.4% and 64.2% respectively. Early tumor stages (I/II) were associated with significantly improved EFS and OS compared to stage III and stage IV (3-Y EFS 83.3% vs. 63.8% vs. 18.2%, (p-value<0.001) and 3-Y OS: 95.7% vs.94.7% vs. 66% respectively, p-value<0.001). Initial tumor extension into IVC was associated with inferior EFS compared to other stage III local FH-WT (36.5% vs. 63.3% respectively, p-value = 0.049). Blastemal predominance after chemotherapy had no statistically significant impact on prognosis, although a trend towards inferior outcomes was noticed (3-Y EFS 20% vs. 56.3%, p-value=0.253). Median time to start radiotherapy was 27 days which didn't reflect on outcome.
Conclusion: Outcome for early stage WT was comparable to international results, while metastatic WT had a significantly worse outcome. FH-WT with IVC thrombus has to be treated aggressively for a better outcome. Radiotherapy delay might not affect local recurrence in WT.

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TREATMENT AND OUTCOMES OF ANAPLASTIC WILMS' TUMORS IN EGYPT

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Background/Objectives: Wilms tumor (WT) is the most common renal tumor of childhood. Unfavorable Anaplastic WT histology accounts for 5-10% among wilms' tumor. It is considered to be resistant to the regular treatment and carries worse prognosis. Previous National Wilms Tumor Study group studies had hypothesized that anaplasia is not an indicator of aggressiveness of tumor, but only indicates its resistance to chemotherapy. Our aim is to show demographic data for the patients with anaplastic subtype, clinical presentation, and staging in relation to outcome.
Design/Methods: We included all cases diagnosed as anaplastic WT in the period between August 2007-January 2012, at Children's Cancer Hospital- Egypt. We aggregated clinical data on different treatment modalities, demographics, radiological and pathological finding and final outcome. Follow up was continued till July 2013-average period of 12 months.
Results: Twenty-three cases were diagnosed as anaplastic WT in the defined time interval, accounts for 7% of all WT in our institution with 1.8% (focal) and 5.2% (diffuse) subtypes. Median age of 39 months, range from 13-98 months. Abdominal swelling was the most common presentation. Stages I, II, III and IV represented 5 (21.7%), 2 (8.7%), 9 (39.1%) and 7 (30.4%) respectively. Patients were treated according to different protocols. Out of 23 cases, 7 patients died (30.4%), while 16 (69.5%) patients are alive. By comparing the overall survival of anaplastic WT with other pediatric renal malignancies, it showed a poor overall survival (OS) of 43%. Most of the cases are stage III (39%) and IV (30%) of cases, OS between different stages is (P = 0.019). Stage I had recurrence (40% recurrence rate) and recurrence rate for all stages was 26%.
Conclusion: There is a statistical significant difference of OS between different stages and the higher than expected recurrence and death rates was present in stage I.

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OUTCOMES OF ADOLESCENT WILMS' TUMOR: EXPERIENCE OF A SINGLE CENTER IN EGYPT

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Background/Objectives: Wilms' tumor (WT) is the most common abdominal malignancy in childhood, while its incidence in adults is extremely rare, it represents 0.5% of all renal tumors and 3% of wilms' tumor are reported in adults. Society of Pediatric Oncology (SIOP) 93-01 study, reported a total number of 30 adult patients over 7 years, with a good survival of 4-years overall survival of 83% our aim is to report the outcome of adults patients.

Design/Methods: We included all cases diagnosed as adults wilms' tumor (≥10 years old) between period July 2007 and December 2014 at Children's Cancer Hospital 57357-Egypt. Clinical presentation; demographics, radiological and pathological finding and prognosis is reported.
Results: Out of 447 cases, 12 cases are adult wilms' tumor; it represents 2.7% of all wilms'. Patients ranged from 10 to 14.5 years (Mean; 11.78, and Median 10.77 years), there is equal distribution in gender females (n=7) and males (n=5). Most of the patients had a left renal masses (n=8), while the right kidney had lower frequency (n=4), there were no bilateral cases reported, Stages were II, III and IV as following 3, 3 and 6 respectively. Upfront nephrectomy was done whenever possible and all cases continued a postoperative chemotherapy. The pathological finding were favorable histology (n=11) as following Mixed subtype (n=5), Blastemal subtype (n= 3), Epithelial subtype (n= 3), and a case of diffuse anaplastic histology. The patients' final outcome; alive and in complete remission (n=7), relapsed (n=3) who didn't reach a second remission, stationary case (n=1) and patient died post relapse (n=1).
Conclusion: Adolescent wilms' tumor is a rare entity; most of the cases are with favorable histology but it constitutes a poor prognosis, requiring more aggressive lines of treatment or new modalities for achieving better outcomes, larger number are needed for better reporting about survival outcome.

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ATYPICAL PAEDIATRIC RENAL TUMOURS - OUR EXPERIENCE

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Background/Objectives: Paediatric renal tumours are rare in childhood accounting for less than 5% of all paediatric malignancies. We present a case series of our recent experience with such tumours that have demonstrated atypical behaviour.
Design/Methods: All patients presenting with atypical features of renal malignancy in the last five years were identified from hospital patient records and multidisciplinary documentation. Patient demographics, clinical symptoms, radiological findings and outcomes were recorded and analysed.
Results: Ten patients were identified with a median age at presentation of 4 years (1-13 years). Two patients presented with extensive hepatic involvement. One of these patients had a history of multiple systemic haemangiomata posing a diagnostic challenge requiring an additional liver biopsy and localised liver resection. One patient presented with atypical features of a tri-lobulated Wilm's tumour appearing to be separated by vessels on cross-sectional imaging. Two younger patients presented with bilateral pathology. The first patient was found to have stage V disease requiring nephron-sparing surgery on screening for suspected Beckwith-Wiedemann syndrome. The second patient presented with sepsis and abdominal pain following blunt trauma. Cross-sectional imaging revealed renal rupture and contralateral pyonephrosis associated with a pelvi-ureteric junction obstruction. Follow-up imaging showed a mass on the traumatic side confirmed to be a Wilm's tumour. A unilateral nephrectomy and contralateral pyeloplasty was performed. Three patients presented with extensive local disease. The first had involvement of the collecting system and bladder presenting with haematuria and difficulty voiding. Two older patients presented with inferior vena cava involvement. The presumed diagnosis of these was a Wilm's tumour; however biopsy results confirmed a primitive neuroectodermal tumour in both cases.
Conclusion: Paediatric renal tumours can present with several distinct clinical morphologies. We re-emphasise the importance of an individualised multi-disciplinary team approach in the management of such unusual cases.

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EVALUATION OF THE EFFICACY AND SAFETY OF DEFIBROTIDE TREATMENT IN VENO-OCCLUSIVE DISEASE DUE TO ACTINOMYCIN-D

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Background/Objectives: Veno-occlusive disease (VOD) is a potentially life- threatening complication of actinomycin-D. The clinical signs of the disease are hepatomegaly, sudden weight gain with or without ascites and jaundice. We evaluated the efficacy and safety of defibrotide in patients who developed VOD while receiving Actinomycin-D containing chemotherapy for Wilms tumor.
Design/Methods: Two patients (Patient 1: One year-old male, Patient 2: Three years-old male) were admitted in our unit with the complaint of abdominal mass. Ultrasound and computed tomography of the abdomen identified solid mass in the right kidney of the both patients. Right radical nephroureterectomy was performed and histology revealed Wilms tumor. Postoperative radiotherapy was given and chemotherapy regimens were planned for stage III Wilms Tumor in both of the patients. Abdominal distension occurred and clinical condition of two patients progressively worsened after Actinomycin-D therapy. The patients gained weight and the abdominal ultrasound scan confirmed enlargement of liver and spleen with ascites. Doppler ultrasound revealed reverse hepatic and portal venous flows. Blood tests showed severe thrombocytopenia and very high levels of hepatic enzymes. The coagulation parameters were also abnormal. The patients were treated with life support treatment in intensive care unit. Defibrotide treatment was started with a dose of 20 mg/kg/day in 4 divided doses.
Results: The clinics and laboratory of the patients were improved rapidly after defibrotide. Hepatic and portal venous flows were also recorded normal one week after defibrotide treatment. Defibrotide treatment was maintained for 14 days in both of the patients. These patients completed the chemotherapy protocol without any problem.
Conclusion: Defibrotide, an antithrombotic, anti-ischemic, anti-inflammatory, and thrombolytic single-stranded polydeoxyribonucleotide with fibrinolytic properties is a safe, well tolerated, and efficacious therapy in VOD.

Posters: Retinoblastoma

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CHALLENGES IN TREATING BILATERAL RETINOBLASTOMA IN DEVELOPING COUNTRIES: CHILDREN'S HOSPITAL LAHORE PAKISTAN EXPERIENCE

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Background/Objectives: The Children's Hospital Lahore Pakistan is a tertiary center receiving over 600 new cancer patients per year from all over the country. The purpose of this study was to analyze management and outcome of children with bilateral Retinoblastoma and to discuss the role of Neoadjuvant chemotherapy in developing countries.
Design/Methods: Retrospective review of 36 patients enrolled between January 2014 to January 2015 was done. Data regarding their age, sex, stage, laterality, treatment, outcome and impact of Neoadjuvant chemotherapy was analyzed.
Results: Total 36 patients with age ranging from< 1 to 7 years (93% <5 yrs) were included. M: F Ratio was 1:1.4. 16/36 (45%) presented with bilateral Retinoblastoma and 12/16 (75%) with optic nerve involvement and 23/36(64%) for whole group.17/36(47%) defaulter treatment and 18/36 (50%) refused Enucleation at diagnosis. Only 2/16(13%) had bilateral Enucleation and 9/16(56%) unilateral Enucleation with laser therapy in 5/16(32%). Enucleation was done in 25/36(70%). Total 14/36 (39%) have completed treatment, 7/36 (19%) are on treatment, 10/36 (28%) left against medical advice (LAMA) and 4/36 (11%) expired due to metastatic and progressive disease and sepsis. one patient (3%) relapsed. In the Bilateral group 8/16(50%) have completed Rx, 3/16 (19%) on Rx, 4/16(25%) got LAMA and one patient (6%) expired just post RX due to sepsis. When compared with the previous study presented in SIOP 2014 mortality decreased from 18 to 11% for whole group and 1/16 (6%) for BL RB and defaulter trend decreased from 66% to 47% (17/36) and Neoadjuvant chemotherapy used in 58% cases as compared to 54%.The number of bilateral RB was increased to 45%as compared to 10/56(18%) the number of LAMA increased from 13% to 28%.
Conclusion: Mortality of 11% can further be reduced by early diagnosis, treatment, improved ICU care, efficient Multidisciplinary team management. The Neoadjuvant group needs extensive social support to decrease LAMA rate(60%).

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SIRTUIN1 EXPRESSION AND CORRELATION WITH HISTOPATHOLOGICAL FEATURES IN RETINOBLASTOMA

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Background/Objectives: Sirtuin1 (Sirt1) has been implicated for a dual role as a tumor promoter as well as tumor suppressor. One of the several mechanisms is deacetylation of retinoblastoma protein and thereby inhibiting its tumor suppressor function. Data on Sirt1 expression in retinoblastoma do not exist.
Design/Methods: We assessed expression of Sirt1 in sections of archived tissue blocks of enucleated and exenterated specimens of patients with retinoblastoma by immunohistochemistry. Nuclear staining was considered positive. For analysis, grade 3 stained specimens were compared with the rest. The histopathological features were reviewed and correlated with expression of Sirt1. The clinical and survival data were obtained from database. Effect of Sirt1 expression on survival was analyzed.
Results: Out of 100 retrieved blocks, 6 did not contain any viable tissue. Retrospective data of the 94 patients revealed that median age at presentation was 36 months with male: female ratio of 1.9:1. Fifty-one percent of patients had International Retinoblastoma Staging System (IRSS) stage 1 disease. Of the 94 sections, 89 (95%) expressed Sirt1. Forty-eight percent (45/94) specimens showed grade 3 staining (>75%

of cells) and intensity was 3+ in 53% (50/94). No association was noted with degree of Sirt1 expression and any histopathological features of retinoblastoma specimens. Also, degree of Sirt1 expression did not affect the overall survival (OS) and progression free survival (PFS) in the entire group (5-year OS: 93% vs 86%, p= 0.23; 5-year PFS: 89% vs 88%, p= 0.85) as well as in the sub-group of patients with extraocular and metastatic retinoblastoma (5-year OS: 94% vs 83%, p= 0.33; 5-year PFS: 87% vs 81%, p= 0.66).
Conclusion: Sirt1 was expressed in most of the retinoblastoma samples. However, degree of Sirt1 expression was not associated with any high-risk histopathological feature or survival. The near uniform expression of Sirt1 in retinoblastoma specimens may suggest a pathophysiological and therapeutic role.

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CYTOPLASMIC EXPRESSION OF FOXO3A IN RETINOBLASTOMA PREDICTS HIGH RISK HISTOPATHOLOGICAL FEATURES

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Background/Objectives: Forkhead box (FOX) transcription factors serve critical cellular functions including apoptosis and cell cycle regulation. The downstream mechanisms of cell cycle regulation involve preservation of retinoblastoma protein function, acting as tumor suppressor. Its deactivation by phosphorylation and trans-location from nucleus to cytoplasm leads to cell proliferation. Cytoplasmic expression of FOXO3a has been reported to be associated with higher stage and inferior survival rates in breast and prostate cancers. No study has been reported on expression of FOXO3a in retinoblastoma.
Design/Methods: We assessed the expression of FOXO3a in sections of archived tissue blocks of enucleated and exenterated specimens of retinoblastoma by immunohistochemistry. Cytoplasmic staining was considered positive. The histopathological features were reviewed and correlated with its expression. Clinical and survival data were obtained from the database. Effect of FOXO3a expression on survival was analyzed.
Results: Six of 100 retrieved blocks did not contain any viable tissue. Retrospective data of these 94 patients revealed that median age at presentation was 36 months with male: female ratio of 1.9:1. Fifty-one percent of patients had International Retinoblastoma Staging System (IRSS) stage 1 disease. Of the 94 sections, 68 (72%) were positive for cytoplasmic expression. Choroidal invasion was associated with cytoplasmic FOXO3a (59% vs 35%, p=0.04). A trend was also noted in optic nerve resected margin involvement (12% vs 0, p=0.07). However, the overall survival and progression free survival were not affected by FOXO3a expression in the entire group as well as in the sub-group of patients with extraocular and metastatic retinoblastoma.
Conclusion: Cytoplasmic expression of FOXO3a was frequently found in retinoblastoma specimens. Despite the association of cytoplasmic FOXO3a expression with high risk histopathological features, no effect on survival was noted. Activation by relocation of FOXO3a to nucleus may activate non-mutated retinoblastoma and can be a potential target of treatment in patients with retinoblastoma.

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LOSS OF SPERM DNA INTEGRITY AND CHILDHOOD CANCER

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Background/Objectives: Sperm chromatin integrity is essential in fertilization, proper embryonic development and birth of healthy offspring. Sperm is highly vulnerable to oxidative damage to both nuclear and mitochondrial DNA due to minimal cytosolic anti-oxidants. B-cell Acute Lymphoblastic Leukaemia (B-ALL) and Retinoblastoma (RB) are the most common childhood malignancies but the causative factors are not known. This study was planned to analyze the sperm DNA quality as a possible etiological factor for childhood cancers (B-ALL & RB).
Design/Methods: A total of 75 fathers of children with non-familial RB (n=55), B-ALL (n=20) and 75 fathers of healthy children were recruited for the study. Semen samples were collected and normal semen parameters were analyzed. Markers for Sperm DNA damage such as DNA fragmentation index (DFI) were measured by Sperm Chromatin Structure Assay, 8-hydroxy-2'-deoxyguanosine (8-OHdG) by ELISA and Reactive Oxygen Species (ROS) by Chemiluminiscence assay.
Results: In the fathers of RB, the seminal mean ROS levels were significantly higher (36.086±1.83 vs 20.51±2.71 RLU/s/million; $p<0.05$) than in controls but the difference was not significant between the fathers of B-ALL and controls ($p>0.05$). In the fathers of RB, there was a significant increase in mean DFI levels (31.50±6.67 vs 21.9±9.4; $p<0.001$) but there was no significant difference in DFI levels (26.33±8.36 vs 21.9±9.4;$p>0.05$) between the fathers of B-ALL and controls. In the fathers of RB, the 8-OHdG levels (66.02±2.91 vs 23.10±2.71 pg/ml) were significantly higher ($p<0.05$) but in fathers of B-ALL, the difference in 8-OHdG levels (38.51±3.28 vs 23.10±2.71 pg/mL; $p>0.05$) were not significant as compare to controls.
Conclusion: Increased seminal oxidative stress and sperm DNA damage may be the etiological factors for the development of childhood cancers. Paternal age, smoking, pesticide exposure and alcohol intake are the known inducers of oxidative stress, a major factor causing genome hypermutability & DNA damage which may ultimately cause morbidity & childhood cancer.

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OUTCOMES ANALYSIS OF DIFFERENT ONCOLOGY PEDIATRIC TREATMENT IN ADVANCED STAGE RETINOBLASTOMA IN QUITO ECUADOR

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Background/Objectives: Evaluate different oncology treatment pathways in Stage IV Retinoblastoma including intra-arterial chemotherapy. Retinoblastoma is the most common primary intraocular malignant neoplasia. It represent the 4% of malignant tumors in the principal Pediatric BO Hospital in Quito Ecuador. This neoplasia variants presentation including laterality, focal, genetic etiology and stage. In Ecuador diagnosis may be delayed by clinical manifestation, unknown of pathology in pediatric services, absences of screening protocols. With early diagnosis, 5 year survival and visual preservation is 97% (USA), in Ecuador survival is 70%, otherwise the disease is fatal without treatment. Chemotherapy, radiotherapy, local laser, surgery and new chemotherapy intra-arterial are the protocols used.
Design/Methods: Prospective, descriptive, open.Stadistical database recollected in Pathology Service obtained Retinoblastoma cases and observational evolution of treatment during 8 years.
Results: Forty two patients were diagnosed with histopathology in a Pediatric Hospital between 1994 - 2012, 58% women and 42% men, ages included 1 month to 14 years, age groups were from 1 - 5 years 31.4%, 0 - 1 year 17.3%, 5 - 8 years 17%, 8 - 12 years 17,3%, >12 years 17%. The majority of cases were stage IV representing 38% of cases, followed by stage II 32%. Due conditions of ecuadorian population secondary an low income country, all patients were enucleated, concomitant treatment included chemotherapy in all patients, completed radiotherapy 70%, laser thermotherapy 30% and intra-arterial chemotherapy, first time reported in Ecuador, 1 patient. At the moment this patient presents relapse and enuclation was done. The free survival of the study was 71%.
Conclusion: Almost all patient come in advanced stages of disease, and absence of protocols for different treatment stages limits successful results, new perspectives are being implemented in Ecuador without seeing a favorable outcome, due to the limitation of cases and sources. We recommend a Retinoblastoma national neonatal screening.

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TWO CASES OF SYSTEMIC TROMBOSIS AS A COMPLICATION OF INTRAARTERIAL CHEMOTHERAPY FOR RETINOBLASTOMA

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Background/Objectives: We describe 2 retinoblastoma children with thrombotic events triggered by intra arterial melphalan(IAC) therapy.
Design/Methods: The first patient whom presented due to cerebrovascular events was most likely attributable to local toxicity of the chemotherapy with peripheral embolization. The second case's thrombosis involving the extremity is associated with the catheter and resolved very early after antiaggregan and anticoagulant medication.
Results: Our second case demonstrates the more common presentation while the first case, the more severe one, a transient ischemic attack manifested by confusion and vomiting resulting with perminent right side hemiplegia.
Conclusion: During intraartrial melphalan treatment ophthalmologist must be aware of more serious complications and give information to parents. Either ophthalmologist or oncologist learn the history of the family for clinical thrombosis and if necessary tests for thrombofilia might be done prior IAC.

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IMMUNOHISTOCHEMISTRY OF NOXA PROTEIN IN PRIMARY RETINOBLASTOMA TUMORS

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Background/Objectives: Diagnostic immunohistochemistry (IHC) is widely used to evaluate various intraocular malignancies. The most common primary intraocular tumor in children is retinoblastoma. NOXA is the bcl-2 family protein and represents a mediator of p53-dependent apoptosis. Therefore, the aim of our study is to evaluate the immunohistochemical expression of NOXA protein in retinoblastoma.
Design/Methods: Prospective analyses of 19 primary retinoblastoma over a period of one year were included. Expression of NOXA protein was analyzed by immunohistochemistry (IHC) in formalin fixed paraffin embedded sections and correlated with clinical and histopathological high risk factors (HRFs).
Results: There was a slight male preponderance (58%) & 5/19 (26.3%) were bilateral in our study. Out of 19 cases, 14 were found to be poorly differentiated retinoblastoma (PDRB). Massive choroidal invasion was the most frequently observed histopathological high risk factor. Expression of NOXA was seen in 10/19 (52.63%) retinoblastoma cases. Expression of NOXA protein was statistically significant with various histopathological high risk factors.
Conclusion: Immunohistochemistry is being used increasingly in the prognostic assessment of tumors. IHC revealed NOXA as a poor prognostic marker in retinoblastoma. This provides important prognostic information that can guide clinical management and researchers to find molecular target in intraocular tumors.

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CLINICAL PROFILE, RISK FACTORS AND OUTCOME OF ORBITAL RETINOBLASTOMA AT A TERTIARY CARE REFERRAL CENTRE IN INDIA

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Background/Objectives: Management of orbital retinoblastoma (RB) remains a challenge in developing countries. The purpose is to study the clinical profile and outcome of orbital RB in Indian children and to analyse risk factors for metastatic disease.
Design/Methods: Medical records of children who presented to the RB clinic of our tertiary care referral centre between 2011-13 and were diagnosed as RB with orbital invasion were retrospectively reviewed. Treatment consisted of a multimodal protocol that included neo-adjuvant chemotherapy, enucleation, orbital radiotherapy and adjuvant chemotherapy. Those children who had CNS disease at presentation were treated either with multi-modal therapy or were advised palliative care.
Results: Orbital Retinoblastoma accounted for 29% (77/265) of all cases diagnosed with RB during the study period. Of the 77 cases with orbital spread at presentation, CNS metastasis was noted in 17 (22%) cases. Risk factors for metastatic disease at presentation included bilateral disease (p=0.03) and a longer lag period (p=0.04). Other factors such as age (p=0.74) and gender (p=0.633) had no significant association with metastasis. The follow up period ranged from 12-36 months. Survival rate at last follow-up was 75.4% for non-metastatic cases and 18% for metastatic cases (p=0.0001).
Conclusion: Orbital RB accounted for a high proportion of RB cases in our series, underlining the need for awareness campaigns to facilitate early detection. Bilateral disease and delay in seeking healthcare are significant risk factors for metastatic disease. Although locally invasive non-metastatic orbital RB can be managed with multi-modal protocol, CNS metastasis is associated with a poor prognosis for survival.

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A REVIEW OF DIAGNOSIS AND TREATMENT OF RETINOBLASTOMA IN AUCKLAND , NEW ZEALAND FROM JANUARY 2000 TO DECEMBER 2014

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Background/Objectives: Sixty Nine cases of Retinoblastoma (RBL) were identified in New Zealand. This study investigates the epidemiology of RBL, specifically in the North Island.
Design/Methods: This is a retrospective chart review (patient demography, staging, treatment and outcome) of 53 patients with RBL who were seen in Auckland only.
Results: Of 36 unilateral RBL patients, there were 19 European, 7 Maori, 3 Cook Island Maori, 6 Pacific Islanders and 1of Asian descent. Fourteen patients had High Risk Histology in enucleated specimens and received 3 drug adjuvant chemotherapy. The OS of this group is 100% at 4-136 months after treatment. They all have good vision in the remaining eye. No severe late effects have been documented yet.Thirteen of 14 patients presenting with bilateral disease (7 European, 5 Maori,1 Pacific Island, and 1 Asian) received local therapy to the remaining eye and concomitant chemotherapy. All have survived. Only 1 patient received local Radiotherapy, relapsed locally and was salvaged with High dose chemotherapy & ABMT and is alive 9 years later. One patient needed the 2nd eye enucleated and is free of disease 9 years later.One patient had both eyes salvagedOne European patient that presented with trilateral disease and is alive at 13 years from treatment. Two patients who presented with metastatic disease did not survive.83% of unilateral RBL cases presented with a group E eye according to the International Intraocular Retinoblastoma Classification (IIRC).These were enucleated soon after diagnosis. All group D eyes and 2 group C eyes were also initially enucleated.
Conclusion: Despite the majority of our patients being diagnosed with advanced group eyes, the superb treatment of a well defined and organized multi disciplinary team has resulted in 100% OS for patients with unilateral, bilateral and trilateral disease. Metastatic disease (Stage 4a& 4b) at diagnosis is still incurable in our unit.

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A RETINOBLASTOMA PROGRAM IMPROVES OUTCOMES AND ACCESS TO CARE FOR PATIENTS IN RESOURCE LIMITED SETTINGS

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Background/Objectives: Clinical outcomes for patients with retinoblastoma are excellent with early detection and multidisciplinary management. Implementing a RB program addresses multiple aspects of clinical care that impacts overall outcomes. However, resource limited settings particularly public hospitals are challenged by lack of specialists, infrastructure, referral systems and support for treatment. Designing an appropriate RB program in this context is crucial.
Design/Methods: An RB program encompassing early detection campaigns, referral pathway and treatment center, mentoring, RB registry and measuring designated outcomes was implemented in a public tertiary hospital in Davao City, Mindanao, Philippines. Data was collected for patients diagnosed with RB from June 2011 to December 2014. The clinical profile and outcome measures of extra ocular disease percentage, survival and abandonment were documented and analyzed using descriptive statistics.
Results: Fifty-four patients were included in the study. Majority of the patients were male (n=30; 56%), aged 1-5 yrs old (n=49; 91%), unilateral RB (n=37; 69%), and non-Davao residents (n=44; 81%). Leukocoria (n=19; 35%) and proptosis (n=17; 31%) were the most common presenting complaints. Sixty-three percent of patients have advanced disease at presentation (IRSS Stage 3, n=11; 20%; Stage 4, n=23; 43%). There was a three-fold rise in the average number of patients seen per year compared to baseline (n=4, 2005-2010; n-12, 2011-2014) and marked increase in Stage 1 patients in recent 2 years. Overall survival was 35% (n=19) with 19% (n=10) abandonment and 2% (n=1) lost to follow up.
Conclusion: A retinoblastoma program addressing concerns in limited resource settings improves access to care and outcomes for patients.

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MANAGEMENT OF RETINOBLASTOMA IN ALGERIA

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Background/Objectives: Retinoblastoma (RB) is the most common ocular eye tumor in children, with an incidence of 1/15 000 births. Management of patients with retinoblastoma must take into account the various aspects of the disease. The aim of this study is to determine the treatment pattern and outcome of retinoblastoma to raise a reflection on a management policy of retinoblastoma in Algeria.
Design/Methods: This study is a retrospective review of children presenting to a Pediatric oncology unit, Pierre & Marie Curie Center, with a retinoblastoma between 2009 and 2013, tailored treatment strategies were used, including combinations of enucleation, chemotherapy, and radiotherapy, conservatives treatments are made abroad.Tumor control rates and outcomes are reviewed.
Results: 89 children with retinoblastoma were enrolled, 28 bilateral cases (31%) and 61 unilateral (69%), Among the 61 with unilateral involvement, enucleation was performed for a majority (90%). 11 of these patients had neoadjuvant chemotherapy for extraocular or optic nerf extension. Furthermore, in 28 patients with bilateral involvement, 20 (71%) eyes were enucleated and 3 patients were enucleated both eyes

after conservative treatment failure. Overall survival was 94% and relapse free survival 92%.
Conclusion: pediatric oncology team has acquired a certain technicality in the treatment of retinoblastoma, however, it is made difficult because of the unavailability of conservative treatment in Algeria, the implementation of these means will allow to facilitate the management and improve outcomes.

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SECOND MALIGNANT TUMORS:THE SWORD OF DAMOCLES OVER SURVIVORS OF RETINOBLASTOMA

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Background/Objectives: Although retinoblastoma(RB) is the most curable pediatric malignant tumor,long-term survivors,specially hereditary cases,have an well-known increased risk of developping second malignant tumors(SMT).We review the patients(p) diagnosed with SMT within our National Reference Unit for Retinoblastoma.
Design/Methods: Review of clinical records of 91p:67 new diagnosis,24p referred from other hospitals:12p for follow-up,5p for treatment,4 parents with RB,3p for genetic study.Descriptive analysis.
Results: Unilateral 48(53%),bilateral 42(46%),trilateral 1(1%).Median age at diagnosis 12 months(m)(range 1m-5years(yr).Confirmed hereditary cases 43(5 unilateral).Follow-up:median 73m(range 4m-56yr),31p>10yr.External RT:12p, brachytherapy 16p.SMT in four females diagnosed and treated for hereditary bilateral RB during the first year of life.Mean age at diagnosis of SMT:21,7 yr(range 13-28yr). Patient 1: Diagnosed at age 1m:bilateral enucleation.At age 28 year old basal cell carcinoma on left foot was diagnosed.Alive 5yr after complete excision. Patient 2:Diagnosed at age 2m:right eye enucleation,cryotherapy and external radiotherapy on left eye.At age 27 year old right nasal leyomiosarcoma was diagnosed:progression after polychemotherapy and exitus 27m after SMT diagnosis. Patient 3: Diagnosed at age 4m:VEC chemotherapy(vincristine,carboplatine and etoposide) x6 and bilateral external radiotherapy(RT).At age 13 year old,left nasal leyomiosarcoma was diagnosed.Treatment according to EpSSG-2005 strategy:ifosfamide and adryamicine x5,left orbit exenteration with complete resection,external RT(60Gy) and ifosfamide x2.Alive after 12m of follow-up with good quality of life. Patient 4: Diagnosed at age 6m:polychemotherapy (vincristine,cisplatin,etoposide,adryamicine and cyclophosphamide),cryotherapy on right eye and external RT(40Gy) on left eye.At age 22 month old she presented right eye recurrence:VEC x6+ brachytherapy.In December-14,at age 19 year old left naso-orbital undifferentiated sarcoma was diagnosed:good clinical response after 3 cycles of IVADO(vincristine,doxorubicine,ifosfamide,D-actynomycine).After imaging evaluation local treatment with radical surgery and/or radiotherapy will be planned apart from maintenance chemotherapy.
Conclusion: SMT are the sword of Damocles over long-term survivors of hereditary RB.Germline RB1 gene mutation,external RT and alkilating agents are the main risk factors.The role of brachytherapy is not defined yet.Individualized follow-up strategies and guide recommendations for current and future treatment protocols must be stablished.

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FAMILIAL RETINOBLASTOMA; SINGLE EXPERIENCE OF A TERTIARY CANCER CENTER IN JORDAN

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Background/Objectives: Familial retinoblastoma Aseel Ghanem,MD, Ibrahim Al-Nawaiseh, MD, Yacoub A. Yousef, MD, Department of Surgery/ Opthalmology, King Hussein Cancer Center, Amman, Jordan. *Objective*: To evaluate the difference in outcome of management of retinoblastoma between the proband (first affected patient in the family) and the other affected patients in the same family.
Design/Methods: Fourty two patients with familial Retinoblastoma. Retrospective Review of the medical records and Ret-Cam images between 2003-2015.
Results: Out of 200 Retinoblastoma patients in our registree, 42 (21%) patients were familial; 17 were probands and 25 were second or third affected family members. There was 62 affected eyes; 23 eyes for probands and 39 eyes for the other affected family members.In proband, all patients (100%) had at least one eye enucleated, 15(52%) of the affected eyes were enucleated, and 9(31%) of the affected eyes were radiated. In the other hand, in the other affected family members, only 20% had one eye enucleated, 4 (20%) of the affected eyes were enucleated and no single patient received radiation. The Eye salvage rate was significantly higher in the other affected family members than the probands in this series (p=0.0206).All patients who were diagnosed by screening (before having signs or symptoms) had both eyes salvaged with excellent visual outcome and without need for radiation or even chemotherapy.At the last day of follow up, 1 (7%) of the probands was dead due to metastasis, and 1 (7%) had second malignancy (osteosacrcoma in the field of radiation), while no single case in the other family members had metastasis or was dead.
Conclusion: Awareness of families of the possibility of retinoblastoma (by having one person in the family affected with this diseases), and adequate screening (even in absence of genetic testing) showed significantly higher rate of eye salvage in patients with familial retinoblastoma.

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COMBINED SYSTEMIC CHEMOTHERAPY AND INTRA-ARTERIAL CHEMOTHERAPY AS PRIMARY CURATIVE TREATMENT OF RETINOBLASTOMA

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Background/Objectives: The treatment of retinoblastoma is consistantly evolving, current goal of the treatment is not only survival but also saving the eye, saving the vision and minimizing complications following therapy. From early 2000s, Intra-arterial chemotherapy (IAC) has been introduced in the similar context. Our center started IAC in 2010 and have experienced 100 times of IAC treatment.
Design/Methods: From January 2001 and December 2014, among 23 retinoblastoma patients treated with IAC in our center, 11 patients (13 eyes, 2 bilateral) who had IAC for primary curative aim were evaluated. Each patient received both systemic chemotherapy and IAC. For IAC, femoral arterial puncture is done and microcatheter is positioned into the ophthalmic artery during 30 minutes of melphalan infusion.
Results: Median age of total 11 patients was 18.8 months at diagnosis (range, 4.0 to 34.1 months). The Interntational Classificaion of Retinoblastoma (ICRB) sorted the eyes as group B (n = 1), stage C (n = 2), group D (n = 4), or group E (n = 6). Only two eyes initially received IAC and then systemic chemotherapy proceeded. Most eyes had systemic chemotherapy first for one to five cycles. Three to five times for each patient, total 50 times of IAC have been performed to 13 eyes. Except for the eyes of one patient who received IAC abroad, other eyes alternatively repeated IAC and systemic chemotherapy. Focal therapies such as thermotherapy, laser photocoagulation, cryotherapy and intravitreal chemotherapy injection were treated to 11 among 13 eyes (84.6%). There was no death during follow up duration of 29.6 month (median, 6.3 to 55.7 months). Overall eye salvage rate is 72.2 ± 13.8 %. Three of thirteen eyes (23.1%) were enucleated.
Conclusion: Primary IAC for the retinoblastoma patients was tolerable and effective. Alternate systemic chemotherapy and IAC was a promising option for advanced retinoblastoma.

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EVALUATION OF AN INTERACTIVE RETINOBLASTOMA GENETICS WORKSHOP FOR CLINICIANS IN KENYA

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Background/Objectives: Genetic testing is integral to care for inherited disorders in high-income countries, while low- and middle-income countries like Kenya have limited genetic testing and counselling services. Genetic testing will likely become widespread in Kenya within the next decade, yet there has not been a concomitant increase in genetic counselling resources. To address this gap, we designed an interactive workshop for clinicians in Kenya focused on the genetics of the childhood eye cancer retinoblastoma. The objectives were to increase retinoblastoma genetics knowledge, build genetic counselling skills and increase confidence in those skills.
Design/Methods: The workshop was conducted at the 2013 Kenyan National Retinoblastoma Strategy meeting. It included a retinoblastoma genetics presentation, small group discussion of case studies and genetic counselling role-play. Knowledge was assessed by standardized test, and genetic counselling skills and confidence were self-reported by questionnaire.

Results: Knowledge increased significantly post-workshop, driven by increased knowledge of retinoblastoma causative genetics. One-year post-workshop, participant knowledge had returned to baseline, indicating that knowledge retention requires more frequent reinforcement. Participants reported feeling more confident discussing genetics with patients, and had integrated more genetic counselling into patient interactions.
Conclusion: A comprehensive retinoblastoma genetics workshop can increase the knowledge and skills necessary for effective retinoblastoma genetic counselling.

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EXPRESSION OF NADPH OXIDASE AS A REACTIVE OXYGEN SPECIES MARKER IN RETINOBLASTOMA

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Background/Objectives: Reactive Oxygen Species (ROS) have been shown to enhance proliferation of cancer cells. NADPH Oxidases (NOX4) are major intracellular source of reactive oxygen species and elevated ROS levels are often found associated with cancer, apoptosis resistance, tumor cell invasion etc. Under oxidative stress conditions, excessive ROS can damage cellular proteins, lipids and DNA, leading to fatal lesions/mutations in cell that contribute to carcinogenesis. Therefore, the purpose of this study is to examine the expression of NOX4 protein in human retinoblastoma.
Design/Methods: Immunohistochemical (IHC) expression of NOX4 protein was analyzed in 72 prospective cases of primary enucleated retinoblastoma specimens and then validated by western blotting. Cytoplasmic staining was considered as positive and graded as weak/negative, moderate and strong. Expression of this protein was correlated with clinical parameters, tumor differentiation, and various histopathological high risk factors (HRFs).
Results: The tumor was poorly differentiated in 75% with extensive necrosis in 61.66% cases. Calcification was found in 28.33% cases. Massive choroidal invasion was the most frequently observed histopathological high risk factor in 33.3% cases. In addition, optic nerve cut end and retrolaminar invasion was seen in 28.3% cases, iris & ciliary body in 15% whereas scleral invasion was found in 11.66%. One or more than one HRFs were identified in 28/72 cases. NOX4 protein was expressed in 71.6% primary retinoblastoma cases by immunohistochemistry. NOX4 was statistically significant with massive choroidal invasion and poor differentiation.
Conclusion: This is the first study to show the expression of NOX4 protein in retinoblastoma tumor. Our results revealed that NOX4 was highly expressed in human retinoblastoma. Therefore, retinoblastoma tumor may exhibit greater ROS stress than normal cells. Investigating NOX4 might be helpful for developing therapy with combination of ROS-eliminating strategies in the management of retinoblastoma patients.

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DELAYED DIAGNOSIS, THE CRITICAL LANDMARK RISK FACTOR IN MANAGEMENT OF RETINOBLASTOMA

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Background/Objectives: One of the clinical landmark risk factors in managing retinoblastoma is early diagnosis for increasing the survival of these patients. The main idea of this study was to recognise delayed diagnosis in children with retinoblastoma to assess the degree and cause of delays from presenting symptoms to starting treatment of retinoblastoma.
Design/Methods: A retrospective review of all children with proven retinoblastoma, who presented to MAHAK hospital in Tehran, Iran from April 2007 to Dec 2011, was performed. Data was analysed by SPSS version 19 with Chi-square test.
Results: There were 157 (91 boys) children eligible for study. The mean age was 1.21±0.11 years with the mean interval of the delayed diagnosis 3.4±0.53 months. Classification of D group in both unilateral (93 patients) and bilatera tumors was the largest category. The significant relation (P-value=o.o5) delay diagnosis time and tumor grouping was evident. The most frequent symptoms were leukocoria and strabismus respectively. Age was significantly lower in the subgroup of bilateral tumor than unilateral retinoblastomas (0.6±0.12 years versus 1.6±0.15 years). There was late diagnosis in subgroup of extraocular retinoblastoma than intraocular (8.7±2.9 months versus 2.9±0.52 months).
Conclusion: The suggestion of authors is early referring to ophthalmologists and pediatric oncologists, educational programs around signs and symptoms such as leukocoria, strabismus and inflammatory abnormalities through national media. In conclusion, early diagnosis of retinoblastoma can be the critical landmark risk factor in managing those patients because the delay in the diagnosis account for highly advanced clinical and poor prognosis of the therapy.

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EXPRESSION OF VASCULAR ENDOTHELIAL GROWTH FACTOR AND KI-67 PROTEIN IN CHEMOREDUCTION FAILED RETINOBLASTOMA

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Background/Objectives: To study the immunohistochemical expression of vascular endothelial growth factor (VEGF) and Ki-67 protein and to determine its association with clinico-histopathological features in enucleated eyes of chemoreduction failed retinoblastoma (Rb).
Design/Methods: This was a prospective cum retrospective study conducted after obtaining ethical clearance. According to International Classification of Intraocular Retinoblastoma, patients with group C and group D Rb underwent enucleation because of chemoreduction failure were included in our study.
Clinico-histopathological features along with expression of VEGF and Ki-67 by immunohistochemistry were correlated.
Results: Total of 53 eyes was included. 14 eyes had group C and 39 had group D Rb. All patients underwent chemoreduction with focal treatment. 18 eyes (18 patients) failed chemoreduction, out of which 15 eyes were enucleated. Failure rates were 14% in group C and 41% in group D Rb. Histopathology showed viable tumor cells in all enucleated specimens. High risk features were found in 67% cases. There was significant association of poorly differentiated tumor with high risk features. Positive expression of VEGF was found in 47% eyes and Ki-67 in 93% eyes. No statistical association was found of VEGF and Ki-67 protein expression with clinico-histopathological features.
Conclusion: Failure rates of chemoreduction was 14% in group C and 41% in group D retinoblastoma. Presence of viable tumor, high risk features, and Ki-67 expression were found in most of the enucleated retinoblastoma specimens suggesting their possible role in chemoreduction failure.

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RETINOBLASTOMA: CHANGING PARADIGM IN INDIA - EXPERIENCE FROM A TERTIARY CARE CENTRE

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Background/Objectives: Retinoblastoma (RB) is the most common intraocular malignancy in childhood. When treated early and appropriately, especially in intraocular RB, it has a high survival rate with lesser morbidities. The developing countries share larger burden of disease with lesser survival rate. This study aims to throw light on the changing paradigm in clinical and epidemiologic factors of retinoblastoma.
Design/Methods: This is a retrospective descriptive study of children with retinoblastoma followed up in the Pediatric Oncology Clinic at our Centre from a period of August 2011-2014. Clinical and epidemiological profile of these children are described.
Results: A total of two eighty six (38%) outof 752 patients enrolled in to the pediatric oncology clinic over a period of 3 years from August 2011-2014 were diagnosed with retinoblastoma. There was a male predilection (M: F = 1.6:1). One third (33%) of these children had extra ocular extension. Forty five percent (n=130) of the total burden had bilateral disease. Fifty eight percent of intraocular tumors were bilateral against 20% advanced disease being bilateral. Overall 207/286 children were on follow up and have either completed or receiving treatment. 35(12%) children were loss to follow up. Thirty six children (12%) had either progressive disease or have expired.
Conclusion: The data reveals a sharp contrast in the clinical and demographic profile of Retinoblastoma when compared to that of developed countries. Retinoblastoma is major contributor (38 %) of pediatric oncology cases at our Centre, compared to 4% of total cases in developed countries. Advanced disease contributed to 33%, in contrast to 5% in developed countries. We observed a very low loss to follow up (only 12%) of cases owing to the efficient tracking system. High incidence and burden of the disease makes early screening and timely referral imperative for better outcomes in management of retinoblastoma.

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PROGNOSTIC SIGNIFICANCE OF HIGH MOBILITY GROUP PROTEIN IN PRIMARY RETINOBLASTOMA

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Background/Objectives: High mobility group proteins are the members of non histone nuclear factors associated with cell proliferation, differentiation and neoplastic transformation. High mobility group (HMG) proteins are a newly recognized protein regulating cancer cell tumorigenesis, expansion and invasion. Patients who have histopathological high risk factors (HRFs) are more prone to metastasis and recurrence. However, the role of HMG protein is still unclear in retinoblastoma.
Design/Methods: Prospective analysis of 60 primary enucleated retinoblastoma cases over a period of one year. Expression of HMGA1 was analyzed by Immunohistochemistry (IHC) in formalin fixed retinoblastoma specimens and their results were confirmed by western blotting. Expression of HMGA1 protein was finally correlated with clinical and histopathological parameters.
Results: A total of 60 eyes were taken of which 12(17.39%) eyes had bilateral involvement. Ages ranged from 7months to 8years. 45 (75%) cases were reported as poorly differentiated tumors. Histopathologically, 12(20%) had massive choroid invasion, 16(23.33%) had optic nerve invasion, 6 cases each had sclera and ciliary body invasion. Strong expressions of HMGA1 were seen in 55.07% cases. Western Blotting was performed to confirm the immunohistochemistry results. Expression of HMGA1 was statistically significant with poor differentiation (p=0.0440), and with HRF (p=0.0166).
Conclusion: Overexpression of HMGA1 is seen more frequently in poorly differentiated tumors and those with, histopathological high risk factors. HMGA1 could serve as a poor prognostic marker in retinoblastoma. Better understanding of the molecular mechanisms underlying HMGA1 function could yield novel therapeutic approaches to anti-cancer strategies.

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ADVANCED PRESENTATION AND ABANDONMENT : CHALLENGES IN THE MANAGEMENT OF RETINOBLASTOMA IN LOW / MIDDLE INCOME COUNTRIES (LMICS)

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Background/Objectives: The profile of Retinoblastoma(RB) in LMICs differs greatly from that in more affluent settings.This study evaluated the clinical/epidemiological profile and outcome of RB at a paediatric oncology centre in India.
Design/Methods: Retrospective study of all children diagnosed with retinoblastoma between January2009 and December2014. Patients with extraocular/optic nerve involvement were staged using lumbar puncture and bone marrow examination. Patients with advanced intraocular disease and/or no useful vision underwent upfront enucleation.They received 6 cycles of systemic chemotherapy (carboplatin,etoposide,vincristine,cyclophosphamide) in case of high-risk post-operative histopathology.Patients with early stage disease were considered for focal therapies +/- systemic chemoreduction.Extraocular disease warranted 12 cycles of chemotherapy and local radiotherapy.Since 2013,intra-arterial chemotherapy(IACT)has been used at our centre.
Results: In 188 patients(male:female-1.2:1),median age at presentation was 2years(unilateral 2.5years;bilateral2 years).Unilateral and bilateral disease were 71.2% and 28.7%.Median duration of symptoms was 2.35 months (range15days – 2years),with leucocoria (83%) being the commonest presentation. Over two-thirds(68.6%)had group E disease.28%patients had advanced stage(IRSS stage III+ stage IV)at presentation,with extraorbital disease in 12%.Two-year EFS and OS of the entire cohort were 79.4% and 80.5 %. By stage,2-year EFS and OS were : stage1(EFS-96.7% ,OS-96.5%), stage2(EFS -88%,OS-91.4%),stage3(EFS-53.3%,OS-67.1%),and stage4(EFS-15%,OS-12 %).Survival outcomes were poorer when massive choroidal involvement was noted on histopathology of enucleated specimen($p<0.01$) .Of the 16 patients who received IACT,enucleation could be avoided in 10. Abandonment of treatment in the entire cohort was 15%.However, with increased use of ocular salvage strategies like IACT, and improvement in social/financial support abandonment rates dropped from 26% in 2010 to 2.6% in 2013 and 2014.
Conclusion: The outcomes in our patient population are lower than described in Western literature due to delayed presentation, and a higher proportion of advanced stage disease.Improvement in social and financial support systems, and newer modalities of ocular salvage have helped decrease abandonment, and improve outcomes of RB in LMICs.

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GENITOURINARY RHABDOMYOSARCOMA OUR EXPERIENCE USING MULTIMODAL THERAPY

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Background/Objectives: To study the clinical profile and outcome of children with genitourinary Rhabdomyosarcoma (RMS).
Design/Methods: Retrospective review of children treated for Genitourinary RMS at Christian Medical College, Vellore, India from Jan, 2004 – Jan, 2015.
Results: Sixteen children (11 boys, 5 girls) aged 1.5 - 14 years were included. Primary site of tumour was bladder/prostate (BP RMS) in 8 and non bladder/prostate (NBP RMS) in 8. NBP sites were vagina in 3 and one each from the following areas; testis, para-testicular, urethra, para-vesical and scrotum. 11 had embryonal, 4 had botryoidal and 1 had alveolar RMS. Tumour size was >5cm in 75%. Multimodal treatment including chemotherapy (CT) [IVA/VAC], Surgery (Conservative/ Radical) and Radiotherapy (RT) (1440 Gy -5040 Gy) was used depending on clinical stage and operability. Among those with BP RMS, two are currently on treatment; two had disease progression and four achieved CR (complete remission) of which one relapsed. Among three in CR, one had radical surgery, RT and CT; one had radical surgery and CT; and one had CT and RT. Children who had radical surgery required lifelong clean intermittent catheterization.Among those with NBP RMS, 6 achieved CR and 2 had progressive disease. Two children achieved CR with CT and R0 resection; one child with para-vesical RMS with intra-abdominal metastasis achieved CR with R2 surgery and individualised CT. Three children with vaginal RMS relapsed with CT alone.
Conclusion: Majority of children presented with tumours larger than 5cm at diagnosis. All 3 girls with vaginal RMS relapsed. Children who had multimodal therapy had better outcome.

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CORRELATON OF E-CADHERIN AND β-CATENIN mRNA AND PROTEIN LEVELS IN EWING SARCOMA AND PRIMITIVE PERIPHERAL NEUROECTODERMAL TUMORS

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Background/Objectives: Ewing sarcoma (ES) and primitive neuroectodermal tumors (pPNET) are part of Ewing sarcoma family of tumors with very aggressive biology. The lack of differentiation has led to difficulties in understanding tumors histogenesis. It was shown that EWS and pPNET could express cytokeratins, suggesting the partial epithelial differentiation indicative of intercellular junctions, including the tight cell-cell junctions.
Design/Methods: We analyzed 12 specimens of primary tumor tissue of patients with EWS and pPNET. The specimens were obtained by diagnostic biopsy fixed in 4% buffered formalin and embedded in paraffin. For E-cadherin and β-catenin expression analysis we used: RT-PCR and immunohistochemistry (IHC) method with specific antibodies. IHC included the analysis of pan-cytokeratin (AE1/AE3), epithelial marker. All the specimens were previously analyzed by standard histopathology methods, including the IHC positive expression of membrane glycoprotein CD99 and RT-PCR analysis of specific translocation t(11;22)(q12;24) EWSR1/FLI1, which provided the definitive diagnosis.
Results: IHC: 3 specimens had low positivity of pan-cytokeratin – in individual cells or small clusters. 11 specimens were positive for membrane β-catenin, and 2 were positive for membrane E-cadherin. One specimen showed nuclear staining for all 3 markers in individual cells. RT-PCR: 11 specimens were positive for β-catenin and 2 for E-cadherin.
Conclusion: IHC and RT-PCR methods were used to determine and compare the results of E-cadherin and β-catenin expression in EWS tumor specimens and there was a strong correlation between this two methods. Expression of β-catenin by RT-PCR and mainly non-expression of E-cadherin are in accordance to existence of cell-cell adhesive receptors. Partial epithelial differentiation was determined by positive expression of pan-cytokeratin obtained by IHC in 25% of primary tumor specimens. Further studies could clarify possible significance of these findings.

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OUR SURGICAL EXPERIENCE WITH RHABDOMYOSARCOMA IN CHILDREN

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Background/Objectives: Rhabdomyosarcoma is the most common soft tissue sarcoma in children. Surgical method is important for diagnosis, staging, treatment and long term follow-up. We aimed to evaluate the results of rhabdomyosarcoma patients whom we operated.
Design/Methods: Between 2008-2015 the records of rhabdomyosarcoma patients were retrospectively reviewed. Gender, initial complaints, age at surgery, size and site of the tumor, histological subtype, metastasis, surgery, chemotherapy, radiotherapy and survey of the patients were evaluated.
Results: The median age of 8 patients was 30.6 months (16-60 months). All of the patients were male. Initial complaints were abdominal distension, inability to urinate, constipation, swelling on the pelvis, mass on the perineum noticed after falling, subdiaphragmatic mass detected by tests after falling from bike. One patient also had itching and jaundice. Tumor size was 5-9cm for 6 patients and ≥ 10cm for 2 patients. Four patients had pelvic tumor. The origin was prostatic urethra in 3 patients and pelvic floor muscles in 1 patient. Others were located in perineal region, iliac region, portal hilus and subdiaphragmatic area. Seven patients underwent tumor excision and two of them also underwent cystectomy. Tumor and liver biopsy were performed in 1 patient. Pathological results were embryonal rhabdomyosarcoma for 8 patients. Thoracal rhabdomyosarcoma was detected in the postoperative second year in the patient with perineal tumor and it was resected. All patients had chemotherapy and 7 patients had radiotherapy according to IRSG (International Rhabdomyosarcoma Study group) IV treatment guidelines. Median survival time was 29.1 months (13-49 months). Two patients died 13 and 29 months after the surgery.
Conclusion: Surgery of rhabdomyosarcoma is a controversial subject. As the survival times increased the quality of future lives of the patients gained importance. As a result multidisiplinary treatment of rhabdomyosarcoma patients is important.

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RHABDOMYOSARCOMA: A SINGLE INSTITUTIONAL EXPERIENCE FROM A MIDDLE INCOME SETTING

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Background/Objectives: To evaluate the outcomes of children with biopsy proven rhabdomyosarcoma through a period of protocol transition from 1990 - 2010.
Design/Methods: All data was collected retrospectively by folder review. All patients included in the study were diagnosed between 1 January 1990 and 31 December 2010.
Results: One hundred and fifteen patients with rhabdomyosarcoma appeared on our institutional registry between 1990 and 2010. Forty patients were excluded. Of the remaining 75 patients, 34 were female and 41 male. Thirty seven patients had embryonal histology and 18 were alveolar. Patients by stage and group were: Stage 1 (20); Stage 2 (5); Stage 3 (37) and 13 stage 4. Primary disease sites included 17 para-meningeal tumours, 15 head and neck (non-orbital / non-para-meningeal), 11 pelvic (non-bladder, non-prostate), 9 extremity, 6 bladder, 6 vagina, 5 abdominal, 5 orbital and 1 in which no primary was found. By protocol division, 28 patients were treated on the current protocols introduced after 2005, 5 were treated with new protocols introduced in 2003 and 42 on protocols used prior to 2003. With respect to treatment toxicity the main complication was febrile neutropaenia. Twenty eight patients relapsed and only 2 patients were salvaged. Two patients died of infection during chemotherapy, 2 died of refractory / progressive disease, 1 was lost to follow up and 4 died of late secondary malignancies. Thirty eight patients are alive and disease free (5 year OS 61%: stage 1- 80%; Stage 2- 80%; Stage 3- 51%; Stage 4- 42%).
Conclusion: The unit treats proportionally larger numbers of patients with rhabdomyosarcomas with adverse anatomical primaries. Toxicity has been acceptable with very few deaths from infection (2/75). The salvage rate post relapse was dismal (2/28). There is a trend to suggest that protocol revision has impacted positively on survival (OS: pre-2003: 54.1%; 2003-2005: 59.4%; post 2005: 64.2%).

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BREAST METASTASES IN RHABDOMYOSARCOMA: A CASE SERIES

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Background/Objectives: Rhabdomyosarcoma(RMS) is the most common soft tissue sarcoma in children.The most common site of metastasis is the lung. Breast metastases are rare.
Design/Methods: All cases with breast metastasis within a cohort of 200 RMS patients followed in the Istanbul University, Oncology Institute during 1990-2014 are assessed.
Results: There were three adolescent girls with breast metastasis. Two had breast metastases at diagnosis, one during follow-up. All had alveolar histology. Case1: A thirteen-year old girl was diagnosed with rhabdomyosarcoma of the lower extremity with regional lymph node metastases. She received treatment for a year with complete response. Five months after terminating treatment, a mass was detected in her left breast. Tru-cut biopsy revealed rhabdomyosarcoma. Despite chemotherapy, the breast mass progressed and new metastatis were detected in bone and abdomen. She underwent radical mastectomy and further chemotherapy. She is alive for 15 months after breast metastasis. There is no recurrence in the breast, axillary region and primary site; but progression at other sites. Case2: A thirteen-year old girl was diagnosed with rhabdomyosarcoma in the sphenoid sinus. There were metastases in breasts, ovaries, pancreas, bones at diagnosis. Tru-cut biopsy from the breast mass revealed RMS. There was significant regression in the primary site and complete response in all metastatic sites after four courses of chemotherapy. Radiotherapy was given to the primary site. Leptomeningeal metastasis developed after one year from diagnosis.The patient was died with progressive disease sixteen months after diagnosis. Case3: A fourteen-year old girl was diagnosed with RMS at the perineal region. There were bilateral breast and bone metastases at diagnosis. She was treated with IRS-3 protocol. She died from progressive disease in the first year.
Conclusion: The prognosis is poor in breast metastasis of RMS. Mastectomy may be an option for chemotherapy-resistant cases. Breast metastasis should be considered when evaluating adolescent girls diagnosed with RMS.

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GH INJECTION-SITE SARCOMA OCCURRING IN NEUROBLASTOMA SURVIVOR

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Background/Objectives: Second malignant neoplasms (SMN) are serious late events in childhood cancer survivors (CCS). Late endocrinological toxicities are also common and lead to a frequent use of growth hormone (GH) in this population.
Design/Methods: A 13 month-old female was diagnosed with MYCN stage IV neuroblastoma. She was successfully treated with etoposide based courses, surgery and high dose chemotherapy with stem cell rescue. Twelve years later, the patient was started on substitutive recombinant GH therapy due to a progressive growth delay. Injections were performed in both thighs with a maximum dosage of 0,35 mg per kg per week. While on treatment the patient presented a mass of the left thigh on one of the injection site. Imaging was consistent with a hematoma. However, the mass had to be surgically removed secondary to acute pain caused by a local progression. Pathology revealed a Ewing-like ESWR1 negative CD99+ CIC-DUX4 sarcoma with lymph node involvement. Despite chemotherapy, a second surgical resection and radiotherapy the patient died from local and metastasis progression.
Results: SMN are not uncommon in CCS. The role of radiatiotherapy is widely recognized, chemotherapies such as anthracyclines and particularly at high doses have been shown to be independent risk factors for SMN. GH has an intrinsic proliferative effect but has not been correlated with SMN in CCS. Upon subcutaneous injection a substantial part of GH is locally degraded with on-site activity. Thus previous chemotherapies could constitute a first hit and added with local GH effect have led to the development of this SMN.
Conclusion: Both previous anti neoplastic therapies and GH injections contributed to the development of this injection site CIC-DUX4 sarcoma.

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AN INSIGHT INTO MECHANISM OF SIRTUINS DE-ACETYLATION FUNCTION

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Background/Objectives: Sirtuins are histone de-acetylases that were first discovered in yeast. There are seven sirtuins in mammals, they share the same catalytic domain but with different enzymatic activity, cellular localization and various substrates. Sirtuin-a(SIRT1) is the most studied mammalian Sirtuins.
Design/Methods: In our project, we ran IP to test protein interactions of SIRT1 and its different substrates. Then several Sirtuin inhibitors were used with different concentration to break down those interactions. After treatment, an antibody-based probe-ligase-amplification method was used to detect these interactions.
Results: We have found that in Rhabdomyosarcoma and synovial sarcoma, SIRT1 has interaction with histones and some non-histone chromatin proteins such as SSX, TLE1, H3, H3K9, etc. Interactions were also observed in cytoplasmic lysis. These interactions can be inhibited by Sirtuin inhibitors, like tenovin-6 and entinostat at 4uM and 10nM.
Conclusion: Therefore, we believe that our findings may help understanding the mechanism of how Sirtuin inhibitors work.

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EPITHELIOID SARCOMA WITH PLACENTAL METASTASES IN A PREGNANT ADOLESCENT FEMALE: CASE REPORT

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Background/Objectives: Epithelioid sarcoma (ES) is an uncommon subtype of soft tissue sarcoma that occurs at a median age of 23-40 years at diagnosis. Malignancy in pregnancy is also regarded as an infrequent phenomenon, with an occurrence estimated at about one per 1,000 births.
Design/Methods: Case of a 17 year old gravid female diagnosed with ES metastatic to the placenta.
Results: Seventeen year old G1P0 female presented at 31 weeks gestation with an ulcerated wound involving her right fifth digit. Lesion initially appeared as a small wart at age 10 but started ulcerating over the past year. Two months prior to evaluation, she developed large masses over her right chest wall and axilla. Biopsy confirmed ES, and staging revealed widely metastatic disease. Given the significant morbidity with high dose ifosfamide and doxorubicin therapy in a gravid patient with minimal curative benefit, decision was made to defer therapy until after the delivery of the infant. She was induced at 34 weeks gestation and therapy initiated; the patient clinically deteriorated shortly after and died. Placental pathology demonstrated intervillous invasion of ES.As most cases of infant disease occurred within the first 12 months, decision was made for whole body surveillance MRI every 3 months for the first year of life. At 10 months of age, the infant remains free of disease.
Conclusion: There are no guidelines concerning appropriate surveillance of infants born to mothers with sarcoma and placental metastases. Reports of fetal spread propose that intervillous invasions may place infants at considerable risk for disease. This is the first reported case of epithilioid sarcomatous placental invasion in a pediatric patient. With many non-teratogenic chemotherapeutic agents available, the option of therapy should be offered to a pregnant patient to possibly decrease the risk of metastatic spread to the placenta and, therefore, decrease the risk of disease in the infant.

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RHABDOMYOSARCOMA EXPERIENCE: A SINGLE INSTITUTION'S RESULTS

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Background/Objectives: We reported clinical features and treatment results of children diagnosed with rhabdomyosarcoma (RMS) in our institution.
Design/Methods: Medical records of patients with RMS whose treatment and follow up had been carried out in our institution between 1988 and 2015 were analyzed retrospectively.
Results: There were 44 patients with a median age of 72 (13-204) months.The primary tumor site was head and neck in 66%; genito-urinary in 18%; gluteal in 12%; paraspinal in 2% and intraabdominal in 2% patient. Biopsy was performed 64% and primary surgery 36% patient at diagnosis.The tumor histology was embryonal in 91% and alveolar in 9% cases. Clinical group (CG) distribution of patients: CG 1: 4 (9%), CG 2: 3 (7%), CG 3: 34 (77%), CG 4:3 (7%). Primary surgery was resulted with total resection in only 3 patients."The Intergroup Rhabdomyosarcoma Study – IRS" -based treatment regimens were used in 37 patients, COG ARST0431 protocol was used for other 7 patients.Thirty-six patients received conventional radiotherapy to the primary tumor site, two patients to metastatic sites.Delayed surgery was performed in six patients and complete resection was achieved in three of them.The median follow up time was 50 months (range 2 – 162), EFS was 58% at 5 and 10-years; overall survival was 66% at 5 and 10-years. Relapse/progression was developed in 9 head and neck, 4 genitourinary, one intraabdominal and one gluteal RMS. Therapy related death was not seen.; median relapse/progression time was 18 months (range: 20 days – 32 months). Nine relapsed patients died from progressive disease; one patient with Li-Fraumeni syndrome died at 10th month of treatment.
Conclusion: Half of our patients had advanced stage disease, and 84% of patients was in clinical group 3-4. Treatment response had been affected by tumor site. Local control was problem particularly in parameningeal and genitourinary RMS. Survival rates are acceptable.

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INFLAMMATORY MYOFIBROBLASTIC TUMOUR (IMT) AFFECTING PAEDIATRIC PATIENTS: A STUDY OF 46 PATIENTS WITH EMPHASIS ON HISTOPATHOLOGIC DIAGNOSTIC ISSUES

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Background/Objectives: Inflammatory myofibroblastic tumour (IMT) commonly affects children and young adults. Histologically, they display a variety of patterns and hence overlap with other lesions of myofibroblastic origin. Approximately 50% of IMTs show Alk1 rearrangement. Alk positivity is a promising predictive marker for treatment response to crizotinib. We aim to review the histology of IMTs affecting paediatric patients along with discussion on differential diagnoses and ALK positivity.
Design/Methods: A total of 46 patients below age of 15 years diagnosed with IMT at various sites are included. Review of clinical details, imaging findings, histopathology and immunohistochemistry was done. Differential diagnoses were considered and discussed.
Results: Age range of patients was from 3 months to 15 years. M: F ratio was2:1. Various sites were involved (head neck region: 12, GI tract : 12, lung and mediastinum: 9, bladder: 4, pelvis:3, others:6). Surgical resection was performed on 14 patients. Histologically, myxoid / vascular pattern was the commonest. Small biopsy precluded a definitive diagnosis of IMT in 5 patients. Three IMTs with spindle cell morphology were difficult to differentiate from low grade myofibrosarcoma while two IMTs with fibrous morphology were indistinguishable from fibromatosis. ALk positivity was seen in 30% of tumours. One of the pancreatic lesions resembled IgG4 associated disease.
Conclusion: Our series demonstrates that IMTs affect a wide range of anatomical sites in children. Histologically, typical myxoid/ vascular pattern aided diagnosis in most patients. However, in spindle cell type of IMT, low grade myofibrosarcoma needed to be excluded. Lack of atypical mitoses and absence of cellular atypia were deciding features. Similarly, IMT with fibrous pattern resembled fibromatoses. Thus we acknowledge a histologic overlap of IMT with other myofibroblastic tumours which can impact clinical behaviour and treatment decisions. The incidence of Alk positivity was 30% in our series which is lower than reported in literature.

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MAPPING THE INCIDENCE OF KAPOSI SARCOMA AMONG CHILDREN IN SUB-SAHARAN AFRICA

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Background/Objectives: Annually, there are over 163,000 children diagnosed with cancer worldwide. Infection with human immunodeficiency virus (HIV) increases the risk of many cancers. Kaposi sarcoma (KS) is a common HIV-associated malignancy and is more common where human herpes virus 8 is endemic, such as in equatorial sub-Saharan Africa (SSA). The majority of children with HIV reside in SSA. The overall incidence of KS among children in SSA is unknown due to few national cancer registries, under-reporting, and limited diagnostic capabilities. This review compiles available incidence data on KS among children in SSA and maps geographical burden of disease.
Design/Methods: PubMed and Google Scholar were searched for all available studies and registries documenting incidence of KS among children in SSA using key words "pediatric", "Kaposi sarcoma" and the respective country name. Studies that did not report pediatric-specific data were excluded.

Results: Sixty-four studies and two registries were evaluated from 48 countries in SSA. Six case-control studies and one registry were included. Incidence data were extracted and visually mapped. All included studies came from Eastern and Southeastern Africa with a notable absence of data from Swaziland, which has the world's highest HIV prevalence. After indirect adjustment for pediatric population, the incidence of KS among children ranged from 0.09 per 100,000 person-years in the equatorial nation of Kenya to 160 per 100,000 person-years in the neighboring equatorial country Uganda.
Conclusion: There is a dearth of epidemiological information on KS among children in SSA. Contrary to adult studies, which report the incidence of KS being highest in equatorial SSA, this review suggests that living in equatorial SSA may not increase the risk of KS among children. Larger national and regional studies are needed to determine overall burden of disease for KS among children in SSA and to further elucidate the association between geographic location and KS.

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RADIOLOGY OF RHABDOMYOSARCOMAS IN CHILDREN: A PRIMER FOR THE ONCOLOGIST

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Background/Objectives: Rhabdomyosarcomas are the most common soft tissue tumour in children and account for 5-8% of childhood cancers , and 19% of all paediatric soft tissue sarcomas. Overall ~65% of all rhabdomyosarcomas are diagnosed in patients under 10 years old. There is a slight male predilection (M:F 1.67:1 7) with Caucasian children are affected more often than other races.
Design/Methods: Rhabdomyosarcoma usually manifests as an expanding mass; symptoms, however, depend on the location of the tumour. 40% of the tumours occur in head and neck region, including the orbits. Outcome of rhabdomyosarcomas varies with the location of the primary site. The natural history, pattern of metastatic spread, treatment, and prognosis of childhood rhabdomyosarcoma vary with the anatomic site of the lesion. The orbit,head and neck (parameningeal) and genitor urinary (non bladder/prostate) tumours represent the most prognistically favoured tumours. Factors important with regard to prognosis includes large tumours (>5cm in size), invasive tumours and locoregional lymph nodes. These prognostications can be determined at CT scan and MRI.We present characteristic radiological features of paediatric rhabdomyosarcomas in different locations, with their prognostic features.
Results: Radiology plays an important role in initial diagnosis, prognostication, staging and monitoring response assessment of rhabdomyosarcomas in children.We intend to present characteristic radiological features of paediatric rhabdomyosarcomas in different locations, with their prognostic features.
Conclusion: Rhabdomyosarcomas are the most common soft tissue tumour in children. Pediatric Oncologists should be aware of the various radiological features, which are significant in prognostication and response assessment of these tumours in children.

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MALIGNANT RHABDOID TUMOR OF THE LIVER

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Background/Objectives: The aim of the study was to analyze clinical data and therapy
Results: in a cohort of patients with malignant rhabdoid tumor (MRT) of the liver treated in federal cancer center in Russian Federation.
Design/Methods: Sixteen patients with extracranial MRT were treated during the period of 02.2012-01.2015. Four (25%) patients with MRT of the liver were included in this analysis. We analyzed age at diagnosis, alpha-fetoprotein level, stage of the disease (according to Intergroup Rhabdomyosarcoma Study criteria), presence of initial tumor rupture and therapy response. All diagnosis were established by histopathologic examination and confirmed by lack of nuclear expression of INI1. Patients were treated according to European Rhabdoid Tumor Registry recommendations.
Results: Diagnosis was verified on the 1st year of life in all 4 (100%) cases. Median age was 6.75 months (range 1-11 months). M:F ratio was 4:0. There was no elevation of alpha-fetoprotein level at diagnosis. Only 1 (25%) patient had localized disease, 3 (75%) patients had distant metastases. Localization of metastases included lungs; lungs and the opposite lobe of the liver; lungs, left adrenal gland and peritoneal metastases. Two (50%) patients had initial tumor rupture. All patients had IRS IV (1 patient with localized disease due to tumor rupture). Surgery was done in 2 patients (50%): delayed R0 resection (1), initial R1 resection and secondary R0 resection (1). 2 (50%) patients had unresectable tumors. Median number of chemotherapy cycles was 5.5 (range 4-9 cycles). Outcome: 1 (25%) patient - alive with no evidence of disease for 24 months; 3 (75%) – died due to early progression.
Conclusion: Our data confirmed unfavorable prognosis due to advanced stage of the disease and poor response to therapy. However intensified dose-compressed chemotherapy and aggressive surgical resection could be potentially curative in subset of patients.

P-555

TOXICITY AND FEASIBILITY OF CISPLATIN-ADRIAMYCIN-METHOTREXATE BASED CHEMOTHERAPY IN CHILDREN WITH OSTEOSARCOMA AT A COMPREHENSIVE CANCER CENTRE IN DELHI, INDIA

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Background/Objectives: Osteosarcoma is the most common primary bone tumor of childhood. To improve on historically sub-optimal results, a dedicated musculoskeletal unit established in 2009 and a new protocol initiated. To study demographic profile, treatment related toxicities, outcome and survival of patients with osteosarcoma treated with Cisplatin-Adriamycin-Methotrexate (100 mg/m2-75 mg/m2-12g/m2) chemotherapy as in EURAMOS-1.
Design/Methods: Medical records of 47 children ≤ 18yrs, treated during 2009-2013 were reviewed. Toxicities were assessed using CTCAE ver 4.01, and survival by Kaplan Meier method.
Results: Pretreatment demographic and disease characteristics included median age 15 yrs (5 – 18 yrs), with 68% males (32/47), BMI<-2 (Z score) in 14/47 patients; primary extremity tumor in 96% (45/47), large tumors(>8cm) in 87% and non-metastatic disease in 75% (35/47) patients. Limb salvage surgery was possible in 36 patients while 3 underwent amputation. The most common surgical complication was wound infection (5).HUVOS grade III and IV necrosis occurred in 62% (24/39) cases. Clinically significant toxicities observed with Cisplatin-Adriamycin (190 cycles) and methotrexate (432 cycles) included mucositis grade III/IV in 6%(11/190), 5%(24/432) cycles, febrile neutropenia in 20%(38/190), 1%(5/432) cycles, hospitalizations for supportive care in 22%(43/190), 8%(34/432) cycles respectively. Each patient required an average of two hospitalizations for toxicity and delay in next cycle of chemotherapy was observed in 2 cycles per patient. At the end of treatment 35/47 patients remained in remission, 4 progressed, 6 abandoned therapy and there were two therapy related deaths. Event free survival (EFS) was 53%, there were 9 relapses, and none were salvaged. Favorable prognostic factors for EFS were absence of metastasis (62%, 25%, p0.005) and >90% necrosis (78%, 27%, p0.01); median follow up for survivors was 33 months.
Conclusion: This EURAMOS-1 based protocol was feasible in our setting with modest survivals and limb-salvage in most patients. Febrile neutropenia was the commonest toxicity requiring hospitalization. Abandonment reduction strategy is needed.

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THE CLINICAL CHARACTERS OF NON-RHABDMYOSARCOMA SOFT TISSUE SARCOMAS—A RETROSPECTIVE STUDY IN A SINGLE INSTITUTION IN 11 YEARS

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Background/Objectives: The purpose of the study is to summarize the clinical characters of the non-rhabdomyosarcoma soft tissue sarcomas.
Design/Methods: We performed a retrospective analysis of all the data of non-rhabdomyosarcoma soft tissue sarcomas in our hospital in 2003-2014. We followed-up all the patients by telephone or letter to obtain their condition post-operation.
Results: There were 55 cases in total. 1. There were 8 pathological types: synovical sarcoma, fibrosarcoma, PNET, hyalocyte sarcoma, acinous soft tissue sarcoma, embryonal sarcoma, malignant small cell sarcoma and extraosseous Ewing's sarcoma. The case load of these 8 pathological types were 14(25.45%), 15(27.27%), 10(18.18%), 5(9.09%), 4(7.27%), 3(5.46%), 3(5.46%) and 1(1.82%), respectively. 2. There was a difference about tumor location among the eight sarcomas. (P<0.01) 3. There was no difference about the therapeutic protocols. (P>0.05) Radical operation and radical operation plus chemotherapy were the popular therapeutic protocols. 4.There was a

difference about the use of chemotherapy($P<0.01$).The utilization of chemotherapy in PNET, malignant small cell sarcoma, acinous soft tissue sarcoma and embryonal sarcoma were 100%, while the utilization of chemotherapy were 42.7% in other four sarcomas. 5. The survival rate was 49.09%, the loss to follow-up rate was 12.73% and the mortality rate was 38.18%. The two-year survival rate was 50.91% and five-year survival rate was 18.18%.
Conclusion: There were several types in soft tissue sarcomas, and they needed to be diagnosed by pathological examination. The non-rhabdomyosarcoma soft tissue sarcoma should be performed radical operation or radical operation plus chemotherapy.

Posters: Supportive Care/Palliative Care

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IMPACT OF SOFT TOUCH THERAPY IN PALLIATIVE AND END OF LIFE CARE AMONG CHILDREN WITH CANCER

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Background/Objectives: A qualitative study was conducted to investigate the impact of Soft Touch Therapy in Palliative and End of Life care, among children with cancer. It was observed that most of the children in palliative and end of life care reported persistent pain with increased heart rate, anxiety, aggression, irritation and distress.
Design/Methods: After a review of the literature, soft touch therapy was provided randomly for those children who had irritated, aggressive, anxious and distressed behavior. For this purpose, a sample of *N=480 was selected from Children Cancer Unit, The Indus Hospital, Karachi. A qualitative change in behavior was observed, in terms of reduced pain, anxiety, irritation and aggression, while heart rate returned to normal slightly. The study lasted for two years, all through which necessary precautions had been kept in mind.
Results: The results show a great impact of soft touch therapy for pain management and other psycho-social factors, in children with cancer.
Conclusion: Soft touch therapy has the potential to improve the quality of life as well as the well-being of children in palliative and end of life care.*Number of Patients.

P-558

THE DEVELOPMENT OF SUPPORTIVE CARE GUIDELINES TO ENHANCE OUTCOMES OF CHILDREN WITH CANCER IN THE CARIBBEAN

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Background/Objectives: Non-communicable diseases such as cancer are emerging as an increasingly significant cause of childhood mortality. In high-income countries (HIC), childhood cancer survival is more than 80%, compared to 10-30% in low and middle income countries (LMIC). Established paediatric cancer centres in HIC like the Hospital for Sick Children (SickKids), Toronto, Canada are well positioned to share clinical expertise with counterparts in resource-constrained countries. Launched in March 2013, the SickKids-Caribbean Initiative (SCI) aims to enhance care for children with cancer and blood disorders in 6 Caribbean countries: The Bahamas, Barbados, Jamaica, St. Lucia, St. Vincent and the Grenadines and Trinidad and Tobago. In order to prevent deaths due to complications of treatment interventions, intense protocol regimens must be matched with appropriate supportive care.
Design/Methods: In consultation with Caribbean clinicians, 5 priority areas in supportive care were identified: Febrile Neutropenia; Chemotherapy-induced nausea and vomiting; Hyperleukocytosis; Tumour Lysis Syndrome; and Transfusion Medicine. Specialists developed a survey for each respective area, which were then circulated to Caribbean clinicians. Existing international and SickKids clinical practice guidelines were used as a reference to draft documents integrating survey feedback about current practice and available resources.
Results: At an upcoming workshop, SCI representatives will review each of the 5 documents, with consideration paid to local institutional implementation and adherence. These will then be further adapted for institutional use in each country, and a clinical delegate from each institution will be responsible for developing an implementation plan for their clinical setting and finalizing the documents for local use.
Conclusion: Appropriate strategies need to be developed for the Caribbean clinical and social setting, as resource-constraints create challenges for disease management and supportive care. Through standardizing supportive care practices based on the best available evidence, SCI hopes to contribute to increasing survival in the Caribbean.

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PALLIATIVE CARE NEEDS OF FAMILIES OF CHILDREN WHO DIE FROM CANCER: A GHANAIAN STUDY

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Background/Objectives: In developing countries, a high percentage of children with cancer present at an advanced stage. Often treatment for curative intent is not feasible in such cases and the children are given palliative care. Ensuring palliative care is effective and addresses the needs of the children and their families is important. The objective of this study was to obtain feedback from parents of children who had died from cancer to get to know their experiences and their needs. This would inform improvements to the palliative care service.
Design/Methods: This qualitative study was undertaken at the Paediatric Oncology Unit in Accra, Ghana. A questionnaire with open-ended questions, was administered to a sample of parents whose children received palliative care and had died from cancer in 2014. Informed consent was obtained.
Results: Ten families were approached and six agreed to be interviewed. Parents were of the opinion that cancer could not be cured. They all understood that palliative care was to make the child relieve symptoms "until their peaceful death". Of note is that although almost all the children had received morphine for pain relief, half of them stated it was inadequate. They all had an input into their child's care. Although parents felt the relationship with professionals was good, two were dissatisfied as "professionals hardly understand us". Of the three families that encountered the clinical psychologist, two were not impressed, in quotes "he forgot every patient is unique". Improvements suggested included "individualized care", privacy and more spiritual input.
Conclusion: Palliative care should form an important component of Paediatric Oncology training for health workers in developing countries so that there will be effective symptom control and they will be responsive to the individual needs of children and families.

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THE INCIDENCE OF NEUTROPENIC FEVER THE FIRST 6 MONTHS OF ANTI-CANCER THERAPY IN A SWEDISH COHORT OF CHILDREN AGED 7-16 YEARS

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Background/Objectives: Children treated for cancer are at risk of significant complications and even death during neutropenic fever (FN) episodes. There is a knowledge-gap of factors predicting risk of severe infections, which leads to great variation in clinical practice in the management of FN. In this nation-wide study we investigated the incidence of antimicrobial treatments among children aged 7-16 years during the first six months after start of cancer treatment.
Design/Methods: From January 2004 -May 2006, children newly diagnosed with cancer and starting therapy (n=145) were invited to participate and 101 accepted (70%). Disease and treatment related data were collected from the participant's medical records; including information on FN and laboratory data as well as demographic data. An episode of infection was defined as the individual period of time use of oral or intravenous antimicrobial treatment in association of symptoms of infection.
Results: 230 episodes of antimicrobial treatments were identified in 80 of the 101 children (79%) during the first six months of cancer treatment. Each child was in median prescribed two (range 0-7) antimicrobial treatments. Microbial cultures were obtained in 89 % (n=204) of the episodes. Children diagnosed with sarcoma were more often receiving antimicrobial treatment whereas children diagnosed with central nervous system (CNS) tumours and Hodgkin lymphoma more seldom received antimicrobial treatment. Children diagnosed with acute lymphoblastic leukaemia and CNS tumours were to a larger extent undergoing 1-2 episodes whereas children sarcoma and acute myeloid leukaemia were to a larger extent undergoing >2 episodes. We will also provide data on positive blood cultures and the presence of anti-microbial resistance.

Conclusion: The majority of the children received antimicrobial treatment during the first six month of treatment for cancer. Children with sarcoma were identified as a "high-risk" group for FN together with AML patients.

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EVALUATION OF DO NOT RESUSCITATE (DNR) ORDERS AT A SINGLE CENTER IN JORDAN

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Background/Objectives: : Do not resuscitate orders (DNR) are crucial in planning end-of-life care. Successful discussion of these orders depend on family background, care giver's perceptions and patients conditions.
Design/Methods: We retrospectively analyzed charts of patients who had DNR orders placed between January 2006 and December 2011. We analyzed demographics, DNR order documentation, and timing of DNR orders in relation to diagnosis and death.
Results: We evaluated the charts of 76 patients (44 males). The median age at diagnosis was 5 years (range, 0 to 16.7). DNR orders were obtained from first attempt in 55 patients (76%). The majority of orders were obtained by primary oncologist (92%), while the rest were placed by palliative care team and intensive care consultants. Orders were placed in the outpatient clinic (48%), in-patient unit (41%) or intensive care unit (11%). The median duration from DNR order placement to death was 2.1 month (range, 0 to 25) and was significantly longer for patients with solid tumors (3.4 months) in comparison to CNS tumors (1.6 months) and Leukemia/Lymphoma patients (0.4 months); p=0.022.
Conclusion: Our study showed no clear obstacles in placing DNR orders among our patients. We believe that better analysis requires better documentation of the process including all unsuccessful attempts to place the order. Patients with leukemia/lymphoma in our center should have end-of-life planning done at an earlier stage.

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CYTOMEGALOVIRUS INFECTION IN CHILDREN AFTER BONE MARROW TRANSPLANTATION: RISK FACTORS, CLINICAL ASPECTS AND OUTCOMES

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Background/Objectives: CMV infection remains the most common and potentially severe viral complication in patients given HSCT.
Design/Methods: This study was a retrospective analysis of clinical, laboratory and outcome data of all pediatric patients underwent BMT, at KFSH&RC-J, from July 2005 to June 2014 to identify the risk factors associated with the development of CMV in post BMT patients and their outcomes. A p-value of < 0.05 was considered statistically significant.
Results: 95 pediatric patients were admitted for BMT. The mean age was 6.5 ± 4 years. Out of males were 63 (66.3%) and females were 32 (33.7%). Majority of patients have hematological malignancy (n=31; 32.6%); out of them ALL (n=9), AML (n=15), lymphoma (n=7), followed by beta-thalassemia (n=13), sickel cell anemia (n=8), aplastic anemia (n=6), fanconi anemia (n=3), solid tumors (n=19, 20%) including neuroblastoma (n=16) and medulloblastoma (n=3) and HLH (n=5; 5.3%) and others miscellaneous disorders (n=11, 11.6%). Allogeneic transplant (n=71; 74.5%) and remaining were autologous transplant (n=24; 25.7%).CMV reactivation was observed in 29 patients (29/95; 30.5%) within 100 day of post BMT. Out of them majority were asymptomatic (n=21; 77.8) and remaining (n=9 ; 22.2%) had clinical manifestation/organ involvement (Liver, Skin, GIT and CNS).Age < 5 year ($p= 0.043$), AML (p=0.019), positive pre-transplant CMV status (p=0.007), conditioning regimen containing ATG ($p < 0.041$), allogeneic BMT ($p < 0.027$) lymphopenia $< 300/mm3$ (p=0.049) were identified as risk factors for CMV reactivation. 36 (37.9%) patients developed GVHD and overall 27 (28.4%) patients were expired. Both outcome variables were statistically significant GVHD (OR: 5.4; 95% CI: 2.42-12.18) and mortality rate (OR: 8.1; 95% CI: 2.51-25.61) in patients with CMV reactivation.
Conclusion: Young age, AML, positive pre-transplant CMV status, ATG containing conditioning regimen, allogeneic BMT and lymphopenia were identifiable factors associated with development CMV reactivation in post BMT pediatric patients.

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USE OF COMPLEMENTARY AND ALTERNATIVE MEDICINE (CAM) IN PEDIATRIC CANCER PATIENTS: SNAPSHOT OF DATA FROM RIYADH, SAUDI ARABIA

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Background/Objectives: Despite the use of CAM globally there is no authorized body governing its use in a heavily cultured population such as Saudi Arabia.The objectives was to define prevalence and patterns of use of CAM by pediatric cancer patients at King Faisal Specialist Hospital & Research Centre in Riyadh, Saudi Arabia.
Design/Methods: A cross sectional study was conducted by interviewing parents of children with cancer at a single institute from 2013-2014.
Results: A total of 228 parents were interviewed. Median age of parents was 37 years (17-66), and 82.8% had post primary or more education. Out of the 228 interviewed parents, 224 (98%) said they have used some form of CAM either in the past or current treatment of their child. Herbs were used by 23% (55/224), dietary supplements by 46% (103/224), and a combination of both by 98% (220/224). Among herbal remedies, the most common type used was olive oil (60%), followed by black seeds [Nigella sativa seeds] (41%), garlic (16%), and kurkum (9%). The dietary supplements that were utilized included honey (48%), camel's milk (11%), and Royal Jelly [queen bee's honey] (4%). In regards to alternative treatments, 95%, recited verses from Al-Quran, 82% used holy water from the ZamZam Spring in Makkah Al-Mukaramah, followed by 9% who reported using perfumed oils. In this sample, 53% of parents used CAM occasionally for their child, and around 40% used it on daily basis. Overall, 61% of parents were satisfied by the use of CAM; however nearly 60% used them without the knowledge of the treating oncologist.
Conclusion: The high incidence of use of CAM among our pediatric cancer patients warrants establishing a regional module for integrating CAM with cancer therapy and underlines the importance of health care professionals asking routinely about the use of CAM in this population.

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ASSESSMENT OF GRIEF AMONG HEALTH CARE PROVIDERS AT A TERTIARY HOSPITAL IN THE PHILIPPINES AFTER A DEATH OF A PATIENT WITH CHILDHOOD CANCER

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Background/Objectives: Death is inevitable and people handle death differently. This study aims to evaluate the intensity of grief experienced by the health care providers (HPs) after the death of a pediatric cancer patient.
Design/Methods: A prospective cross-sectional descriptive study was done to measure the intensity of grief among HPs who experienced bereavement from a death of a pediatric patient with cancer using the Texas Revised Inventory of Grief (TRIG).
Results: A total of 105 respondents participated in the study (80% response rate) which included medical interns (14%), nurses (28%), pediatric residents (30%), fellows (19%), consultants (7%) and "others" (2%). Pediatric residents showed a more intense level of past grief (p=0.0238) and present grief (p=0.0141) compared to the rest of the respondents. Consultants scored the lowest percentile TRIG scores pertaining to absence of grief, followed by 51.7% of nurses. Those belonging to the age group of 41-50 years old showed significant intensity of grief for the past and present grief (p=0.0303 and p=0.0137, respectively). Only a small number of the study participants (3%) had palliative training and only about half of the respondents (53%) sought some emotional support after experiencing bereavement. There is no statistical difference in the level of grief among male and female respondents.
Conclusion: Children with cancer are an endearing special group of patients, such that when a child with cancer dies, an indelible mark is left behind especially among those who took care of them. Everyday encounter with these patients endears them to their HPs. For this reason alone, grief is experienced by the HPs most especially when their patient dies. Experiencing grief can be a long process to endure; hence emotional and psychological support is important because when grief is ignored or suppressed, it may become a source of stress and even dysfunction.

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HIGH MORTALITY FROM CARBAPENEM RESISTANT GRAM NEGATIVE SEPTICEMIA IN THE NEUTROPENIC CHILD IS A SIGNIFICANT CHALLENGE IN INDIA

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Background/Objectives: Morbidity and mortality from gram negative septicemia (GNS) in children with cancer is well recognized. Increasingly multidrug resistant infections, including carbapenem resistant, are being reported. Our objective was to identify the

prevalence, resistance patterns and outcomes of GNS in children with cancer at our centre.
Design/Methods: We retrospectively analysed data of all newly diagnosed and treated pediatric (0-18 years) cancer patients in 2 centres in New Delhi who had positive gram negative bacterial growths in their blood cultures in the year 2014. Bacterial resistance to various antimicrobial agents was determined. Outcome after septicemia was documented.
Results: 256 blood cultures were done on 129 children (median 1 blood culture/child, range 0-16 blood cultures/child). Of these 45(17.6%) were positive with 27(60%) gram negative bacteria (*Escherichia coli* 8, *Klebsiella pneumoniae* 8, *Pseudomonas aeruginosa* 6, *Enterobacter cloacae* 3, *Acinetobacter baumanni* 2), 15(33.3%) gram positive bacteria and 3(6.7%) fungal. Resistance to piperacillin/tazobactam, amikacin and meropenem were seen in 68%, 51.8% and 63% of the gram negative bacterial isolates respectively with resistance to all three in 48.1% of isolates. There were no deaths with gram positive bacterial or fungal septicemia, but 5 deaths in the 14 children with 27 episodes of GNS giving mortality rates of 35.7% per GNS child and 18.5% per GNS episode respectively. Factors associated with GNS mortality were disease group (leukemia/NHL/transplant 27.8% vs solid tumours 0%, p=0.13), neutrophil count (ANC<0.5 45.4% vs ANC>0.5 0%, p=0.006) and carbapenem resistance (resistant 29.4% vs sensitive 0%, p=0.12). 5 out of 6 (83.3%) children with carbapenem resistant GNS who were also neutropenic died. There were no deaths in children with GNS who either had carbapenem sensitive growths or were not neutropenic.
Conclusion: Septicemia in children with cancer is characterized by GNS which are often multidrug resistant (including carbapenem resistant) and carry a high mortality when accompanied by neutropenia.

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DEVELOPING IMMUNIZATION SOLUTIONS FOR CHILDREN WITH CANCER IN INDIA: A QUALITY IMPROVEMENT INITIATIVE

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Background/Objectives: Children with cancer need special considerations regarding their (and their siblings/parents) immunization during and after their cancer treatment. Several guidelines are available in the resource rich countries, but these are not completely applicable in the Indian context. We aim to address this gap by developing guidelines and advocating for their implementation.
Design/Methods: Firstly, a survey was conducted among clinicians treating children with cancer in India to understand current practices. Secondly, existing guidelines were gathered from across the world. Simultaneously, the Indian Academy of Paediatrics Committee on Immunization (IAPCOI) was contacted for their recommendations. All this information was collated and gaps or contradictions identified.
Results: The survey of 37 institutes from 21 centres in India identified areas of homogeneity (eg. contraindicated vaccines, time gap between end of therapy and re immunization) and areas of heterogeneity (varicella exposure prophylaxis, influenza vaccinations). Based on this, draft guidelines were developed and then disseminated to the members of the North India Paediatric Oncology for feedback. The guidelines are now finalised and include recommendations for the index child, siblings and parents, both during and after end of treatment and take into account the index child's age and previous immunisation status.
Conclusion: Guidelines for immunisation of children with cancer (and their siblings/parents) have been developed and tailored to the Indian context. Efforts are now ongoing to adopt and disseminate these recommendations and to advocate for their implementation.

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INTERVENTIONS OTHER THAN ANTICOAGULANTS AND SYSTEMIC ANTIBIOTICS FOR PREVENTION OF CENTRAL VENOUS CATHETER-RELATED INFECTIONS IN CHILDREN WITH CANCER - A COCHRANE SYSTEMATIC REVIEW

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Background/Objectives: Use of central venous catheters (CVC) in treatment of children with cancer is associated with infective complications. This systematic review aimed to find which interventions, if any, are effective in preventing CVC-related infections in children with cancer. Antibiotics and anticoagulants were excluded as they have been examined in other Cochrane reviews.
Design/Methods: A systematic search of electronic databases (CENTRAL, MEDLINE, EMBASE and CINAHL(R) from inception till Oct 2014) was done. We also searched reference lists of relevant articles and international conference proceedings. Procedures for study selection, data extraction and quality assessment were specified *a priori*. The primary outcome was catheter-related blood stream infection (CRBSI) and secondary outcomes were catheter associated infection (CAI), exit infection, tunnel infection, pocket infection and premature removal of the catheter.
Results: The search strategy yielded 922 articles. Seven trials involving five different interventions were included. Two trials (n=680) compared flushing CVC with urokinase (with or without heparin) versus heparin alone. There was non-significantly decreased CAI (Rate Ratio 0.72, 95%Cl 0.12-4.41) in the urokinase arm. Two trials (n=183) compared flushing CVC with taurolidine versus heparin alone. There was non-significantly decreased CAI (Rate Ratio 0.54, 95%CI 0.06-5.25) in the taurolidine arm. One trial reported a statistically significant reduction in CRBSI in the taurolidine group. One trial (n=307) compared ethanol lock with heparin locks and showed a statistically significant reduction in CAI in ethanol lock group. One trial (n=113) compared frequency of catheter dressing change every 15 days versus every 4 days and found no difference in premature catheter removals. One trial (n=83) found no difference in premature catheter removals when insertion site was internal jugular or subclavian vein.
Conclusion: A lack of adequate studies reporting standard outcomes from making any definitive conclusions about the effectiveness of individual interventions for prevention of CVC-related infection in children with cancer.

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THE DEVELOPMENT OF CORE DATA SETS AND OUTCOMES - IMPROVING THE QUALITY OF PAEDIATRIC PALLIATIVE CARE RESEARCH IN CHILDREN WITH CANCER

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Background/Objectives: Palliative care research in children with cancer is complicated by small, heterogeneous sample populations. Meta-analysis allows combining and contrasting of results from multiple studies to identify concordance/disagreement, requiring consistency in research design, outcome definition and data reporting. We analysed these elements of research studies exploring the measurement of health related quality of life in children dying from cancer.
Design/Methods: MEDLINE, EMBASE, CINAHL and PsychINFO were searched using a Child Health Filter and defined search (+/-Thesaurus/MESH terms). The Cochrane Database of Systematic Reviews was screened. 7601 citations were identified. Using predefined inclusion criteria, 810 were included for subsequent review against clear exclusion criteria. After final rejection of 'maybes' and duplicates, 22 were included for data extraction.
Results: Research was predominantly cross-sectional - only 5 studies describing longitudinal assessment of outcomes. 11/14 interview based studies conducted a single interview. Definition of the palliative phase and the timing of cross sectional analysis was inconsistent. Most studies were single centre. Variation was noted in the statistical parameters used to report demographic/sample data, age ranges, and stage of life where age was reported (e.g. death vs diagnosis). Data on children dying from cancer could often not be extracted from children with other conditions or stages of cancer.Reporting, grouping and subanalysis of diagnoses was inconsistent - no studies used diagnostic codes (e.g ICD-10).
Conclusion: Paediatric palliative care research opportunities are scarce and precious. Consistency in study design and result reporting is therefore imperative to facilitate meta-analysis, and the reproducibility and generalisability of findings. There is need for a clearly defined core data set and reporting standards to be included in future research, with consensus on the definition of outcomes used and palliative care terminology.

P-569

RESEARCH GOVERNANCE AND STUDY DESIGN IN PALLIATIVE CARE RESEARCH IN CHILDREN WITH CANCER

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Background/Objectives: Asking children dying from cancer, and their families, to engage in palliative care research is sensitive and challenging. However, published research has demonstrated that high quality studies are possible, ethical and acceptable, and can inform future research design and conduct to improve the quality and benefit derived.
Design/Methods: MEDLINE, EMBASE, CINAHL and PsychINFO were searched using a Child Health Filter and defined search (+/-Thesaurus/MESH terms). The Cochrane Database of Systematic Reviews was screened. 7601 citations were identified. Using predefined inclusion criteria, 810 were included for subsequent review against

clear exclusion criteria. After final rejection of ´maybes´ and duplicates, 22 were included for data extraction.
Results: 10 of 22 studies described difficulty generalising research findings, citing causes including single centre research, low response/recruitment rates and poorly validated instruments/tools. Other limitations cited included small heterogenous populations, lack of standardised diagnostic/symptom classification/coding/definition, researcher bias, retrospective study/recall bias, and a lack of longitudinal research. One third of studies contained no consideration of research limitations.Good practice included active determination of children's ability/appropriateness to participate (e.g. sickness, young age, recent diagnosis), indentification of parental distress and need for psychological support, children's ability to assent/consent for themselves, impact of research on daily life (e.g. long distance), stipulating minimum time since bereavement, and ensuring support/follow-up post-research.
Conclusion: Palliative care research in children with cancer is sensitive and challenging, especially in the transition from curative to supportive care. There is a need therefore for excellence and transparency in both study design and conduct, high quality monitoring and safeguarding of research participant welfare, and to learn from previous research.

P-570

SYMPTOMS AT THE END OF LIFE IN CHILDREN DYING FROM CANCER

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Background/Objectives: The aim of this study was to identify published literature and research on symptoms and problems experienced by children with cancer during the palliative phase of their life, identify problems with symptom management and determine how trends in reporting could inform future research and studies.
Design/Methods: MEDLINE, EMBASE, CINAHL and PsychINFO were searched using a Child Health Filter and defined search (+/-Thesaurus/MESH terms). The Cochrane Database of Systematic Reviews was screened. 7601 citations were identified. Using predefined inclusion criteria, 810 were included for subsequent review against clear exclusion criteria. After final rejection of ´maybes´ and duplicates, 22 were included for data extraction.
Results: Pain (15/22 studies), fatigue (10/22), gastrointestinal (7/22) and respiratory (7/22) symptoms, were the most prevalent symptoms cited. Symptoms were generally reported in the context of 'all participants', and not considered in the context of different age groups or developmental stages. Only some studies considered symptom prevalence and intractability with regard to other subcategories, such as diagnosis (e.g brain tumours) or time since entering palliation. In terms of statistical analysis there is marked inconsistency in reporting parameters such as age groups, disease classification, sex, treatment received, and length of palliation. Of concern is the low percentage of TYA data reported and extractable from the identified literature (3/18 studies with adolescents).
Conclusion: Despite effective analgesia and clinical experience in its management, pain remains the most prevalent symptom at the end-of-life in children with cancer. Given small patient numbers and acknowledged problems treating and managing teenagers and young adults (TYA), TYA data is not extractable from the majority of published results and findings. There is a need for consistency in the presentation and statistical treatment of published research findings, and availability of subcategory data.

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DETERMINANTS AND CHARACTERISTICS OF PARENTAL INVOLVEMENT IN QUALITY OF LIFE STUDIES IN CHILDREN IN THE PALLIATIVE PHASE OF CANCER

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Background/Objectives: Approximately 260 children with cancer die from their disease each year in the UK. Despite children as young as 5 being able to self-report, both retrospective and prospective paediatric palliative care research remains patients dependent on parent and carer proxy reporting. As part of a larger systematic review the characteristics and determinants of parental involvement in clinical research was explored.
Design/Methods: Clearly defined search terms and a Child Health Filter were used to search MEDLINE, EMBASE, CINAHL and PsychINFO. All search terms where matched to the Thesaurus/MESH Terms of each database where relevant. The Cochrane Database of Systematic Reviews was searched, with a manual search of known studies and research for relevant texts. 7601 citations were identified. Using predefined criteria, 810 were identified for initial inclusion and review against a set of clear exclusion criteria. After removal of duplicates and discussion of 'maybes', 22 citations were included for review and data extraction.
Results: Parental recruitment was around 69% of those eligible. 31% of parents were fathers and 61% were mothers. The reasons cited for increased maternal involvement studies was that mothers were the primary caregivers, that fathers were primary providers (financial), that fathers found it more difficult to participate in both retrospective and prospective studies and paternal mental health. Reasons for involvement in studies included a desire to contribute to the care of others, hope, lengthening time with their child, and that participation in research improved the frequency and quality of communication whilst receiving palliative care.
Conclusion: Parental recruitment in palliative research in children with cancer is motivated and affected by multiple factors. These factors, for both prospective and retrospective studies are a potential source of bias in considering the health and quality of life needs of children dying from cancer and need further dissemination to improve the quality of future research.

P-572

HOSPITAL VOLUNTARY INCIDENT-REPORTING SYSTEM: A 4-YEAR SURVEY ON DRUG-RELATED PROBLEMS IN PEDIATRIC ONCOLOGY

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Background/Objectives: Hospital and healthcare providers strive to deliver the safest care possible. However, drug-related problems are commonly reported. In 2011, a hospital incident-reporting system was implemented as part of the Quality Assurance system to improve patient safety and quality of care. Each incident is discussed by a multidisciplinary team of experts and preventive or corrective actions are defined and elaborated.
Design/Methods: A 4-year retrospective analysis of drug-related incidents as collected from the incident-reporting system was performed in a pediatric hemato-oncology ward. Incidents were further subclassified. All drugs involved were categorized according to the Anatomical Therapeutic Chemical (ATC) classification system of the WHO, which enabled to identify these classes of drugs that were most frequently involved.
Results: A total of 125 out of 196 (63.7%) (nearly) reported incidents involved drugs. For 94 out them (75.2%), the ATC level could be retrieved or defined. Class L (antineoplastic and immunomodulating agents) was most commonly involved and represented 53.2% (n= 50) of drug-related incidents. This was followed by classes B (blood and blood forming organs, more especially perfusion solutions) (16.0%, n=15), J (anti-infectives for systemic use) (12.7%, n= 12), N (nervous system) (6.4%, n= 6), A (alimentary tract and metabolism) (5.3%, n=5), H (systemic hormonal preparations) (3.2%, n=3) and V (various drugs) (3.2%, n=3).
Conclusion: Drugs were very frequently involved in the incident reporting system and mainly included antineoplastic and immunomodulating agents. This might reflect the profile and complexity of a pediatric oncology ward. Preventive actions include optimization of an electronic medication/chemotherapy prescription/administration program (especially for antineoplastic/immunomodulating agents and perfusion solutions), as well as introduction of new or revision of existing guidelines for supportive care agents (anti-infectives, pain medication, chemotherapy induced nausea and vomiting). Finally, it must be mentioned that an underreporting of incidents is suspected.

P-573

THE REASON WHY THE RAPID RESPONSE TEAM WAS CALLED FOR THE ONCOHEMATOLOGIC PATIENTS IN A BRAZILIAN GENERAL HOSPITAL

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Background/Objectives: In THE REPORT TO *ERR IS HUMAN,* the Institute of Medicine concluded that many deaths occur in hospitals in the United States as result of errors. One initiative promoted by the Institute for Healthcare Improvement, recommended strategies to decrease the number of preventable inpatient deaths; one of the recommended strategies was the implementation of a rapid response team (RRT), also known as a medical response team who are available 24 hours per day, for evaluation of patients not in the ICU who develop signs or symptoms of clinical deterioration. Pediatric inpatients manifest deterioration for several hours before cardiopulmonary arrest so RRTs have the potential to be an effective intervention in pediatric inpatients. *Objective*: Analyze the reason why the RTT was called to attend pediatric oncohematologic patients during 2014.
Design/Methods: A retrospective analysis of the pediatric oncohematologic inpatients attended by the RTT in 2014.
Results: There were 64 callings for the pediatric RTT in our institution, 25% were for oncohematologic patients. The base diagnostics were febrile neutropenia, neuroblastoma, bone marrow transplantation and ALL; the causes for the RTT callings were: fall (25%), convulsion (6%), sepsis (19%), respiratory failure (13%) and others

(37%). All the patients were evaluated for the ICU pediatrician, that took conduct and after revaluation sent or not the patient for the ICU. Only one patient was sent to the ICU, all the others remained in their units under the staff care.
Conclusion: The RTT may have caused a significant reduction in the number of cardiorespiratory arrests in oncohematological pediatric patients because all of them who presented any symptom of deterioration were evaluated and taken care by the team, independent of the cause of the calling. None of the evaluated patients developed cardiac arrest.

P-574

UNCOMMON FEATURES OF NEUROBLASTOMA IN CHILDREN: A REPORT FROM A SINGLE INSTITUTION IN ALGERIA

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Background/Objectives: Neuroblastoma is the most common extra cranial solid tumor in childhood. It's a tumor characterized by a large spectrum of clinical and biological heterogeneity. However, if classical manifestations are well known, neuroblastoma continues presenting with atypical and exceptional symptoms that makes it a real enigmatic disease. A series of one hundred sixty seven patients with neuroblastoma is reviewed to report on atypical clinical characteristics at initial diagnosis or within evolution, and to analyze treatment features.
Design/Methods: We performed a retrospective study from 2005 to 2014, in a Pediatric Oncology Unit of CHU de Beni Messous. One hundred sixty seven patients with neuroblastoma were registered. They were evaluated by biochemical and imaging investigations, classified and treated according to the conventional protocol regimens.
Results: There were four patients presenting with paraneoplastic neurological symptoms including opsoclonus-myoclonus ataxia syndrome OMA, bulbar syndrome, and polyradiculoneuritis .Two patients had a cardiomyopathy, and three patients developed central nervous metastasis. We observed two cases with multifocal neuroblastoma .Two children exhibited a secondary acute leukemia at the end of treatment.Survival rates were poor in patients with central nervous system involvement and secondary acute leukemia, except those with OMA and cardiomyopathy.
Conclusion: Patients with paraneoplastic symptoms exhibited a delay in diagnosis; while metastasis to the central nervous system, and secondary leukemia were associated with poor prognosis.

P-575

FEASIBILITY AND BENEFITS OF HYPNOSIS IN A PEDIATRIC CANCER CENTER

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Background/Objectives: Hypnosis is an efficient method to reduce pain and anxiety induced by invasive medical procedures and by diseases such as cancer. While they are easier to hypnotize than adults, children behave differently under hypnosis. They are less limited by cognitive stereotypes and have a more permeable boundary between imagination and reality. However, during procedures, children often fidget, appear restless and require sustained and animated hypnotic suggestions. We performed an observational study to determine the feasibility and the benefits of hypnosis in a pediatric cancer center.
Design/Methods: Two psychologists and one pediatric oncologist of the center were trained to hypnosis with a particular focus on pediatrics. Hypnotic techniques were proposed to the children and their families as alternative or complementary approaches for pain and/or anxiety management related to disease, treatment or invasive medical procedures. Patients younger than 3 years or with vulnerable psychological profile (autism, psychosis) were excluded.
Results: From February 2014 to February 2015, 66 sessions of hypnosis were achieved in 22 pediatric patients (age 4 to 17 years) treated for cancer and hematological diseases. The most common indications were lumbar punctures (23 in 8 patients), pain management (19 in 3 patients), anxiety management (11 in 9 patients), placement of venous catheter (6 in 3 patients), placement of nasogastric tube (2 in 2 patients). For some invasive procedures (30/66), hypnosis was associated to analgesics and a mixture of nitrogen monoxide and oxygen (MEOPA). Hypnosis did not increase the duration or the cost of the procedures. Patients reported it as a positive experience and preferred it to MEOPA alone or sedation with propofol for the following procedures.
Conclusion: Hypnosis is an inexpensive and not time-consuming method that can be easily implemented in a pediatric cancer center to improve the wellness of patients and their families.

P-576

MICROBIOLOGICALLY-DOCUMENTED INFECTIONS AMONG CHILDREN WITH FEBRILE NEUTROPENIA IN A PEDIATRIC-ONCOLOGY UNIT IN NORTH INDIA

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Background/Objectives: Bacterial (15-25%) and fungal (2.6-5%) infections contribute to morbidity and mortality in children with cancer. This study analysed the spectrum of microbiologically-documented infections (MDI) and attempted to identify the risk-factors.
Design/Methods: Children with febrile neutropenia (FN) were prospectively evaluated over 1-year. Culture-positive bacterial infections were included. Invasive fungal infections (IFI) were classified as 'proven', 'probable' and 'possible' using EORTC/MSG (2008) criteria. Risk-factors for MDI were analysed.
Results: MDI was documented in 82/414 (19.8%); 59 (14.2%) had isolated bacterial infection (IBI), and 16 (4.3%) had IFI. Eight (9.7%) had polymicrobial sepsis. Sites: blood (92.5%), urine (3%), pus (3%) and stool (1.5%). Commonest bacterial isolates E. coli (17.9%), S. aureus (13.4%) and K. pneumoniae (10.4%). Drug-resistance demonstrated: MRSA (22%), ESBL and carbapenem-resistance (50% and 17% of Gram-negative isolates). All patients with IFI had underlying haematological malignancies (81.2% ALL, 18.7% AML). IFI were 'proven' in 37.5%, 'probable' in 37.5%, and 'possible' in 31.2%. Fungi isolated: Mucor (2), Aspergillus (5), Candida (2) and Pseudallescheria (1). Twenty-six-percent (109/414) developed complications: metabolic (15.4%), fluid-refractory shock (12%), respiratory failure (12%), ICU admissions (6.7%), neutropenic enterocolitis (5.3%), acute kidney injury (4.5%) and encephalopathy (3.9%). Mortality rate was 10.3% (43/414); 21% due to IFI, and 39.5% to IBI. MDI were associated with complications (OR 4.44; 95% CI 2.6-7.4) and death (OR 8.6; 95% CI 4.3-16.8) ($p < 0.001$). IFI resulted in 50% mortality. Chemotherapy interval $\leq$7 days (OR 3.6; 95% CI 1.6-7.6), a clinical focus of infection (OR 1.9; 95% CI 1.1-3.4), and platelet count $<20000/\mu$L (OR 2.1; 95% CI 1.0-4.5) at admission were predictive of MDI in multivariate analysis.
Conclusion: MDI in children with malignancies result in complications and mortality. Drug resistance is a concern needing antibiotic stewardship. Developing a risk score for identification of high risk febrile neutropenia children at admission might improve outcomes.

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PAEDIATRIC PALLIATIVE CARE MODEL IN A DEVELOPING COUNTRY; EXPERIENCE AT THE CHILDREN HOSPITAL, LAHORE

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Background/Objectives: Palliative care is an emerging discipline worldwide. Palliative care unit was established at Childrens hospital, Lahore in 2009 with guidance from Dr Aziza Shad. A four bedded room is allocated for supervised by a dedicated team of doctor, psychologist, pediatric nurse and social workers. Aim of this study is to evaluate demographics and services provided to the paediatric palliative care patients at the Children hospital, Lahore.
Design/Methods: A retrospective review done of patients admitted in the paediatric palliative care ward from Jan 2009 till Dec 2014. Medical records were reviewed, data analyzed regarding patient number, diagnosis, indication for palliative care, outcome and psychological support provided.
Results: Palliative care services provided to 541 patients. Median age 6 years(3-14 years). M:F 1.5:1. Newly registered patients 49(64%), 92(36%) repeat admissions. Acute Myeloid leukemia 167(31%), relapsed acute lymphoblastic leukemia120 (22%) ,neuroblastoma 29(5%) . One hundred and forty one (26%) patients expired, 83(16%)lost follow up, 314(58%) still on follow up. Morphine used for pain management in syrup/ injectable form. Psychological support was provided to all of them. Currently our palliative care program is hospital based. There are future plan to extend palliative care at home, provide oral morphine for extended period.
Conclusion: Palliative care is essential right of child when curative treatment is not an option. Good supportive/palliative care should be available throughout the journey.Aim of such treatment is to make patient is pain free throughout treatment and any respiratory distress and anxiety at end of life is managed with appropriate psychological support and anxiolytics/sedatives. In Pakistan, access and use of morphine is limited and there are no algorithms for proper end of life care.Palliative care should be recognized as an essential component of health care and both health care professionals and the general public need education about palliative care.

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PAEDIATRIC ONCOLOGISTS IN JOHANNESBURG MAKE APPROPRIATE REFERRALS TO THE PAEDIATRIC INTENSIVE CARE UNIT (PICU) TO ENSURE APPROPRIATE ALLOCATION OF SCARCE RESOURCES

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Background/Objectives: The decision to admit a child to a state-funded PICU is based on the probability of immediate and long term survival, in the context of severe resource constraints. The aim of this study was to determine whether referrals by paediatric oncologists to PICU were appropriate and to challenge the perception that all oncology patients have poor prognoses and should thus be refused admission to PICU.
Design/Methods: A retrospective descriptive audit of all PICU admissions over a 12-year period was performed. Indications for admission, underlying oncology diagnoses, survival rates and causes of death were analysed.
Results: One hundred and seven patients were admitted 120 times. The average duration of stay in ICU was 3.5 days (range 1 to 76 days). Underlying diagnoses were central nervous system tumours (48.7%), solid tumours (34.7%), haematolymphoid malignancies (9.9%) and other tumours. Indications for admission included post-operative care (107), neutropaenic sepsis (10) and other (4). The mortality rate of the oncology patients was 15.8%, compared to an overall mortality rate for PICU patients of 13.8%. Six of the 10 patients admitted for neutropaenic sepsis died. Of the 107 admissions for post-operative care, 11 patients died from treatment complications. The five year survival rate for oncology patients discharged from PICU was 62%. Most deaths occurred as a result of surgical complications (31.6%) and neutropaenic sepsis (31.6%).
Conclusion: In this setting, oncology patients admitted to PICU have a relatively low mortality rate, implying that selection criteria for PICU admission are sufficiently stringent. As there is no validated scoring system for admission of oncology patients, the decision to admit a patient to PICU should be based on the overall projected prognosis of the oncological condition. Paediatric oncologists should refer patients with an expected good prognosis, and refer only those patients with neutropaenic sepsis who do not have multi-organ failure.

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SELF-ESTIMATION OF PHYSICAL ACTIVITIES DURING CANCER TREATMENT - A COMPARISON OF SUBJECTIVE AND OBJECTIVE DATA ASSESSMENT

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Background/Objectives: Due to a lack of exercise recommendations in pediatric oncology, exercise adherence should be supervised with the help of parameters describing the subjective exertion. Therefore, it is essential that children and adolescents are capable of reflecting their own patterns of physical activities with respect to the amount and intensity. The present study investigated how reliable children with cancer are able to self-estimate their physical activities during acute treatment.
Design/Methods: In the course of a previous study on physical activities (Götte *et al.* 2014), a sub-group (n=29) was evaluated with the objective assessment tool StepWatch™ Activity Monitor (*SAM*) in addition to the self-reporting with a questionnaire. The results of the two instruments were compared with regard to 'daily minutes of walking' and 'amount of moderate-to-vigorous physical activities' (*mvpa*). For the SAM measurements, walking was defined as an intensity of >20 and moderate activity as >50 gait cycles per minute.
Results: The patients were 13.8±2.8 years of age and 3.4±2.0 months after initial diagnosis of various tumor entities (45% leukemia, 31% bone tumors, 24% others). The Bland-Altman plots indicated an average under-estimation of the questionnaire by 3.4 min., with the limits of agreement ranging from -104.2 to 97.3 min., i.e. a fairly symmetrical under- and over-estimation. The *mvpa* deviated by -3.1 minutes (limits of agreement -132.5 to 126.2 min.). The comparison for the days with at least 60 min. of *mvpa* showed a marked difference with 3.1±2.6 self-reported days versus only 0.1±0.4 measured days.
Conclusion: The results of this pilot work indicate that patients may not reliably self-estimate their physical activities. Therefore, exercise therapy should also incorporate counseling of self-competence with respect to perception of physical activities. A possible solution would be a self-supervision of activities with commercial activity trackers (e.g. fitbit) which is an approach we are just evaluating in our institution.

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NETWORK ACTIVEONCOKIDS TO ENHANCE EXERCISE PROMOTION FOR PEDIATRIC PATIENTS WITH CANCER IN GERMANY

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Background/Objectives: Feasibility of physical activities and exercise in pediatric oncology during and after treatment has been proven and evidence for positive effects is increasing [Baumann *et al.* 2013; Braam *et al.* 2013]. However, exercise promotion programs are not yet generally established and are currently offered only in selected hospitals. Therefore, a nationwide network called *ActiveOncoKids* was founded to link and extend existing programs offering exercise for pediatric patients with cancer as well as to establish sustainable funding possibilities.
Design/Methods: The network was established in 2012 and comprises sports scientists, physiotherapists, medical doctors and psychologists. Network meetings are organized every two years for all network members and twice a year within a smaller steering group to discuss current progress, problems, and potential scientific collaborations.
Results: Since the establishment we were able to successfully support additional hospitals and sports clubs in implementing exercise programs for pediatric patients with cancer, to compose multi-centric research applications, to cooperate with health insurance companies and to gain the confidence of medical professionals. Although we progressed well so that about 20% of Clinics of Pediatric Oncology are now offering exercise programs for children and adolescents with cancer (starting with 9% in 2012), sustainability could not be achieved yet and most projects are not financially secured.
Conclusion: As a next step we plan to evaluate training programs and adjust methods of assessments to scientifically evaluate the efficiency of exercise in large multi-centric studies and draft risks, contraindications as well as entity-specific aspects of training control. Furthermore, transnational collaborations are required to exchange local experience and carry out joint scientific studies and working groups.

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SIMULATION AND TRAINING OF SKILLS FOR NURSES AND DOCTORS IN PEDIATRIC ONCOLOGY

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Background/Objectives: In emergency medicine, simulation and training programs are well established. A specific program for skills training and simulation in pediatric oncology is lacking. Therefore, we developed a three-step training and simulation program for staff members in pediatric oncology.
Design/Methods: First, an analysis of needs was performed via a questionnaire-based survey. Empathy, communication skills as well as practical skills (performing a lumbar puncture, bone marrow aspiration) and knowledge-based topics (side-effects of chemotherapy, complication management, and transfusion medicine) were identified as hot topics. According to these needs, a concept composed of three modules was set up.
Results: In the first module, staff members learn 'basic principles" of pediatric oncology. Using commercially available models, lumbar puncture and central venous line management could be trained. A model for simulation of bone marrow puncture was not yet available and therefore newly developed. Besides, communication was trained and challenged in hands-on exercises. One focus was set on the diversity of pedagogical methods to enhance the learning success. The second module contains more problem-orientated tasks. The participants receive challenges which have to be resolved in small teams (management of given complications, e.g. tumor-lysis syndrome). The third module focusses basically on team-based tasks. The quests are complex and feed-back is spotlighted. After completion of the course, the participants felt more self-confident in their job and this effect was sustainable.
Conclusion: Staff members in pediatric oncology have manifold challenges to master. High quality performance needs knowledge, empathy, and practical as well as communication skills. To train and develop these skills a multidisciplinary program for employees in pediatric oncology was established resulting in amelioration of workplace satisfaction. Acknowledgements: This project receives funding of "Verein fuer krebskranke Kinder Hannover e.V."; the bone marrow model was developed by Marc Dilly and John Rosenthal (Clinical Skills Lab, University Of Veterinary Medicine Hannover).

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THEATER AND PEDIATRIC PALLIATIVE CARE: THE CURTAIN OPENS. HIS SOCIAL VALUE AND THERAPEUTIC POTENTIAL

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Background/Objectives: In our background as pediatricians and pediatric oncologists there is a lack of spaces related to other disciplines such as theater. It is not often that we have the chance of performing arts activities that promote and help staff from other professional perspectivesObjectives:Spread the project that has been performed in our pediatric hospital of the play written by the Indian Nobel Prize winner R.Tagore, The Post Office, adapted and performed exclusively by health personnelShow the video trailer of the work doneServe as an example for the continuity and dissemination of such initiatives within the pediatric oncology community.
Design/Methods: MaterialAdaptation made from the original work of R. Tagore, The Post OfficePerformed using a cast of pediatricians (attending doctors and residents), assistants, nurses and pediatricians and four of their daughters.Directed by a pediatrician trained in theaterThere have been 3 performances in local theaters with more than 700 tickets sold Produced for the benefit of the Association for Pediatric Palliative Care ChildrenMethodPreparation for the play has been the driving element for teamworkThey have worked on the scenery and stage aspects (stage presentation, speech, memory, emotional aspect of death and lost).
Results: The aspects that have been worked on have been very helpful in acquiring skills that can help us to improve other aspects needed as professionals working with patients, families in difficult situations such as a child in palliative care.There have also been social and profitable results with a significant economic contribution to our association dedicated to Children in Palliative Care.
Conclusion: The generous and unique effort of multidisciplinary collaboration among people doing creative projects reciprocally enriches our personal skills and teamwork.

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PREDICTIVE VALUE OF SERUM PROCALCITONIN IN FEVER IN PEDIATRIC ONCOLOGY PATIENTS: EXPERIENCE FROM INDIA

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Background/Objectives: There is paucity of data on the role of inflammatory biomarkers in management of fever in immunosuppressed. Procalcitonin (PCT) has been observed to have better discriminatory ability for serious infections. Objective: To evaluate the role of PCT as a predictor for microbiologically documented infections (MDI) in pediatric oncology patients.
Design/Methods: Pediatric oncology and transplant patients (on chemotherapy or having neutropenia) with fever were enrolled (2007-2015). Correlation of PCT with MDI was made. PCT was not used to guide therapy decisions.
Results: Data from 1023 episodes of fever were available for evaluation. 590 (57.6%) episodes were classified as febrile neutropenia [Absolute Neutrophil Count $<1000/\mu L$]. 225 (22%) episodes had MDI. PCT level at admission ranged from 0.05 to 560 ng/ml ($\geq$0.5ng/ml in 43.8%). Gram positive, gram negative, fungal, viral, mycobacterial and parasitic infections constituted 53(23.5%), 89(39.5%), 51(22.6%), 30(13.3%), 1(0.4%) and 1(0.4%) cases respectively. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of PCT ($\geq$0.5 ng/ml) for MDI were 56.35%, 59.02%, 19.26% and 85.04% respectively, while those for bacterial infections alone were 53.8%, 57.98%, 15.96% and 89.43% respectively. These values, when evaluated for fungal infections alone were 48.89%, 57.31%, 5.14% and 95.95% respectively. These values, when evaluated for blood stream infections alone (bacteremia or fungemia) were 60.75%, 58.47%, 14.65% and 92.72% respectively. In febrile neutropenia episodes, sensitivity, specificity, PPV and NPV for MDI were 52.78%, 60.58%, 23.08% and 85.13% respectively, while those for bacterial infections in febrile neutropenia were 50.7%, 59.54%, 14.17% and 90.17% respectively. At a PCT $\geq$1.0 ng/ml, specificity and PPV for MDI improved to 76.96% and 30.8% respectively.
Conclusion: Procalcitonin level at the onset of fever in immunosuppressed patients is not a sensitive biomarker for microbial infection (sensitivity of 50-60%) and cannot be individually used for decision-making in management. However, it has good NPV (85–93%) for microbial infections.

P-584

SPECTRUM OF MICROBIOLOGICAL INFECTIONS IN PEDIATRIC ONCOLOGY PATIENTS: EXPERIENCE FROM A TERITARY CARE CENTRE IN NORTH INDIA

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Background/Objectives: In developing countries, infections pose the major challenge in curing pediatric malignancies. Data on spectrum of infections in pediatric oncology from developing countries is sparse. To analyze the spectrum of microbiological infections in pediatric oncology patients diagnosed at our center.
Design/Methods: Microbiological data of pediatric oncology patients evaluated for fever from 2007 to 2015 were analyzed.
Results: There were 1023 episodes of fever evaluated. Of these, 225 (22%) had microbiologically documented infections. Since 2012, >90% patients had central venous access devices. Gram positive, gram negative, fungal, viral, mycobacterial and parasitic infections constituted 53 (23.5%), 89 (39.5%), 51 (22.6%), 30 (13.3%), 1 (0.4%) and 1 (0.4%) cases respectively. Among 53 gram positive infections, organisms included Staphylococcus aureus(11.3%), Coagulase negative staphylococcus(65.7%), Enterococcus fecium(13.2%), Enterococcus fecalis(3.7%) and Streptococcus pneumoniae(1.8%). Among 89 gram negative infections, organisms included Klebsiella pneumoniae (29.2%), Escherichia coli (16.8%), Pseudomonas aeruginosa (15.7%), Acinetobacter species (8.9%) and Stenotrophomonas maltophilia (5.6%). Pseudomonas putida, Pseudomonas stutzeri and Proteus mirabilis were identified in 2 cases each. Salmonella typhi, Salmonella typhimurium, Nocardia, Chryseobacterium and Elizabethkingia meningoseptica were isolated in one each. Among fungal infections, invasive aspergillosis was diagnosed on the basis of galactomannan assay (in 34 cases). Fungus was isolated from body fluids in 17 cases. These included Candida albicans(5), Candida tropicalis(3), Candida parapsilosis(3), Candida glabrata(1), Candida haemulonii(1), Candida pelliculosa(1) and Trichosporon asahii(2). Documented viral infections included Cytomegalovirus, Dengue, Epstein-Barr virus and Herpes simplex virus, which were found in 19, 5, 4 and 1 cases respectively. One child was found to have cysts of Cryptosporidium parvum in stool examination. With advancing years, there is no significant difference in the detection rate of microbial infections.
Conclusion: Gram negative bacteria are still the major isolate at our center. Gram positive isolates have shown reduction over the years probably as a result of better nursing care of central lines.

P-585

PAIN MANAGEMENT IN MOROCCO: REPORT FROM THE MOROCCAN SOCIETY OF PEDIATRIC HEMATOLOGY AND ONCOLOGY

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Background/Objectives: To improve the quality of pain management in Moroccan pediatric oncology, a first program was developed in 2005 through the My Child Matters (MCM) initiative. To consolidate the achievements and to roll out the program to other PO units, a new project has been initiated on 2014 by The Moroccan Society of Pediatric Hematology/Oncology with the support of the Lalla Salma Foundation Prevention and Treatment of Cancer.
Design/Methods: To assess the current situation of pain management in Moroccan pediatric oncology a parent/patient and healthcare providers surveys were conducted.
Results: Eighty one caregivers were assessed. Seventy nine (90%) of them were using morphine, 17 (20%) have protocols and policies of pain management, 13 (17%) documented pain management in chart, 71 (88%) were poorly satisfied of pain management in their unit and all of them requested training.The second survey covered 156 children with cancer from the five Moroccan pediatric oncology units. Among them 150 suffered from pain (96%), 85 related to the disease, 46 related to procedure and treatment and 19 related to both. Pain was severe in 82 cases (55%) and the majority reported to doctors about pain. Procedural pain was mainly related to lumbar puncture and bone marrow aspirate. Sixty seven patients (48%) received medication to prevent procedural pain. Majority of patient/ parents reported an impact on their emotional, physical and social functioning. Majority of parents requested information and communication about pain management.
Conclusion: The MCM program allowed us to develop educational materiel and to overcome our reluctance to prescribe morphine. The ongoing project includes continuous education, training, policies and procedure development. We will reconduct the same surveys after the full implementation of the program to assess its impact.

P-586

IN VITRO INDUCTION OF SPERMATOGENESIS FROM TESTES OF CYCLOPHOSPHAMIDE-TREATED SEXUALLY IMMATURE MICE

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Background/Objectives: Spermatogonial stem cells (SSCs) proliferate and differentiate to all types of premeiotic, meiotic and postmeiotic cells. Cyclophosphamide (CP) belongs to the group of alkylating agents' drugs. It has a gonado toxic effect and may cause azoospermia. To evaluate the possibility of induction spermatogenesis in vitro from testes of CP-treated sexually immature compared to mature mice.
Design/Methods: 7 days-old (immature) and 8 weeks-old (mature) ICR mice were divided into two groups: CP group (CP) and control group (CT). Immature mice were injected intraperitoneally (i.p) with 100 mg/kg CP once a week during 3 weeks, while the mature mice were injected every week with 200 mg/kg for 6 weeks. Mice of the CT group were injected with saline. Mice were sacrificed every week after the last injection (ALI) for 4-7 weeks. Testicular cells were isolated from 0.5- 3 weeks ALI. Cells were cultured in three-dimension (3D) cultures in the presence or absence of purified Sertoli cells (SCs) from immature normal mice. The presence of premeiotic, meiotic and postmeiotic cells were examined before and after 4 weeks culture, by immunofluorescence staining using specific antibody for each marker.
Results: CP treatment significantly reduced testicular and body weight during the 4 weeks ALI in the immmature mice while during 6 weeks of the matue. A significant damage of STs was detected in the testes of CP groups compared to CT; this was in parallel to the testis weight. An increase/induction in the percentage of some premeiotic (PLZF, a-6-integrin, GFR-a, OCT4) meiotic (BOULE, LDH) and postmeiotic (PROTAMINE, ACROSIN) positive cells was examined in 3D cultures that contained SCs compared to cultures without SCs. This increase was not observed in cultures from mature mice.
Conclusion: Our results show for the first time the possibility of spermatogenesis induction in vitro from CP-treated immature mice.

P-587

SUCCESSFUL OUTCOME OF MUCORMYCOSIS WITH ANTIFUNGAL TREATMENT AND SURGERY IN A CHILD WITH ACUTE LEUKEMIA

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Background/Objectives: Mucormycosis is a fungal infection with a high morbidity and mortality in children with hematologic malignancies. We present a pediatric case treated successfully with antifungal agents and surgery and further continued with oral posaconasole during maintenance chemotherapy.
Design/Methods: Retrospective assessment of a case.
Results: An 8 year old boy was treated for precursor B cell ALL with BFM-ALL protocol. At the end of the first phase of delayed intensification (protocol II), he was hospitalised with febrile neutropenia. Cefepime iv was initiated after obtaining cultures. At 48 hours, fever continued and the patient began to complain of mild pain in the left orbita. There was no pathology in the examination by the ophtalmologist and otolaryngologist. An MRI revealed orbital cellulitis and sphenoid sinus infection. Voriconasole iv was initiated, after a day, periorbital swelling was observed, iv amphotericin B was added since we could not rule out a mucormycosis infection. After 5 days, fever continued and in MRI signs of progressive infection and periorbital abcess formation was observed. Surgical drainage, curettage and an absorbable gelatin sponge containing liposomal amphotericin B was inserted locally. Fever subsided in 24 hours. Chemotherapy was initiated again. No pathogen was detected in cultures. Mucormycosis was diagnosed by pathology. Liposomal amphotericin was continued during delayed intensificaton and the first month of ALL maintenance treatment. Then antifungal treatment was continued with oral posaconazole as ambulatory treatment for a total of 6 months of antifungal treatment. The patient has remained in remission for ALL and free of fungal infection.
Conclusion: Mucormycosis is a fungal infection with a high morbidity and mortality in children with hematologic malignancies. Suspecting a fungal infection, timely diagnosis and appropriate agressive treatment including antifungal treatment and surgery are key component for a successful outcome.

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ANTIMICROBIAL TREATMENT, AGRESSIVE SUPPORTIVE TREATMENT (INTENSIVE CARE UNIT-ICU, EXTRACORPOREAL MEMBRANOUS OXYGENATION -ECMO, GRANULOCYTE TRANSFUSIONS) MAY SAVE LIFE IN SEPTIC SHOCK IN PEDIATRIC ALL

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Background/Objectives: Systemic fungal infections and tiphilitis are complications with high mortality rates during leukemia therapy. Early identification of infection, antimicrobial therapy and aggressive intensive care support decreases mortality.
Design/Methods: Case report.
Results: A seven-year-old boy with acute lymphoblastic leukemia developed neutropenic fever after completion of remission induction chemotherapy . Empiric antibiotics were started after obtaining cultures. Fever subsided, but recurred. Liposomal amphotericin B was added. Clinical status deteriorated within hours and he was transferred to ICU. Acute respiratory distress syndrome (ARDS) developed, was intubated. Candida tropicalis grew in blood culture. Stool was positive for Clostridium difficile. Metronidazole, caspofungin and linezolid were added. Despite aggressive supportive care, he continued to detoriorate. Granulocyte transfusions were given 11 times. Hemofiltration for fluid overload was done, chest tubes were placed for pneumothorax. He was put on ECMO- extracorporeal membranous oxygenation for 55 days due to severe ARDS . Candida parapsilosis grew on blood culture during ECMO. Micafungin was added. He was kept on micafungin prophylaxis after the completion of his antifungal therapy. He had CMV reactivation and hemophagocytic syndrome, responded to IVIG and gancyclovir. Acinetobacter baumanii was identified in his tracheal aspirate which responded to meropenem. He had a respiratory detorioration on the 95th day of his ICU stay, was diagnosed with pulmonary hypertension and treated with iloprost and sildenafil. He was weaned off the mechanical ventilator as his lung parenchyma restored. He was off of the ventilator to oxygen support via nasal cannula on the 145. day, was transferred to hematology ward after 147 days in ICU. Bone marrow evaluation showed morphologic and cytogenetic remission for preB-ALL. He continues on his modified chemotherapy.
Conclusion: Systemic fungal infections and tiphilitis continue to be life threatening in immunocompromised hosts. Aggressive intensive care support, granulocyte infusions and ECMO can decrease mortality and morbidity.

P-589

INFECTIONS WITH RESPIRATORY VIRUSES IN CHILDREN WITH CANCER IN ISTANBUL AT THE LAST YEAR

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Background/Objectives: Respiratory virus (RV) infection can cause significant morbidity and mortality in pediatric cancer patients. The aim of this study is to identify the RV infections in children with cancer presenting with signs and symptoms of respiratory tract infection.
Design/Methods: During January 1st 2014- January 1st 2015, all children with cancer presenting with signs and symptoms of respiratory tract infection were assessed for RV infection. Specimens were collected by nasal swabbing. Samples were assessed with algorithms and molecular techniques (rRT-PCR) suggested by CDC and WHO in the reference Virology laboratory, of Istanbul University.
Results: Samples of 74 respiratory tract infection episodes of 51 children with cancer were evaluated with simultaneous detection of 20 respiratory viruses. A respiratory viral pathogen was obtained in 43 (58%) of the analyzed samples.Rhinovirus (n=11, 25%) and concomitant detection of two viruses (18%) were the most frequently isolated pathogens. Other viruses were Coronavirus (13.9%), Respiratory Syncytial Virus (13.9%), Metapneumovirus (4.6%), Bocavirus (2.3%), Parainfluenza (9.3%), influenza A (H3N2) (9.3%). Four (9.3%) had severe pneumonia (One Rhinovirus + Coronavirus, others Rhinovirus, Metapneumovirus, Respiratory Syncytial Virus) and 11 (25.5%) had mild lower respiratory tract infections. Patients with febrile neutropenic episodes and

pneumonia were hospitalized and broad spectrum antibiotics were administered. The other non-neutropenic and mild respiratory tract infections were treated with supportive approach as outpatient. Patients with influenza were treated with oseltamivir. There were no deaths due to respiratory tract infectons in our series.
Conclusion: Viruses are a major cause of respiratory tract infections in children with cancer. Oseltamivir is effective in treatment of influenza in children with cancer. Since there are no effective antiviral agents for some respiratory viruses, infection control and early diagnosis are important to prevent spreading of infection. In most cases, hospitalization and supportive care is needed to reduce morbidity and avoid mortality.

P-590

STATUS OF PARTICIPATION IN PHYSICAL EDUCATION AT SCHOOL AFTER TREATMENT FOR PEDIATRIC CANCER

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Background/Objectives: Physical education (PE) at school aims at promoting the children's physical and psychosocial abilities and contributes to the development of a long-term active lifestyle. In Germany, pediatric patients with cancer are often not attending school and therefore cannot participate in PE during acute treatment. Undergoing cancer therapy, the children's physical activity levels are reduced dramatically (Winter *et al.* 2009) and physical limitations persist throughout adulthood (Ness *et al.* 2009). The primary objective was to analyze the status of participation in PE, because it has not yet been sufficiently examined whether pediatric patients return to PE following cancer treatment. Secondly, barriers which handicap reintegration should be identified.
Design/Methods: Data was collected using a standardized questionnaire of the KiGGS-study (German Health Interviews and Examination Survey for Children and Adolescents) supplemented by questions related to PE and reasons against participation. Using this instrument enables comparison with age- and gender-related reference values of healthy children.
Results: Patients with cancer (n=114; m=61%) 13.5±4.0 years of age and 10.6±9.6 months post-treatment attending school since at least two months were included (leukemia/lymphoma 46%, bone tumor 25%, brain tumor 16%, other solid tumor 14%). Although 72% of the patients desired participation in PE, 38% were not participating to full extent, whereof 17% reported no participation at all and 21% mentioned partly participation. Most problems became obvious in patients treated for bone tumors (68% partly/non-participation). Identified barriers included: personal (physical/psychosocial), social (parents/classmates) and structural reasons (teacher/curriculum).
Conclusion: Contrary to the patients' motivation, a high percentage is not participating in PE at school within two years post-treatment. Initial attempts of a reintegration program at our department and detailed examination of barriers showed that these can be successfully conquered by communication, professional advice and support for patients, teachers and parents.

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ENHANCEMENT OF PHYSICAL ACTIVITY LEVELS IN PEDIATRIC PATIENTS WITH CANCER DURING ACUTE CANCER TREATMENT: DEVELOPMENT OF A TWO-PART EXERCISE MODEL

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Background/Objectives: Reduced physical activity levels (Winter *et al.* 2009) in children with cancer additionally increase the cancer-related burden and presumably lead to further persisting problems like reduced motor performance during (Götte *et al.* 2015) and after treatment (Kesting *et al.* 2015). Furthermore, patients ask for supervised training sessions and individual support to be motivated (Götte *et al.* 2014). The objective was the implementation of a training program for pediatric patients during cancer treatment.
Design/Methods: During the last six years a supervised and individually-tailored training program is offered for children aged 4-21 years during treatment with various entities and different physical limitations at our local department. Contents are adapted to sports history, personal goals, medical condition and age-related physical education topics. Intensity varies from low, moderate to high loadings, depending on the patients´ condition.
Results: The training program could be feasibly implemented at the local stationary and ambulant pediatric cancer ward. Patients show high acceptance, but frequent presence of physical complaints also underline the need of a broad range of exercise methods that allow a minimum program even under poor general condition. Futhermore, no exercise promotion was offered during home stays.
Conclusion: This program provides individual and safe enhancement of physical activity at the cancer ward. To expand exercise promotion and include home stays during treatment as well, we are currently evaluating a two-part model consisting of 1) a supervised exercise intervention during in-patient stays and 2) a personal training schedule comprising of individual goals and exercises for home stays. Activity trackers (fitbit) provide feedback about daily steps during home stays and regular communication (mail, phone, face-to-face) ensures support and safety. This special offer could be a feasible alternative to cancer sports groups which are difficlut to realize for pediatric patients with cancer due to limited incidence and large catchment areas.

P-592

MINDFULNESS AND EFFECTIVE OBSERVATIONAL SKILLS: IMPROVED QUALITY OF CARE FOR PEDIATRIC PATIENTS WITH CANCER

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Background/Objectives: Children Cancer Unit in Indus Hospital caters to the underprivileged hence people from all over Pakistan and Afghanistan, come to the hospital for treatment. Ensuring that each child receives the quality of care he or she deserves is a struggle which health professionals face. Accuracy and objectivity are essential components of patient care, and specifically where pediatric patients are concerned who may not be able to verbalize their physical or psychological discomfort or distress as well as adults, hence it becomes imperative that nurse technicians are able to identify sources of distress or discomfort in pediatric patients with cancer.
Design/Methods: A pilot study was carried out on 12 students who were enrolled in the nurse technician program in the Children Cancer Unit (CCU), Indus Hospital.
Results: The nurse technicians were then tested in observational skills in wards in Children Cancer Unit then taught mindfulness skills, after the training they were tested again in their observational skills with pediatric patients with cancer. A qualitative analysis of the data revealed that their observational skills had improved remarkably post intervention and the students were able to accurately gauge signs of physical and psychological distress or discomfort in pediatric patients.
Conclusion: Inaccurate or biased reporting can be a major hurdle in pediatric care, making health professionals overlook symptoms that may be life threatening because effective observation skills are missing. The quality of care for pediatric patients is already compromised because most of the time they are not able to voice accurately their concerns and symptoms which may be causing them distress.The data yielded the result that mindfulness skills can be used effectively to gather objective and accurate information regarding patients, thus improving quality of care.

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REIKI USED IN ALLEVIATION OF PHYSICAL AND PSYCHOLOGICAL DISTRESS IN END OF LIFE CARE IN CHILDREN WITH CANCER

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Background/Objectives: Children suffering from cancer are in excruciating pain especially when they are in the end of life care phase. In order to improve the quality of life in the end of life stage it becomes a priority to reduce physical and psychological distress. Reiki, a complementary alternative energy therapy is used for alleviation of stress, anxiety, increasing relaxation and improvement of the overall quality of life in children with cancer while reducing physical and psychological distress.
Design/Methods: Hundred sessions of Reiki were carried out over a period of two years on children with cancer who were on end of life care in Children Cancer Unit, Indus Hospital.
Results: Out of the 100 sessions, 80% of the sessions resulted in reduction of physical and psychological distress in patients. Sometimes the children would call the laying of hands over affected areas as 'magic'. Reiki helped alleviate their suffering and gave them respite from the constant excruciating pain that they suffered.
Conclusion: Reiki needs to be a part of end of life care for children suffering from cancer, as this not only provides relief from physical distress but also reduces the psychological distress associated with impending death and progressive disease.

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COLD PACK APPLICATION FOR ALLEVIATION OF PHYSICAL DISCOMFORT IN CHILDREN WITH CANCER AND REDUCTION OF PSYCHOLOGICAL DISTRESS

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Background/Objectives: Since Children Cancer Unit (CCU), Indus Hospital is a philanthropic organization catering to the poor and offering cancer treatment free of cost, medicines are still given through cannulization rather than the central line, which results in physical discomfort and psychological distress in children with cancer.
Design/Methods: After interviewing nurses, doctors and patients it was found that the medicines causing the most physical discomfort and resulting psychological distress, during administration were Vincristine, Levofloxacin, Vancomycine and Potassium Chloride. In a clinical trial of 100 children in the hospital, cold pack application was used on areas of physical discomfort closest to the cannula, while the child was being administered medication.
Results: It was observed that ice pack application while the medicines were being administered via cannula, caused significant reduction in physical discomfort. The ensuing psychological distress of child and caregiver was alleviated, thus increasing treatment compliance.
Conclusion: Children with cancer already have to deal with many adverse effects of the disease as well the side effects of the medication they are taking for treatment be it chemotherapy or radiation. Non pharmacological means need to be utilized more often for the alleviation of physical discomfort in children with cancer so as to prevent toxic overload. And ice packs are a price friendly and effective means of reducing discomfort and psychological distress, when it occurs.

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IMMUNIZATION PRACTICES IN CHILDREN WITH CANCER: A GLOBAL SURVEY CONDUCTED BY SIOP PODC SUPPORTIVE CARE WORKING GROUP

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Background/Objectives: Immunization of children is a cornerstone in public health interventions designed to address vaccine-preventable diseases (VPD). This process is interrupted in the children who develop cancer because of multiple factors. This survey was conducted by SIOP PODC Supportive Care Working Group to assess the prevailing immunization practices for pediatric oncology patients.
Design/Methods: A questionnaire was designed in "PDF form" format and sent to members of working group through emails. Questions included information about availability of vaccines for cancer patients, counselling about VPD for the patients and close relatives, vaccination guidelines for cancer patients and routine prescription of vaccines during and after cancer therapy.
Results: Of 36 respondents from 23 countries, 20 belonged to lower and lower middle income countries (LIC/LMIC), whereas 16 from upper and higher middle income countries (UMIC/HIC). Half of the physicians had more than 10 years experience of treating childhood cancers. The commonest free of cost vaccines included hepatitis-B, haemophilus influenzae type B, pneumococcal and MMR vaccines. In LIC/LMIC (n=20), no free vaccines were available in 35% centres. Prevalence of routine counselling of caregivers about VPD in UMIC/HIC and LIC/LMIC was almost the same (60% vs. 62%). Testing of titres for one or more vaccines was noted in 70% centres of UMIC/HIC, in contrast to only 15% in LIC/LMIC. Annual influenza vaccine was routinely prescribed in 75% patients and 88% of their close relatives in UMIC/HIC, whereas it was provided to 15% and 20% respectively in LIC/LMIC. Seventy percent centres in UMIC/HIC were following some vaccination guidelines, in contrast to 35% in LIC/LMIC. Designed vaccination card was available in only 25% and 20% centres respectively.
Conclusion: Unavailability of vaccines for pediatric oncology patients in LIC/LMIC is a serious concern. There is a need to develop consensus vaccination guidelines during and after cancer treatment based on their availability in different settings.

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PHYSICAL STRENGTH OF CHILDREN WITH CANCER

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Background/Objectives: Treatment for children with cancer affects on children's strength, but the magnitude of the decreased strength and how it affects children's daily life are not revealed in Japan. The objectives of this research were to measure children' physical fitness and identify difficulties in daily life from parents' perspectives.
Design/Methods: The participants were children with cancer and their parents. Of 88 participants, 5 were in-patients, 35 were outpatients, and 48 had completed treatment. We measured height, weight, muscular strength, instantaneous force, flexibility, balancedness. Also, Parents were asked the degree of the strength of their children and how the strength affected their daily life.
Results: The z cores of all scores were calculated based on standardized norm score in Japan. Compared with norm, more than 30% children with cancer were in -2SD of norm score in muscular strength during in-patient and outpatient. When compared the scores between on and off treatment, muscular strength and instantaneous force of on-treatment were significantly lower than that of off-treatment. Children who treated by stem cell transplant (SCT) showed significantly lower height ($p < .001$), weight ($p < .001$), muscular strength ($p = .006$), and instantaneous force ($p = .021$) than those of children who did not have SCT. Regarding parents' perspectives, 13% perceived their children's strength were the same compared with strength before they were diagnosed, and 87% perceived that their children's strength were decreased compared with before they were diagnosed. Difficulties in daily life were seen in walking, fatigue, going up and down the stairs, feeling an inferiority complex, and physical training in school.
Conclusion: The muscular strength is the most affected, and children who had SCT might have severe strength problems. There are various difficulties; physically, emotionally, socially, school, and it is important to give exercise programs to children with cancer.

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PREDICTING THE RISK OF ADVERSE EVENTS IN CHILDREN WITH FEBRILE NEUTROPENIA - VALIDATION OF A CLINICAL RISK ASSESSMENT TOOL

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Background/Objectives: To validate an existing clinical risk assessment tool to predict adverse events (AE's) in children with cancer and febrile neutropenia.[1]
Design/Methods: All patients less than 15 years of age, with confirmed malignancies receiving chemotherapy, who presented with fever (axillary temperature >38°C twice in 24 hours or once >38.5°C) and neutropenia (neutrophil count <500cells/mm^3) were enrolled. A risk prediction score[1] was calculated for each patient and AE's were documented until antibiotics had been stopped and neutropenia resolved. Risk prediction score included: Hb ≥ 9 g/dl, WCC < 0.3 g/L, platelet count <50 g/L, chemotherapy more intensive than ALL maintenance therapy. Adverse events were defined as serious medical complications (SMC), microbiologically defined infection (MDI), and radiologically confirmed pneumonia (RCP).
Results: There were 48 febrile neutropenia episodes in 29 patients of whom 48% had haematological malignancies, 48% solid tumours and 4% CNS tumours (01 January 2014 - 28 February 2015). The male to female ratio was 1:1.6 with a mean age of 69 months (median age 54 months). Adverse events occurred in 11/29 patients with a low risk (score <9) (10 MDIs and 1 SMC including 1 death) and 15/19 (11 MDIs, 3 SMCs, 2 RDPs) with a high risk score (score >9). Based on these interim results the risk prediction model has a sensitivity of 57% and specificity of 73%. The study is ongoing and final sensitivity and specificity is still to be determined.
Conclusion: Based on the interim analysis the risk prediction model does not achieve the targeted sensitivity of more than 90%. Reference: Ammann RA, Bodmer N, Hirt A, et al: Predicting adverse events in children with fever and chemotherapy-induced neutropenia: The prospective multicenter SPOG 2003 FN study. J Clin Oncology 28:2008-2014, 2010.

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PHYSICIAN PERSPECTIVES ON HOSPITAL DETENTION: THE UNEXPLORED PATH

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Background/Objectives: Hospital detention (HoD) can be defined as practices whereby patients are denied release after medical discharge due to families' inability to pay hospital bills. Only recently HoD is being recognized as a global phenomenon with little existing data. Moreover, the perspectives and roles of physicians in relation to HoD are unclear.
Design/Methods: We conducted exploratory analyses to define existing data and gaps to generate ideas for future research on the perspectives of physicians in relation to HoD.
Results: On pilot, anonymized inquiry with over 100 physicians several distinct categories of response emerged. Many reported no knowledge of HoD in their

hospitals. Hearing about it appalled many. Some thought that the issue was very complex and just asking physicians about their role was incorrect and not helpful. Few were involved in hospital administration and thought it inappropriate to conclude that HoD was totally incorrect, since hospitals need to receive payments to continue functioning. It surfaced that in some cases and hospitals, HoD may not be obvious. Hospitals may sign a contract with patients to ensure that patients are legally bound to pay hospital fees for therapy. If they fail, hospitals may use pressure tactics or partially waive fees. Overall, HoD may be grossly underrecognized and underreported. Based on these analyses, areas of future focus for research include: 1) perception surveys with standardized HoD definitions; 2) acknowledging complexity of HoD within health systems such that accountability and transparency may be promoted without blame; 3) working with field-based team members engaged in human rights, health law and policy, governance, and ethics.
Conclusion: The present report highlights the need of exploring perspectives and roles of physicians on HoD practices across settings where different policies may be in place. Being an integral part of health care delivery system, physicians could play a pivotal role in stopping hospital detention.

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IMPACT OF DAY CARE CENTER IN IMPROVING QUALITY OF LIFE OF PPEDIATRIC CANCER PATIENTS BY PROVIDING PALLIATIVE CARE SERVICES NEAR TERTIARY HOSPITALS IN NEW DELHI

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Background/Objectives: One of the most rapidly growing aspect of palliative care service is the need of day care but enough research is not available to prove it.Thus this study was conducted with an aim to assess the impact of a day care center in improving the quality of life (QOL) of pediatric cancer patients by providing palliative care services with a multi-disciplinary team approach near tertiary care hospitals in New Delhi.
Design/Methods: A prospective comparative study was conducted to evaluate the effectiveness of palliative care services in the inpatient department of the day care transition home of Cankids a non-governmental organization. Day care patients were compared with a comparison group who were not provided with any type of palliative care services. In order to examine the effectiveness of day care over time, semi-structured interviews were carried out at entry to study or day care, at 0-1 week, 6-8 week and 12-13 week respectively. The interview schedule included palliative care outcome scale (POS) as a measure of health related QOL in the form of a questionnaire.
Results: Fifty patients randomly selected (80% males, median age-10 years, 75% not residents of New Delhi) over a 12 week period admitted to the day care center for any palliative care service were recruited in the study. The comparison group also consisted of 50 patients (80% males, median age-10 years, 75-80% not residents of New Delhi) requiring palliative care support but were not receiving any and were only receiving standard treatment of cancer at the tertiary center. The difference was statistically significant (p=0.03) when the QOL of study group receiving palliative care services at day care center were compared with the comparison group.
Conclusion: This study demonstrates that patients who were offered palliative care services at a day care had a better QOL.

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REHABILITATION OF CHILDHOOD CANCER PATIENTS- COLLABORATIVE EFFORTS OF SRCC -CENTRE FOR CHILD DEVELOPMENT (CCD) WITH TATA MEMORIAL HOSPITAL(TMH), AND UGAM-CHILDHOOD CANCER SURVIVORS SUPPORT GROUP

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Background/Objectives: To rehabilitate young cancer patients whose psychological and locomotor functions are affected due to treatment by providing therapy sessions in collaboration with SRCC- CCD rehabilitation centre.
Design/Methods: TMH along with Ugam collaborated with SRCC-CCD, multi specialty rehabilitation/therapy centre in Mumbai to offer therapy for young cancer patients who have disturbance of their psychological and locomotor functions. An executive administrator who is Ugam member is in charge of facilitating collaboration. The centre conducts physiotherapy, occupational therapy, speech therapy and educational therapy sessions to evaluate the patients. Patients are given ratings (Good, Fair, Poor) based on the aforesaid evaluation. A monthly report is sent to the hospital giving details of the assessment and the recommendation for follow up. The patient may or may not be advised follow up after giving due consideration to his/her sensory, ADL, psychological, psychosocial and locomotor functions during the evaluation. These evaluations are done free of cost by SRCC-CCD.
Results: A total of 26 patients, median age 8Years(Range 2-15) are beneficiaries.20/26 (77%) are Brain tumor & 6/26(23%) are non Brain tumor patients; 12 reside in Mumbai & 14 are from outside Mumbai. Parental feedback regarding these sessions have been good in 80.8% and fair in 19.2%. Patients have shown overall improvement in their day to day activities after these therapy sessions.
Conclusion: SRCC-CCD has taken exceptional steps for rehabilitation of active cancer patients. These sessions have not only been a boon to the patients and their parents but also to the doctors as they are able to rehabilitate the patients successfully. Implementing such rehabilitation sessions have been imperative for the long term physical and mental development of patients. It is expected that several cancer patients will get benefited by such an activity.

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IMPACT OF SUSTAINABLE FINANCIAL SUPPORT THROUGH INDIAN CANCER SOCIETY(ICS)-CANCER CURE FUND (CCF) FOR TREATMENT OF CHILDHOOD CANCERS AT TATA MEMORIAL HOSPITAL(TMH)-MODEL FOR DEVELOPING COUNTRY

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Background/Objectives: With the non-availabilty of state sponsored or insurance based health care model in developing countries, many children with cancers do not get treatment due to lack of finances. Having evolved an incentive based financial model to address this serious issue we show way forward for sustainable solution for cancer care.
Design/Methods: In 2011 HDFC AMC in joint initiative with ICS launched mutual fund scheme to provide financial assistance to needy cancer patients for treatment by tapping investors who would be willing to donate whole or part of dividend for the ICS- CCFSeven hospitals across India were empanelled by ICS for this project & TMH is one of them.A Due Diligence Team and the Governing Advisory Council of the ICS-CCF fund were established to duly scrutinize the applications from the empanelled hospitals for sanction and disbursement of funds.
Results: ICS has implemented CCF at a Pan India level covering patients from 20 states and has granted financial assistance for cancer treatment of over Rs. 25 crores to 1200 patients till date.141 children(Age 0-15 years) have benefited from innovative venture from Oct2011 to July 2014 at TMH. A total of INR 3,95,55,000 have been sanctioned for them. 53/141(38%)were ALL, 32(23%)PNET, 30 (21%) Lymphoma,12(9%)AML,9(6%) OGS,3(2%)APML and 2(1.%)Others. 39/141 (28%) have completed treatment. 78/141 (56%) are on treatment and 18/141 (13%) have expired. 6/141 (4%) were lost to follow up. 6/18 deaths were due to toxicity and 12/18 were due to disease progression.
Conclusion: Without the help of ICS-CCF most of these 141 patients could not have afforded treatment &succumbed to disease. At median follow up of 16 months 117/141 (83%) are alive with controlled disease. As ICS-CCF supports the entire treatment cost, parents don't have to apply to multiple agencies for funding. It becomes a one-stop process with assured funds leading to reduced treatment abandonment.

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OVERCOMING BARRIERS TO IMPROVING THE TIME TO ANTIBIOTICS IN THE FEBRILE PEDIATRIC ONCOLOGY PATIENT IN THE OUTPATIENT SETTING

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Background/Objectives: Fever is a common complaint in children with cancer in outpatient oncology clinics and emergency departments (EDs) and is a potentially life-threatening complication requiring immediate identification and management with a broad-spectrum antibiotic. We conducted a quality improvement project to decrease the time to antibiotics (triage to administration) to 60 minutes or less in febrile oncology patients with a central venous catheter (CVC) and undergoing treatment.
Design/Methods: We utilized the Model for Improvement methodology and collected baseline data over 6 months. Discussions then occurred with relevant stakeholders (including ED and oncology providers [MDs, NPs, RNs]) to identify barriers to achieving the goal of 60 minutes for antibiotic administration. We subsequently developed interventions and conducted PDSA (Plan, Do, Study, Act) cycles targeted at these barriers over 12 months. Statistical process control charts were used prospectively to analyze data.
Results: Identified barriers included lack of staff and parental education about the importance of timely administration of antibiotics, ED and clinic staff discomfort in administering antibiotic prior to knowing the child's neutrophil count, and difficulty of ED nurses in accessing and troubleshooting CVCs (particularly mediports). The

following intervention bundle was developed: a) Staff education on guidelines in managing a febrile oncology patient; b) Provider education in estimating a patient's neutrophil count; c) Distribution of parental/patient CVC cards; d) ED nurse education to enhance CVC access skills. Median time to antibiotics decreased from 81 to 55 minutes. The overall percent of patients receiving antibiotics in under 60 minutes increased from 36% to 53%.
Conclusion: In discussion with providers caring for febrile pediatric oncology patients, we identified barriers and targeted them to decrease the time to antibiotics over 12 months. While some of these barriers may be institution specific, others may be global barriers that may help to create febrile pediatric oncology patient management guidelines.

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DEVELOPMENT OF CLINICAL PRACTICE GUIDELINES FOR SUPPORTIVE CARE IN CHILDHOOD CANCER IN THE NETHERLANDS - CURRENT VARIATIONS IN SUPPORTIVE CARE PRACTICE

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Background/Objectives: Because of intensive treatment strategies in children with cancer, supportive care plays an increasingly important role. Unfortunately, few evidence-based guidelines are available in this area, which might contribute to suboptimal and conflicting supportive care in children with cancer. In this study our objective was to explore current practice variations in supportive care in children with cancer in The Netherlands.
Design/Methods: We conducted an in-depth review of local guidelines and protocols among all 6 Dutch pediatric cancer centers. The compiled list comprised important supportive care topics and was verified by a pediatric oncologist from each center to assess correspondence with daily supportive care practice in their hospital. Subsequently, we evaluated if the clinical practice in the 6 pediatric oncology centers was concordant (same in ≥5 out of 6 centers), partly concordant (almost the same in ≥5 out of 6 centers) or discordant (same in <5 centers).
Results: The questionnaire comprised 67 questions regarding 14 supportive care topics. We found concordance in 11 of 67 items (16.4%), partial concordance in 6 of 67 items (9.0%) and discordance in 50 of 67 items (74.6%). We explored conformity with three current evidence-based guidelines, which varied but was generally low.
Conclusion: In the Netherlands, major variations exist in daily practice of supportive care for childhood cancer patients. The development and integration of clinical practice guidelines in daily practice has the potential to greatly contribute to uniform evidence-based practice, and thereby contribute to better outcomes of childhood cancer patients. Development and implementation of these guidelines is the next step in our project.

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EFFICACY AND TOLERANCE OF LIDOCAINE 5% PATCHES IN NEUROPATHIC PAIN AND VASO-OCCLUSIVE SICKLE-CELL CRISES PAIN IN CHILDREN: A PROSPECTIVE MULTI-CENTER CLINICAL STUDY

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Background/Objectives: Neuropathic pain and pain related to bone vaso-occlusive crises in children are often treated with pain killers responsible for many side effects. Lidocaine patches are recommended for treatment of neuropathic pain in adults but is not evaluated in children.The purpose of this study was to evaluate the safety and efficacy of Lidocaine patches5% in the pediatric population.
Design/Methods: Trial design: phase II, prospective, open, non-randomized and multi-center study. Patients, 6 to 21 years-old, suffering from neuropathic pain or superficial bone vaso-occlusive crises were proposed to participate. The rate of success was defined by the rate of patients who, during at least 2 out of 3 consecutive days, show a decrease of 2 points or more on the Visual Analogue pain Scale (VAS) between Lidocaine 5% patch application and a measurement made after 12 hours. Using a one-stage Fleming design, 39 patients had to be enrolled and a minimum of 29 successes (74 %) was necessary to conclude that the treatment was effective. Tolerance was determined by the rate of patients with adverse reactions according to the criteria of the National Cancer Institute Common Terminology Criteria for Adverse Events v4.0.
Results: Forty patients were enrolled in the study and 39 were analysed. On Day 1, VAS scores were significantly reduced by at least two points in 58.97% of the patients. 48.6% of patients had a decrease of at least two points on the VAS on 2 consecutive days. Only 7.7% of the patients experienced grade 1 or 2 toxicities.
Conclusion: The use of Lidocaine5% patches allows reducing intensity of pain in half of our population study. However we can't conclude to an efficacy using the statistical design beforehand established. Nevertheless, considering the good tolerance, we can state that it is safe and could be integrated in the therapeutic arsenal available in pediatrics pain management.

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EFFICACY AND SAFETY OF LOW DOSE KETAMINE AS ADJUVANT TREATMENT FOR REFRACTORY PAIN IN CHILDREN WITH CANCER: A PROSPECTIVE OBSERVATIONNAL STUDY

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Background/Objectives: Pain control is a challenge in children with cancer. Consequences of disease progression, central sensitization and painkillers side effects like opioids induced hyperalgesia can lead to intractable pain despite well conducted treatments. Ketamine, a N Methyl D Aspartate receptor antagonist, has shown to be efficient in relieving cancer pain in adult population. Literature regarding children is scarce.
Design/Methods: This prospective multicentric observational study (approved by French regulatories CCTRIS and CNIL) aims to assess efficacy, safety and opioid-sparing effect of low doses of ketamine added to opioid analgesics to improve refractory cancer pain in children.
Results: Thirty-eight patients (median age 15y.) from 10 French pediatric oncology centers were registered during a 11 months period. All received Ketamine either intravenously (37) or orally (1) as adjuvant treatment for refractory pain. The mean pain score for the overall population has significantly decrease from Day 1 (Mean VAS = 6.7 (2.8)) to Day 3 (Mean VAS = 4.3 (3.2)) ($p < 0.001$). VAS scores were reduced by at least two points in 19 (56%) patients 48h after initiation of ketamine. Nine patients experienced poor tolerance (at least 2 side effects), all with infusion rates lower than 0,05 mg/kg/h. None had limiting toxicities. Concomitant prescription of benzodiazepine has not shown efficiency in controlling side effects. Opioid-sparing effect was highlighted in four patients. 54% of the prescribers and 47% of the patients found ketamine addition "very helpful" even when they did not experienced improvement of pain scores.
Conclusion: The adjunction of low doses of ketamine to opioids analgesics in children suffering from refractory cancer pain allowed reducing intensity of pain in half of our population study. However we can't conclude to an efficacy using the statistical design beforehand established. Nevertheless, Ketamine may be an interesting and safe option for improving treatment of refractory pain in children with cancer.

P-606

TRADITIONAL AND COMPLEMENTARY MEDICINE STRATEGIES IN PAEDIATRIC ONCOLOGY: GLOBAL PATTERNS OF USE

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Background/Objectives: Traditional and Complementary Medicine (T&CM) strategies are frequently sought by paediatric patients with cancer. Patterns of use vary widely across different countries. The current review aimed to characterize the rates, types and reasons for use of T&CM in paediatric oncology, stratified by reporting country income level per World Bank.
Design/Methods: A systematic review of the literature was performed searching MEDLINE, EMBASE, Global Health, CINAHL, PsycINFO, AMED, Cochrane Database and Proceedings First from the date of inception for each database to February 7, 2015. Inclusion criteria comprised children <18 years old representing at least 10% of the participants, who were on active treatment for cancer, with any T&CM use. Exclusion criteria included failure to include at least one of the core outcomes (rate, type or reason for use). All primary study types were included, without language

exclusion. Article screening and data extraction were independently conducted by two reviewers with discrepancies resolved by consensus.
Results: 4088 abstracts were retrieved, with 3062 abstracts screened after duplicates removed. 310 qualified for full-text review. 66 articles from 31 countries reported relevant data; 1 from a low-income country (LIC), 6 from lower-middle-income countries (LMIC), 15 from upper-middle-income countries (UMIC) and 44 from high-income countries (HIC). Reported rates of T&CM use among pediatric oncology patients varied between 59-90% (median 68%) in LIC/LMIC as compared to 6-100% (median 42.7%) in HIC. Publications spanned 1977 to 2014, and reported rates of T&CM use appeared to increase over time. Provision of care from Traditional Healers was reported more frequently in LIC and LMIC than in HIC. Abandonment of conventional cancer care, and delays in diagnosis were associated with T&CM use in some settings.
Conclusion: T&CM strategies are used commonly by paediatric oncology patients worldwide. Integration of T&CM practices into paediatric oncology programs may offer an opportunity to improve treatment adherence and outcomes.

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INFECTION-RELATED MORTALITY IN CHILDREN WITH CANCER: A 10-YEAR STUDY

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Background/Objectives: Many children with cancer die from infection. Nevertheless, the clinical characteristics of infection-related mortality are still poorly understood, yet their understanding may help improve survival. We aimed to analyze infection-related deaths in a Pediatric Oncology Unit (POU).
Design/Methods: Retrospective review of epidemiological and clinical data of children who died between Jan'05-Dec'14 in a POU admitting circa 160 children annually, up to age 16y.
Results: In this 10y period infection caused the death of 29 patients, accounting for 9% of all deaths (N=317) and 60% of the toxic deaths (29/48). Most children were girls (20/29). Eighteen children had hematologic malignancies (15 leukemias, 3 lymphomas), 7 had solid tumors and 4 had central nervous system tumors. Most (25/29) were being exposed to intensive treatment protocols (levels 3/4 of the *Intensity of Treatment Rating Scale 2.0*). Median age of death was 10.2y (IQR 4.4-14.3y). Median time from diagnosis to death was 6m (IQR 2m-1.9y). Nineteen patients met criteria for septic shock, of which 16 were neutropenic (10 leukemias, 2 lymphomas, 3 solid tumors and 1 medulloblastoma). The most common primary site of infection was the respiratory tract (10/29), followed by gastrointestinal (3/29) and skin (1/29); in 15 patients, the primary site of infection was not evident. A pathogen was identified in 16 children - 12 bacterial agents (7 Gram-), 4 fungal agents and 2 viruses. Three patients had co-infections (two Gram- & fungus, one Gram- & Gram+ bacteria). Fifteen patients died in intensive care units, 9 in the POU ward and 5 in the local hospital's ward.
Conclusion: Infections are a major cause of toxic death in children with cancer. To improve their overall survival, especially of those submitted to agressive treatments, new strategies for infection prevention and treatment should be developed, as well as education tools for professionals and families.

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THE ROLE OF BASIC ORAL CARE AND THE NEED OF EVIDENCE BASED-GUIDELINES FOR MUCOSITIS MANAGEMENT IN ONCOHEMATOLOGICAL PAEDIATRIC PATIENTS

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Background/Objectives: Mucositis is a term that describes the inflammatory response of any mucosal surface in the body in response to the cytotoxic effects of oncologic treatment. Oral mucositis is the one that has received more attention, due to its high incidence and impact on patient's quality of life, and there is not a uniform standard management. The aim of this small study is to describe some aspects related with dental health and oral care in an aleatorial sample of pediatric oncohematologic patients.
Design/Methods: A sample of 36 aleatorized patients from "Gregorio Marañón" Hospital-Oncohematology Paediatric Department were analyzed by three odontoestomatologist, in order to describe different parameters in the oral health status, dental care and prevention of oral mucositis.
Results: In this small study we observed that 67% of the patients had never received prior dental boarding. Sweet and cold foods were the prefered by the 36% of them, followed by cold salty ones. This enhances the fact that cryotherapy is effective as pain treatment in mucositis. Only 56% of them had an acceptable oral hygiene at the time of evaluation. Among all the patients evaluated (inpatients and outpatients) 17(47%) had mucositis. All the patients were not brushing their teeth during the treatment. According to the results of our study, patients who received hygiene tips, presented higher degree of mucositis values (probably related with a highest risk of having mucositis, because of a longer neutropenia/drugs/ radiotherapy/type of cancer …) 72,22 % of the patients did not receive treatment for mucositis but 11,11% reported that chlorhexidine was the best option for its healing.
Conclusion: There is a need to unify criteria and to develop preventive and therapeutic protocols for clinical applicability, (which will include pharmacological and non-pharmacological treatments, teeth brush, cryotherapy …) This is the aim of a new biggest study that we have just begun.

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FACTORS CONTRIBUTING TO PLACE OF DEATH IN CHILDREN AND YOUNG PEOPLE DYING FROM CANCER: A SYSTEMATIC REVIEW OF THE LITERATURE

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Background/Objectives: Despite significant increases in survival from childhood cancer it remains the most significant cause of death in children and young people. Paediatric Palliative Care is an evolving subspecialty whose primary aim is to work with young people and their families to improve their quality of both life and ultimately their death. Internationally there is increasing emphasis on involving patients and carers in decision making during palliation-including decisions regarding locations of death and dying. The aim of this literature review was to determine the preferred place of death and identify the factors influencing this decision.
Design/Methods: Embase, Medline and Cumulative Index to Nursing and Allied Health Literature (CINAHL) were searched from 1998-2014 using the terms: 'child', 'cancer', 'place' and 'death'. 3 independent reviewers assessed articles for relevance and inclusion.
Results: 22 studies were included from 15 countries. The majority of studies were retrospective reviews of death certificates or medical records. Four studies used semi-structured questionnaires given to bereaved parents and three were prospective studies. Location of death varied significantly. Home deaths ranged from 9-79% and hospital deaths from 27-81%. A minority of patients died in hospices, ranging from 3.1-35.5%.
Conclusion: Internationally there are significant differences in the location of death of children and young people dying from cancer. This review identified many factors contributing to place of death: patient demographics, disease diagnosis and stage, time from diagnosis, geography, cultural beliefs and socioeconomic status. The most significant were: Availability of Paediatric Palliative Care services and the ability to provide end of life care in the preferred place of death. A key role of palliative care is to facilitate parent and patient choices. Health professionals should ensure the development of flexible services which can provide the care required at the location of choice and be powerful advocates for this uniquely vulnerable group.

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MANDATORY NATIONAL POLICY FOR RESUSCITATION PLANNING IMPROVES DECISION MAKING AND COMMUNICATION AT THE END OF LIFE IN CHILDREN AND IS WELCOMED BY CLINICIANS

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Background/Objectives: In May 2010 National Health Service (NHS) Scotland published Europe's first fully integrated national policy for Do Not Attempt Cardiopulmonary Resuscitation (DNACPR) decision making and communication. The Scottish Government led the development of this policy. A Paediatric education package was made available on line (Children and Young Adult Acute Deterioration Management-CYPADM) and local champions appointed to provide training and change working patterns.
Design/Methods: Using The Scottish Paediatric Surveillance Unit (an epidemiological sub group of the Royal College of Paediatrics and Child Health) clinicians were sent a monthly questionnaire asking if they had any end of life discussions with families. Positive responses generated a follow up email asking about the consultation.
Results: Over 2 separate 1 year periods (2011-12 and 2013-14) 127 positive responses were obtained and 99 follow up questionnaires completed (response rate 78%). The age range of individuals involved was 0.5-27 years, with increased use of the form at the extremes of the range. The form was useful in neonatal and transition settings. Uptake reflected the population distribution across the nation, with most forms filled for people living in the Central Belt. Over 95% of clinicians rated form use as easy or very easy. A similar proportion rated the policy as very good or excellent.

Conclusion: Policies which facilitate an integrated approach to DNACPR decision-making and communication children have been implemented across Scotland. Quality measures have been developed to assist Health Boards in further establishing the impact of these policies on patient care.

P-611

A MANAGED AND SUPPORTED TELEHEALTH NETWORK DELIVERS EQUITABLE, HIGH QUALITY END OF LIFE CARE TO CHILDREN DYING OF CANCER, ACROSS THE NATION, IRRESPECTIVE OF GEOGRAPHY

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Background/Objectives: The Scottish Managed Service Network (MSN) for Children and Young People with Cancer was established by the Scottish Government to ensure equity of access to, and the provision of care to the population of Scotland irrespective of location. Managerial and secretarial support was provided to the network independent of health boards. Despite recent work suggesting the number of children with a life limiting or threatening diagnosis is much greater than thought, it remains rare and providers are often isolated both physically and intellectually. Weekly telephone and monthly video multi disciplinary meetings began in May 2014, linking professionals across disciplines and sites.
Design/Methods: A retrospective review of MDT attendance logs and review of service.
Results: A median of 7 professionals attended phone conferences (IQR 5-8) and a median of 13 attended video conferences (IQR 10-15). Hospice, community, secondary and tertiary care paediatric and nursing staff always attended. Allied health professionals attended as the meetings became established. Paediatric Haematologists did not attend. Professionals were clear that the meetings enhanced working practice and welcomed the formal structure provided by the MSN. The meeting was universally rated as "The most important MDT I attend".
Conclusion: The use of proformas to frame case discussions was welcomed. The meetings would not happen without managerial support from the MSN. More needs to be done to engage with haematology colleagues Impact on practice: Improved integration of care and development of quality indicators has rapidly improved practice delivery to a uniquely vulnerable patient group.

P-612

WHERE DO CHILDREN WITH CANCER DIE AND WHAT FACTORS EFFECT DECISION MAKING ABOUT THIS? A SYSTEMATIC REVIEW OF THE LITERATURE

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Background/Objectives: Childhood cancer remains the single most common cause of death in children and young adults in the developed world. As the survival rates have improved, so too has the use and availability of paediatric palliative care. In the UK and Europe there is an increasing emphasis on the facilitation of choice for patients and carers. Factors believed to effect choice in regard to location of death include availability of services, cultural beliefs, type of disease and socioeconomic status.
Design/Methods: Embase, Medline and Cumulative Index to Nursing and Allied Health Literature (CINAHL) were searched from 1998-2014 using the terms: 'child', 'cancer', 'place' and 'death'. Articles were assessed for relevance.
Results: Twenty two studies were included from 15 countries. The majority were retrospective reviews of death certificates or medical records. Four studies used semi-structured questionnaires, three were prospective studies.Location of death varied significantly. Home deaths ranged from 9-79%, hospital deaths from 27-81% and hospice deaths from 3.1-35.5%.
Conclusion: There are significant differences across the world and even between regions within a single country, in the location of death of children and young people dying of cancer. One of the key roles of palliative care professionals is to facilitate parent and patient choices. A deep understanding of obstacles to optimum delivery of care is required of clinicians delivering end of life care to children and their families. Where absent/poor service provision or socio economic factors restrict choice, evidence should be collected and presented to funding agencies to highlight gaps in the equitable delivery of care to a uniquely vulnerable group.

P-613

RISK FACTORS FOR SEVERE OUTCOME IN NEUTROPENIC ENTEROCOLITIS; A SYSTEMATIC REVIEW

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Background/Objectives: A systematic literature review was carried out to evaluate best existing evidence on prognostic factors for outcome of neutropenic enterocolitis (NEC) or typhlitis. A well known potential life threatening complication of the treatment of malignancies. The reported mortality rate in both adults and children varies from 8% - 50%.
Design/Methods: Databases (MEDLINE, CENTRAL and EMBASE) were searched for relevant studies. All studies describing risk factors for outcome were included. Information about study characteristics, treatment, outcome and prognostic analysis were abstracted and the quality of each article was assessed.
Results: A total of 15 studies met the inclusion criteria and reported on risk factors for the outcome of NEC. All had methodological limitations, regarding the internal and external validity. Four studies evaluated possible prognostic factors in a multi- or univariate analysis resulting in 8 potential relevant factors. Two studies with high quality performed multivariate analysis showed that the diagnosis of Non Hodgkin Lymphoma conditioning pretransplant with busulfan/cyclofosfamide and acute myeloid leukaemia receiving high dose cytarabine indicated a significant prognostic factor for poor outcome of the typhlitis episode. Two studies with univariate analysis showed that the radiological finding of bowel wall thickening >10mm and the laboratory findings of CRP>150 mg/L and IL-8 > 1000pg/ml were found as prognostic markers.
Conclusion: This systematic review summarizes the available evidence to identify the prognostic factors relevant for the outcome of typhlitis/neutropenic enterocolitis and provides the evidence on which to base further prospective studies and possibly create a prediction rule for outcome of typhlitis/neutropenic enterocolitis in both adult and paediatric oncology.

P-614

DELIVERING BAD NEWS AND ADVANCED COMMUNICATION SKILLS CURRICULUM FOR PEDIATRIC ONCOLOGY TRAINEES

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Background/Objectives: Effective communication is the cornerstone of good patient care. Pediatric oncologists are constantly faced with the challenge of delivering bad news to patients and families. However, a study of pediatric oncologists showed that they had received little training in delivering bad news other than learning from direct observation and lectures. In a more recent survey of trainees in United States pediatric hematology-oncology fellowship programs only 32% of trainees reported receiving communication training. Herein, we present our communication skills curriculum and our pediatric oncology trainees' experience with the training module.
Design/Methods: We implemented a small-group communication skills training module 6 years ago with a goal of providing trainees with a non-threatening, and easily engaging curriculum which allows for self-reflection and experiential learning. The module consists of didactics followed by video recorded role-play sessions using standardized patient actors. These video recorded sessions are followed by self-reflection by the trainee and feedback from session facilitators(pediatric oncologists), co-trainees, and the actor. Simulated scenarios include disclosure of a new oncologic diagnosis, unexpected relapsed/recurrent disease, and caring for the dying patient.
Results: The module focusses on conversation skills which include physician questioning skills, assessing parental/patients' knowledge, presenting information with empathy and in an organized manner, thus aiding shared medical decision making. Surveys were conducted to rate pre-and post-workshop knowledge/confidence levels of trainees(n=18) for various case scenarios. Trainees reported high/very high knowledge post-workshop compared to pre-workshop with scenarios involving discussion of a newly diagnosed cancer, responding effectively to negative emotions and end of life discussions and transition to palliative care($p=0.04$, $p=0.03$, $p=0.01$; respectively). For scenarios involving disclosure of unexpected cancer recurrence, there was no significant difference in reported pre- and post-workshop knowledge levels($p=0.08$).
Conclusion: Our study shows that small-group sessions with formal lectures and video recorded simulated scenarios allowing self-reflection and feedback is an easily implementable and effective training tool.

P-615

RESPIRATORY VIRUSES, A COMMON MICROBIOLOGICAL FINDING IN CHILDREN TREATED FOR CANCER IN SOUTH AFRICA

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Background/Objectives: Febrile neutropenia is a common complication in children undergoing therapy for malignant disease. A bacterial pathogen is only identified in 30-40% of the septic episodes. To prospectively investigate viral infections as possible etiologic agents in children with chemotherapy induced febrile neutropenia.
Design/Methods: Nasopharyngeal aspirates (NPAs) from patients presenting with fever post therapy for a malignant disease were analysed with real time PCR (RT-PCR).
Results: The study included 169 children with cancer, 81 haematological cancer (HM) and 88 solid tumours (ST) and 18 were HIV-infected. 60% were male with a mean age of 7.2 years .There were 531 septic episodes, 332 in HM (mean = 4.10 episodes per patient) 199 in solid tumours (mean = 2.26 episodes per patient) and 48 in the HIV-infected group (mean = 2.67 episodes per patient). Viruses were identified in 60.4% of the septic episodes, 69.7% in HM, 30.2% in ST and 11.3% in the HIV-infected group. Humanrhinovirus (42.6%), Coronavirus (29.6%), Polyomavirus (15.7%) and Parainfluenzavirus (10.8%) were the most commonly observed viruses. 67.8% of viral associated fevers had 1 virus detected and in 32.2% there were two or more viruses (range 0 – 5). 7 (7.1%) of patients died due to a septic event (85.7% blood cancer, 16.7% solid tumour and 28.6% HIV- infected). Eleven viruses were detected in the 7 patients who died (5 Coronavirus, 3 Human-rhinovirus, 2 Influenza A, and 1 Metapneumovirus).
Conclusion: Respiratory viruses are found frequently during febrile episodes in children with cancer. Further prospective studies with viral load determination may elucidate the significance of these viral findings. Early detection of viral infections in this patient group may help to reduce antimicrobial use and help to alleviate the critical issue of microbial resistance.

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VIRAL AND BACTERIAL CO-INFECTIONS IN CHILDREN TREATED FOR CANCER

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Background/Objectives: The aim of the study was to prospectively explore the prevalence of bacterial and viral coinfection in children with febrile episodes (FE).
Design/Methods: Individuals on treatment for cancer who presented with a FE had a full blood count and differential, blood culture and nasopharyngeal aspirate (NPA) for respiratory viruses tested. The NPA was tested using real-time reverse transcriptase PCR.
Results: One hundred and thirty three patients (68% male, mean age 6.69years) with 398 FE (258 HM, 140 ST, 38 HIV-infected) were analyzed for bacterial and viral coinfection. 264 NPAs tested positive for a respiratory virus. 54 were positive for only a virus and 210 had coinfection with a virus and bacteria or fungus (109 gram-positive and 85 gram-negative bacteria, 16 fungi). The odds for FE in a patient with a HM and positive NPA was 1.63 (p=0.051). Amongst those with an absolute lymphocyte count of <500 for longer than 7 days, the OR for coinfection was 1.92 (p=0.006).The OR for coinfection with a positive NPA and blood culture in the HIV-infected patient was 0.376 (p=0.061) and OR for coinfection with Polyoma Ki virus was 0.358 (p=0.04).The time to recovery from the FE was significantly longer in those that had coinfections (p=0.004). 9/123 patients died due to FE. Twenty bacteria were cultured from any septic episode of these patients (9 gram-positive, 7 gram-negative and 4 fungi) and 11 viruses were detected on NPA analysis. 6 patients had at least one positive test for Human rhinovirus.
Conclusion: Bacterial infections are commonly associated with viral infections in children with malignant disease. This study supports interactions between viruses and bacteria in the pathogenesis of severe infections. Future prospective studies are required to explore a temporal association between viral and secondary bacterial infections in the immunocompromised patient.

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BACTERIAL INFECTIONS IN CHILDREN TREATED FOR HAEMATOLOGICAL MALIGNANCY

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Background/Objectives: Childhood cancer cure rates have improved due to intensive chemotherapy which leads to multiple disruptions in immunological protection and increases susceptibility to life-threatening infections.
Design/Methods: Patients diagnosed with a haematological malignancy between April 2009 and March 2011 was prospectively evaluated. At each febrile episode (FE) bloods taken for blood culture, full blood count, C-reactive protein, and procalcitonin and urine sent for culture.
Results: Eighty one patients were enrolled (15 HIV-infected), 61% male, mean age 7.85 years. There were332 FE (4.1/patient); 78.8% with a positive blood culture (77 gram-positive and 181 gram-negative bacteria). 9.2% of FE had a proven fungal infection. 40.9% of FE had one bacteria cultured, 20.2% had two and 38.9% had three or more. 39 *Escherichia coli* were cultured ,79.4% extended spectrum ß-lactamase producers (ESBL); 17 *Klebsiella pneumonia*, 59% ESBL; 12 *Enterobacteraciae*, 50% resistant to Cephalosporins; 85.3% of *Staphylococci* sensitive to Vancomycin and 97.7% resistant to Cloxacillin and 46.9% of *Enterococcus* sensitive to Vancomycin. Septic complications: 26% UTI (39 gram-negative,21 gram-positive,12 fungi),24% clinical pneumonia, 4.3% bacterial meningitis, 13.6% gastroenteritis, 28% mucositis, 30.1% herpes stomatitis and 10% culture-proven tuberculosis. The mean white cell count was 2.7x 10^9/l, the mean absolute neutrophil; lymphocyte and monocyte counts were 2128, 652 and 252 respectively. The mean CRP was 151 mg/ml and PCT was 13 ng/ml. The mean duration of fever was 4.76 days (median 4 days).9(11%) died of the septic episode, only two were admitted to the ICU.
Conclusion: The very high rate of culture proven septic episodes is not recorded in the developed world. Malnutrition, overcrowded wards, lack of adequate nursing personnel, lack of isolation facilities, aseptic techniques and a high prevalence of HIV disease may be contributory factors. In addition, there is a high incidence of antimicrobial resistance. Intensive care facilities are a priority for children treated with high-risk chemotherapy.

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AN INTERVENTIONAL STUDY- NGO MAKING A DIFFERENCE IN THE LIVES OF CHILDREN WITH CANCER : CONDUCTED IN COIMBATORE, SOUTH INDIA

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Background/Objectives: The incidence of childhood cancer is on the rise in India. But India has less than 5 NGOs that work exclusively for children with cancer. The treatment and the indirect expenses make it impossible for a middle-income or lower-income family to afford the whole experience. Ignorance about the disease and social stigma also play a part. Late diagnosis almost always results in death or relapse. Most of the hospitals are also not equipped to treat childhood cancer. Very few hospitals have social service teams or councilors. Not following the protocol, lack of nutritious food and, very low personal hygiene contribute to the alarming relapse rate. The researchers believe that the gaps in the entire spectrum of childhood cancer can be efficiently filled with the services of an NGO. The authors run an NGO for children with cancer and their families.
Design/Methods: This study was run for 18 months among 100 children with cancer and their families. The state of the children before the intervention of the NGO was documented. Then the NGO started working with the children in the key areas like treatment, counseling, food, education, palliative care, and death and bereavement. And after 18 months, the same 100 children were studied to see how the NGO has made a difference in their lives.
Results: The result was that significant improvement was noted.
Conclusion: The authors have concluded that the services of the NGO make a tremendous difference in the lives of the children with cancer.

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VIRIDANS GROUP STREPTOCOCCAL INFECTIONS IN CHILDREN FOLLOWING CHEMOTHERAPY OR STEM CELL TRANSPLANTATION– A TEN YEAR RETROSPECTIVE REVIEW FROM A TERTIARY PAEDIATRIC HOSPITAL

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Background/Objectives: Viridans group streptococcal (VGS) infection is increasing and is now the third most common cause of bacteraemia in paediatric haemato-oncology patients. VGS is associated with high mortality rates due to the potential to cause viridans group streptococcal shock syndrome (VSSS). Despite this, there are no recent paediatric studies describing VGS in children with cancer in Europe to inform antimicrobial therapy. The aim of this study was to describe the characteristics, outcome and resistance patterns of children with VGS bacteraemia undergoing treatment of malignancy or haematopoietic stem cell transplant (SCT) in a tertiary referral centre in the UK.
Design/Methods: Patients aged 0-18 years admitted to a tertiary paediatric haemato-oncology centre with VGS bacteraemia from 2003-2013 were included in the study. All data was collected retrospectively from electronic records and case notes.
Results: 54 episodes occurred in 46 patients. The most common underlying diagnoses were relapsed acute lymphoblastic leukaemia (ALL) [13 episodes], ALL [6 episodes] and acute myeloid leukaemia (AML) [6 episodes]. Streptococcus mitis [35 episodes] was the most frequent organism, followed by strep oralis [10 episodes]. Thirty percent of isolates were resistant to penicillin and 100% sensitive to vancomycin. There were 8 episodes of VSSS (14.8%) – 4 in patients undergoing SCT; 3 in relapsed ALL and 1 with AML. Of these 8 patients, 6 required admission to intensive care and 3 died of multi organ failure.
Conclusion: Patient characteristics were in keeping with known risk factors for VGS bacteraemia although the high risk in relapsed ALL is of note. This observation requires further investigation and may well have management implications. The potentially fatal nature of VGS infection and high incidence of penicillin resistance are confirmed. Research is needed to develop bedside risk stratification scores that identify children at risk of VSSS to guide antimicrobial therapy.

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PHARMACOKINETICS AND ASSOCIATION OF HIGH-DOSE CYCLOPHOSPHAMIDE AND ITS METABOLITES WITH CARDIAC TOXICITY IN PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANT RECIPIENTS

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Background/Objectives: Observed only after administration of high-dose, cardiotoxicity is the dose-limiting effect of cyclophosphamide (CY). CY is activated by the cytochrome P-450 enzymes to form 4-hydroxy-cyclophosphamide (HCY), which is in equilibrium with aldocyclophosphamide. Depending on the cell type, aldocyclophosphamide may decompose to form cytotoxic phosphoramide mustard and the acrolein, or may be oxidized to the inactive metabolite *o*-carboxyethylphosphoramide mustard (CEPM). This report investigates the relationship between the pharmacokinetics of high-dose CY and the cardiotoxicity observed when the drug is used for pediatric hematopoietic stem cell transplant recipients.
Design/Methods: Ten consecutive children ranging from one to 18 years of age who were receiving a high-dose CY (≥ 50 mg/kg/dose) were enrolled. The underlying diseases were acute lymphoblastic leukemia (n = 3), acute myeloid leukemia (n = 2) and others (n = 5). The pharmacokinetics of the CY, HCY and CEPM were evaluated in each patient by analysis of the serial blood samples using liquid chromatography coupled with electrospray tandem mass spectrometry. To evaluate the myocardial damage, all the patients underwent an electrocardiogram (ECG) before every administration of high-dose CY.
Results: No overt cardiac failures were recorded. Serial ECGs revealed a reduction in T-wave and ST segment abnormalities with an increase in NT-proBNP level (1070 pg/ml) in one case. This patient had the lowest area under the concentration time curve (AUC) for CEPM (55.3 μM×h) compared to the other patients (average AUC for CEPM: 126 ± 32.8 μM×h). AUC variability was 2.0x for CY, 12.2x for HCY and 3.7x for CEPM.
Conclusion: We speculate that the patient who developed cardiotoxicity might metabolize CY into active metabolites such as acrolein, more than the inactive metabolite, CEPM. Inter-individual differences in the pharmacokinetics of metabolism of high-dose CY may explain variability in both patient response and cardiotoxicity. A further large-scale trial will therefore be needed to confirm this hypothesis.

P-621

SERVICE EVALUATION OF THE CLINICAL VALUE OF STOOL MICROSCOPY AND CULTURE IN PAEDIATRIC ONCOLOGY UNIT

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Background/Objectives: Diarrhoea is a common symptom in paediatric oncology patients. Although stool samples are still commonly sent for microscopy and culture, the value of these tests in paediatric oncology patients with diarrhoea is not clear. A number of studies suggested the limited role of attempting to isolate routine enteric pathogens as a cause of diarrhoea in hospitalized patients, however the diagnostic value of testing in children with oncological conditions has not been reported. Therefore, we conducted a service evaluation to estimate diagnostic yield of stool cultures in oncology patients.
Design/Methods: Records from the Microbiology Laboratory from September 2009 to October 2014 were reviewed to collect data on the number of stool cultures performed in patients treated at a Regional Paediatric Oncology Unit, Liverpool, UK.
Results: A total of 842 stool cultures from 250 paediatric oncology patients with diarrhoea were performed over the 5-year study period. Ninety three percent (788 samples) of the workload was from inpatients, 6.4% (54 samples) was from oncology day case ward. A significant number of children had more than one stool culture done (average 3.4 samples per patient). Out of 842 samples tested over 5 years only 1 sample was tested positive for *Campylobacter* (0.1 %). Medical records review of the patient who was tested positive showed that the patient presented from the community with a few weeks history of severe cramping abdominal pain, diarrhoea with mucus and weight loss.
Conclusion: A comprehensive service evaluation of all stool culture tests performed in paediatric oncology patients during a 5-year period have demonstrated very low utility of routine stool cultures for patients with diarrhoea. We suggest that the implementation of rational practice guidelines for ordering stool cultures could result in cost savings of approximately £2,200 per year at our hospital and more efficient utilisation of resources.

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AN ACTION RESEARCH: THE PROCESS OF CHANGE DIETARY CONSIDERATIONS AND BEHAVIORS OF CHILDHOOD CANCER PATIENTS AND PRACTICAL INTERVENTIONS FOR ENJOY EATING

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Background/Objectives: Childhood cancer patients lose their appetite due to the adverse effects of the treatment. Sometimes they would no longer eat or have little interest in eating even after the completion of treatment. In addition, hospital environment could not arouse interest in foods and their eating behaviors. Therefore, it is important to provide educational interventions to foster self-management skills on diet sustained even after discharge. The purpose of this study is to provide interventions for childhood cancer patients and to describe the process of change in their considerations and behaviors.
Design/Methods: Participants were childhood cancer patients who were admitted to the Hematology-Oncology ward in Nagano Children's Hospital from May, 2013 to December, 2014. Our interventions were (1) preparation of the environment for enjoyable eating, (2) opening of dietary education classes for patients by multidisciplinary team. In the class, participants were able to touch "the food of today", learn how each nutrient works in their bodies, cook and eat the food, and experience serving participants' cooking to friends who were in the same ward. We collected the interviews of the participants before and after interventions and observational records at the classes. We analyzed these records from the viewpoint of how their dietary considerations and behaviors had changed by actions.
Results: Thirty-four childhood cancer patients participated. As the result of the interventions, following changes were revealed; "trying to eat without their fastidious", "respecting lives of foods", "thinking about the meaning of nutrition", "increasing their motivation to overcome their illness", "enjoying eating", "growing autonomy and self-care" and "expressing their feelings about illness".
Conclusion: By improvement of the environment and educational interventions, the participants showed changes not only just to enjoy eating but also to have interests about nutritional balance and their eating habit.

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THE USE OF PROTHROMBIN COMPLEX CONCENTRATE TO TREAT PURPURA FULMINANS CAUSED BY PROTEIN C AND S DEFICIENCY AFTER VARICELLA INFECTION - A CASE REPORT

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Background/Objectives: Purpura fulminans is a complication of varicella infection causing haemorrhagic infiltration of the skin and increased risk of intravascular thrombosis. It is often caused by a deficiency of protein C or protein S leading to a prothrombotic state.
Design/Methods: We present the case of a 4 year old boy who developed purpura fulminans 1 week after chicken pox infection. He presented with a circumferential skin necrosis to both legs and disseminated intravascular coagulopathy. At diagnosis his protein C and S levels were found to be low at 14.1% and undetectable respectively. He was also found to have a heterozygous mutation for factor V Leiden.
Results: Treatment was started with an IV heparin infusion, IV Immunoglobulins, IV antibiotics and regular infusions of fresh frozen plasma (FFP). It was not possible to achieve adequate Protein S levels using FFP as post infusion his protein C and S levels were 121% and 36% respectively. He also developed pulmonary oedema secondary to volume overload so was switched to infusions of prothrombin complex concentrate (Octaplex). The dose of this was 2ml/kg (25iu/kg) twice daily and his dose of heparin was adjusted to compensate for the heparin this contained. Post Octaplex his post dose protein S levels were 46% which improved to 90-100% over subsequent days. The dose was successfully weaned and stopped after 19 days, following which he successfully maintained his protein S levels independently. During his admission he developed a deep vein thrombosis of his left arm. His heparin was changed to warfarin, without loading. He has now made a full recovery without needing any plastic surgery to his legs.
Conclusion: Purpura fulminans is a rare complication of varicella infection. This is the first reported case where prothrombin complex concentrate has been used alongside heparin to achieve a full recovery without any long term complications or sequelae.

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MANAGEMENT OF TUMOR LYSIS SYNDROME WITHOUT RASBURICASE: A MODEL FOR THE DEVELOPING WORLD

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Background/Objectives: Tumour lysis syndrome (TLS) is a life threatening oncologic emergency. Risk of TLS is determined by tumor type and tumour load and is categorised as low, intermediate and high risk. International protocols for TLS management mandate the use of rasburicase to decrease hyperuricemia mediated renal dysfunction. As it is an expensive medication, we examined whether a judicious protocol of fluid and electrolyte management could effectively manage TLS without rasburicase. This protocol would be important in the resource constrained developing world.
Design/Methods: This prospective study was conducted in Pediatric Hematology-Oncology Unit over a two year period. All the patients with risk for developing TLS were included in the study and treatment was initiated as per our protocol. The patients were categorised based on TLS risk stratification and Cairo-Bishop score.
Results: Sixty patients were recruited in the study. Forty three had Acute Lymphoblastic Leukemia, nine had Acute Myeloid Leukemia and eight had high grade Non-Hodgkins lymphoma. Thirty seven were classified as high risk, 19 as intermediate and 4 as low risk for TLS. Twelve developed hyperuricemia, 7 had hyperphosphatemia, 4 had hypocalcemia and 4 had hyperkalemia. Chemotherapy was delayed due to renal dysfunction in only one patient.Three required PICU care and only one required dialysis. There was no mortality.
Conclusion: Judicious hydration, allopurinol, phosphate binders and frequent laboratory monitoring was used in all our patients. We had an excellent outcome even in the high risk group despite not using rasburicase.

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MIBG THERAPY IS AN ACCEPTABLE OPTION FOR RELAPSED/REFRACTORY NEUROBLASTOMA(NB) IN A LOW/MIDDLE INCOME COUNTRY (LMIC) SETTING: A 10-YEAR EXPERIENCE

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Background/Objectives: 131-MIBG has been used in the treatment of relapsed/refractory NB for the past 30years, with response rates of around 20-40%. It is now used in frontline regimens, often in conjuction with chemotherapy or myeloablative therapy. Data from LMICs is lacking. We describe here our experiences with 131-MIBG therapy in the treatment of NB.
Design/Methods: Retrospective audit of patients with NB at a PaediatricOncology referral centre in India, who received MIBGtherapy in frontline or relapsed/refractory settings from 2005 to 2014.MIBG therapy was administered at the RadiationMedicineCentre, a neighboring institution. Apart from the routine evaluation, all patients underwent 131-MIBG scans and Urinary VanillylmandelicAcid (VMA) levels prior to treatment. A few patients underwent ComputerisedTomograms(CTScans) and/or Fluorodeoxyglucose Positron EmissionTomography(FDG-PET scans). The dose of 131-I MIBG was 10-12mci/kg body weight, and capped at 150mci. Children were isolated after treatment,and caregivers screened for exposure to the agent. Reassessment was done by clinical evaluation,MIBG scans and Urinary VMA levels.
Results: There was data on 31 children who received a total of 46 courses of MIBG therapy(median 1;range1-6courses). Median age was 6years,and male:female ratio 20:11.Intent was palliative in 21patients (total 28courses); most were high risk NB and had received multiple courses of treatment, including AutologousStemCellTranplant in 3/21. Response rate was 45%(12/28), with 4 patients alive at last followup. Median time to progression was 7months.Ten patients received a total of 19 courses of MIBG therapy as part of frontline therapy(inoperable mass- 4 patients, refractory disease- 2 patients, residual post-operative mass-4patients). Response rate was 40%,with 5/10 alive at last followup. The most common toxicity was grade3/4cytopenia, documented in 20%patients, mainly seen in patients with bonemarrow disease.
Conclusion: 1.With the limitations of a retrospective study,MIBGtherapy appears feasible both in relapsed/refractory as well as frontline NB in LMICs, with acceptable toxicities. 2.MIBGtherapy offers a reasonable salvage strategy in LMIC settings,where other aggressive salvage therapies(including High dose therapies) are often not possible. 3.We hope that incorporation of MIBGtherapy in the frontline treatment regimen at our centre in the near future will help improve outcomes in HighRisk NB.

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FEBRILE NEUTROPENIA IN PEDIATRIC ONCOLOGY: A REGIONAL QUALITY IMPROVEMENT STUDY OF GUIDELINES FOR FEBRILE NEUTROPENIA UPTAKE AND TARGETED KNOWLEDGE TRANSLATION

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Background/Objectives: Data was collected to determine knowledge translation effectiveness related to the 2005 APPHON/ROHPPA (Atlantic Provinces Pediatric Hematology Oncology Network) Guidelines for Febrile Neutropenia. These guidelines were developed for the treatment of pediatric oncology patients with febrile neutropenia at healthcare centres in Atlantic Canada. The overall study aim focused on whether the APPHON/ ROHPPA Guidelines for Febrile Neutropenia and associated education improved the treatment of febrile neutropenia in pediatric oncology patients in Atlantic Canada.
Design/Methods: A retrospective chart audit was conducted in twenty-one regional health centres in Atlantic Canada, for the period January 2005 until January 2011. A focused audit of patient charts was conducted to determine health centres' adherence with the recommended Guidelines for Febrile Neutopenia and to assess if any quality improvement opportunities for targeted febrile neutropenia education at health centres in Atlantic Canada could be identified.
Results: In total, 429 cases met the definition of febrile neutropenia as per the indicators outlined in the 2005 APPHON/ROHPPA Guidelines for Febrile Neutopenia. results illustrated a statistically significant difference in "*time to blood culture drawn*" and "*time to administration of antibiotics*" based both on the health centre's (1) Levels of Care designation ($p < 0.001$) and on (2) the treating department or point of entry ($p < 0.001$). Centres and departments within centres who saw more pediatric oncology patients were more likely to follow the recommended times for Febrile Neutopenia treatment.
Conclusion: APPHON/ROHPPA will utilize the results to clarify, communicate, educate and advocate for compliance related to the recommended Guidelines for Febrile Neutopenia. Guidelines for febrile neutropenia at all sites will be clarified, since all require improvement. A re-audit is planned following a period devoted to this clarification and training.

P-627

PRESERVATION OF VARICELLA SEROLOGY TITERS IN PEDIATRIC ONCOLOGY PATIENTS FOLLOWING CHEMOTHERAPY

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Background/Objectives: For pediatric oncology patients, current practice includes administering Varicella-Zoster Immunoglobulin (VZIG) as post-exposure prophylaxis (PEP) against Varicella-Zoster Virus (VZV) and isolating patients for 8 to 21 days. Pediatric oncology patients immune to VZV prior to their cancer diagnosis represent a population likely to preserve immunity against the disease. For this population the need for VZIG and isolation is poorly validated and may be an undue health care cost and inconvenience to patients. Therefore, we assessed VZV serology post-chemotherapy as a marker for persistence of immunity while on chemotherapy.
Design/Methods: Approval from the research ethics board at Children's Hospital of Eastern Ontario (CHEO) was obtained prior to this study. Varicella antibody titers were collected from 500 pediatric oncology patients treated at CHEO. Patients included in this study had positive titers at the time of their malignancy diagnosis and antibody testing at 6-months or 1-year post-chemotherapy treatment.
Results: One hundred and eighty two patients had both positive VZV antibody titers at diagnosis and repeat testing performed post-treatment. Post-treatment,160 (87.9%), 16 (8.8%), and 6 (3.3%) had positive, negative and equivocal VZV antibody titers, respectively. Moreover, 19 (10.4%) had chickenpox and 11(6.0%) developed shingles during chemotherapy or post-treatment but before re-testing for VZV antibody titers. There was no correlation between age or tumour type with preservation of VZV antibody titers.
Conclusion: The majority of pediatric oncology patients with prior VZV antibody titers preserve their VZV immunity post chemotherapy. Consequently, for this population, VZIG PEP and isolation if hospitalized may not be necessary. In Japan and the United Kingdom, acyclovir is used as a cost-effective alternative. For patients VZV seropositive prior to malignancy, further studies to determine the risk factors predisposing these patients to breakthrough disease may identify a subgroup of patients for whom VZIG PEP and isolation in hospital is necessary.

P-628

EDUCATION PROGRAM IN PEDIATRIC PALLIATIVE CARE NURSING: CULTURALLY RELEVANT WITH METHODOLOGY TRAINING THE TRAINER

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Background/Objectives: One of the programs associated with the care of Pediatric Oncology patients are Palliative Care Programs. In many Latin American countries are starting to be formed, lacking some places about programs related to this field of medicine. In most of them there are policies that, sometimes, drive the few existing programs.Latin America is composed of countries that share language, cultural traits and deficiencies in the health system, that make us different as a region and with other nations. Tested in other countries Palliative Care Programs may be partially successful as it requires taking into account the multi-ethnic culture and the various characteristics of each place spiritual expressions.
Design/Methods: In 2013, the program Training in Pediatric Palliative Care Nurses starts (one local nurse). In 2014, the training of nurses in Central America and Caribbean starts for two months rotation in Guatemala. The objective of the program is to achieve qualities as early immersion Palliative Care of an oncological disease although patients are curable (symptom management and emotional support of the patient during the trajectory of the disease), cultural approach to patients in palliative care, understand spiritual variables. It is characterized by professional trainers, and be direct observers of training nurses for two consecutive months, plus a draft for their countries. Methodology: training the trainers. The project will have a multiplier effect in other countries. Be trained to train.
Results: 7 nurses trained. Different countries: Honduras, Haiti, Panama, Dominican Republic, Nicaragua and Guatemala.
Conclusion: Trained nurses are advocates the implementation of palliative care in their hospitals, promote the dissemination of culturally appropriate palliative care in countries that do not yet have care programs for it.

P-629

TOTAL PARENTERAL NUTRITION IN CHILDREN WITH CANCER

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Background/Objectives: The incidence of malnutrition in children with cancer varies between 8% and 60%, depending on the diagnosis and the extent of the disease as well as the type of antineoplastic therapy. Malnutrition is associated with lower tolerance and delay of chemotherapy, more frequent and severe side effects, and compromised immune function. The aim of this study was to show our experience with total parenteral nutrition (TPN) in children with cancer, and point out the importance of nutritional support in pediatric oncology.
Design/Methods: Twenty four children who received TPN during the treatment of cancer at the Children's Hospital Rijeka were included in the study. Indications for starting nutritional support were as follows: body weight below the 10th percentile for age and/or body mass index below the 5th percentile for age at the diagnosis; body weight loss greater than 5% prior to diagnosis or during the treatment; children who refuse or are unable (mucositis, diarrhea) to take food.
Results: The average length of TPN was 19 days (range 6-59 days). Seventy six percent of children had weight gain (median 7.4%; range 1-25%). In 7 (29%) patients mild hepatotoxicity was observed, which did not require discontinuation of chemotherapy. In three adolescents with concomitant steroid therapy, glucose intolerance and need for insulin therapy was observed. Other side effects did not occur.
Conclusion: Our results confirm that TPN is an effective method of establishing protein-energy balance in pediatric patients with cancer. Weight gain was satisfactory, and complications rare and transitory.

P-630

15-YEAR EXPERIENCE OF IMPLANTABLE VENOUS PORT USAGE AT CHILDREN AND ADOLESCENCE: EXPERIENCE OF 4 RUSSIAN INSTITUTES

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Background/Objectives: Intravenous injection is an integral part of the treatment of cancer and many congenital diseases: mucopolysaccharidosis, cystic fibrosis, glycogenosis. Implantable venous ports are the best long-term access to the venous system.
Design/Methods: 3256 patients (3 months. - 17 years) underwent implantation of venous ports: since 1998 2921 patients in the Institute of Clinical Oncology, since 2008 278 patients in the Institute of Pediatric Oncology and Hematology, since 2011 52 patients in Children's Clinical Hospital, since 2012 5 patients in Scientific Centre of Children Health. To access the superior vena cava in 3127 (96%) an internal jugular was punctured, in 129 (4%) a subclavian vena was used. An ultrasound marking of veins came before the puncturing. Using intraoperative fluoroscopic for positioning of distal end of the catheter to the superior vena cava the ports were implanted in 2987 (91.7%) patients, in 269 (8.3) for this purpose an endocardial ECG was made.
Results: Thromboses of port systems was observed in 75 (2.3%) patients, catheter associated bloodstream infections - in 5 (0.15%), pneumothorax - in 5 (0.15%). Migration of a catheter wire to the internal jugular against bloodstream was observed in 138 (4.3%) to the subclavian vein in 92 (2.8%) to the internal jugular vena on the opposite side - in 11 (0.3%). From the first attempt we managed to puncture IJV in 3248 (99.7%), to catheterize in 2915 (89.5%).
Conclusion: The use of ultrasonic marking permits the avoidance of injury to the adjacent anatomical structures and the reduction of the duration of the surgery. The use of an X-ray scanner during the positioning of the port catheter prevents its migration into the cervical veins and enables to place a tip of the catheter into the v. cava superior directly above a right atrium entry site.

P-631

THE ROLE OF VENOUS ACCESS IN PEDIATRIC ONCOLOGY

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Background/Objectives: The treatment of tumors is impossible without a venous access. What kind of properties should it possess? It has to be safe, easy to use, implanted only once during the treatment course and have minimal risks associated with implantation and use. Our aim was to prevent complications of intravenous chemotherapeutic agent administration.
Design/Methods: From 2010 to 2014 we were monitoring the treatment of 228 children (aged 3 months to 17 years) with different tumors. 110 patients underwent 605 subclavian vein catheterization, 118 patients – 118 venous port implantation.
Results: Complications and technical difficulties during catheter insertion were observed in 98.3% of cases, during venous port implantation – in 23% of cases. Complications of subclavian catheter and venous port use were observed in 97.3% and in only 11% of cases, respectively. Subclavian catheters compromised cancer treatment in 45.9% of patients, implantable venous ports – in 1.7% of patients. Each patient with

a subclavian catheter underwent central venous catheterization 4 to 19 times (mean 6 times) during treatment. Catheter dwell time exceeded the recommended limit in all patients except for cases of catheter removal by patients. On multiple occasions all patients were discharged with a subclavian catheter in place.
Conclusion: Venous ports obviously match the criteria mentioned in the introduction. Subclavian catheter use resulted in cancer treatment protocol deviation in almost 50% of cases, thus leading to a poorer prognosis and significantly increasing the number of invasive procedures and instances where general anesthesia was needed.

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STENOTROPHOMONAS MALTOPHILIA INFECTIONS IN PEDIATRIC ONCOLOGY: EMERGING AND POTENTIALLY LIFE THREATENING

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Background/Objectives: *Stenotrophomonas maltophilia* is an emerging multidrug resistant gram-negative bacillus that is ubiquitous in nature. It is of concern in immunocompromised hosts as it is potentially life threatening. We analyzed the clinical characteristics, risk factors and outcomes of pediatric oncology patients with *S. maltophilia* infection at our center.
Design/Methods: Microbiological data of pediatric oncology and BMT patients between 2010-2014 were retrospectively analyzed. Hospital records were analyzed for treatment received and outcome.
Results: *S.maltophilia* was isolated in blood culture of 5 patients. During the study period, out of around 1000 febrile neutropenia episodes, 106 patients had a positive blood culture. Age of patients ranged from 1 to 11 years. Underlying diagnosis was ALL (1), Acute Promyelocytic Leukemia (1), Burkitt lymphoma (1), Aplastic anemia (1), Thalassemia major post cord blood transplant (1). 3/5 had respiratory symptoms, 2/5 had grade 3-4 mucositis and one had chest wall abscess. Pus culture and endotracheal secretions were positive in 2 cases. All had indwelling central venous access device at this time of infection, which was subsequently removed in three. 4/5 patients were neutropenic at the onset of infection. Duration of neutropenia lasted for >3 weeks in 4 patients. All patients received broad-spectrum antibiotics and 2 received steroids prior to illness. Fall in WBC count was noticed in all 5 patients after the onset of infection. The organism was sensitive to Levofloxacin (5/5), Cotrimoxazole (4/5) and Ceftazidime (1/5). All were treated with Cotrimoxazole and 3 received Levofloxacin. Two patients succumbed to the illness. Both patients did not have recovery of neutrophil count till death. In the rest, neutropenia recovered with improvement of sepsis.
Conclusion: Although ubiquitous and less virulent, *S.maltophilia* can cause severe sepsis and death in an immunocompromised host. Removal of indwelling catheter, prompt initiation of appropriate antibiotics and recovery of neutropenia helped in survival.

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BONE MARROW EXAMINATION IN YIELDING CAUSE OF FEVER OF UNKNOWN ORIGIN: EXPERIENCE FROM A TERTIARY CARE HOSPITAL

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Background/Objectives: Bone marrow (BM) examination remains a crucial test in diagnostic approach for fever of unknown origin (PUO). Bone marrow aspiration (BMA), biopsy, culture and other PCR based tests frequently prove helpful in reaching to a diagnosis. We report data of 58 pediatric patients.
Design/Methods: A retrospective analysis of PUO patients admitted at our center during January 2010 to March 2015 who underwent BM examination was done. All patients underwent BMA, biopsy and microbiological tests viz. culture & sensitivity and tests for isolation of mycobacteria viz. gene probe, AFB culture & sensitivity were also sent depending on presenting complains of patient. The demographic and laboratory profile were obtained from hospital records.
Results: During study period, 58 patients were admitted for PUO at our center. Out of 58 patients, 17 patients showed presence of blasts on peripheral smear examination (29%) and thus, were not further analyzed. BM examination revealed diagnosis in 24/41 patients (58%); Hematological malignancy: 12 patients (29%), Hemophagocytic lymphohistiocytosis or MAS: 7 patients (17%), 1 patient: Hodgkin lymphoma (2%), 1 patient (2%): encapsulated fungal spores on biopsy (Cryptococcus) and 1 patient: gene probe for tuberculosis positivity (2%). Two patients showed prominent eosinophilia on BMA and biopsy. None of the 8 patients for whom BM cultures were sent showed growth. Overall, the diagnostic yield of BM examination was 58%. Among the tests for BM examination, the yield of pathological examination was 91%.
Conclusion: BMA, biopsy and microbiological tests are useful for the diagnosis of prolonged fever of unknown etiology in children. In resource constrained set up like ours where extensive work up of PUO is expensive and at times unavailable, BM examination is a relatively cost and time effective modality to help reach a diagnosis in children with PUO. BM culture and other microbiological tests are of less diagnostic significance.

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DIARRHOEA IN CHILDREN UNDERGOING TREATMENT FOR MALIGNANT HAEMATOLOGICAL, ONCOLOGICAL CONDITIONS AND BONE MARROW TRANSPLANTATION (BMT) IN A SCOTTISH CHILDREN'S CANCER UNIT

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Background/Objectives: Diarrohea is a common, potentially serious complication in children undergoing treatment for childhood malignant conditions. Screening of stool is expected to help in management and source isolation of children to prevent spread to others.
Design/Methods: This was a retrospective audit of diarrhoeal episodes over a period of three months from August 2014 and October 2014. All children undergoing treatment for a malignant condition or BMT in a Scottish tertiary treatment centre who had a stool screening during the study period were included. We identified that multiple stool samples were sent for each episode. Being symptom free for 48 hours was considered as remission of an episode. We excluded asymptomatic neutropenic patients as routine samples were sent weekly for this group. Data was obtained from electronic records and case notes. Information collected included diagnosis, symptoms, stool culture & virology results, treatment and outcome.
Results: We identified 35 patients with 63 episodes. Majority of our patients had a haematological malignant condition. Episodes per patient ranged from 1 to 4 with a mean of 1.8. Stool culture was positive in 24 out of 63 episodes with viral PCR being positive in two cases. 13 episodes had vancomycin resistant enterococci and 5 had extended spectrum beta lactamase producing organisms. In 14 episodes there was persistent colonisation. Following the stool culture results, in 9 episodes the antibiotic were changed. In 23 episodes patients were stem cell transplant recipients. These patients had prolonged symptoms and persistent colonisation. Early isolation of children with positive microbiological screen, prevented spread to other patients on the ward.
Conclusion: Diarrhoea is a common side effect of chemotherapy, radiation therapy and bone marrow transplantation. Stool screening was found useful in immunocompromised patients to identify organisms, modify treatment and to isolate patients to prevent spread to others.

P-635

EFFECT OF NUTRITIONAL STATUS AT DIAGNOSES OF PATIENTS WITH NEPHROBASTOMA AT A SINGLE INSTITUTION IN A DEVELOPING COUNTRY OVER TWO 5 YEAR TIME PERIODS

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Background/Objectives: To compare the nutritional status at diagnosis and outcome of patients with nephroblastoma with different stages and nutritional interventions in two time periods.
Design/Methods: An audit was performed on the records of patients with nephroblastoma treated at a single institution from January 2005 until December 2014. The period was divided to compare outcome: group one (2005 until 2009) and Group 2 (2010 until 2014). The initial stage and final outcome were recorded. Anthropometric assessment included: weight, height, triceps skin fold (TSF) and mid upper arm circumference (MUAC). Severe malnutrition was defined as: below two standard deviations of the Z-score; TSF and MUAC under 5th percentile according to Frisancho tables. Nutritional intervention given as oral supplements, enteral (EN) and/or parenteral nutrition (PN).
Results: In the first period there were 50 patients with a mean age of 47 months and in the second were 48 patients with mean age of 49 months, The stages in the two periods were respectively : stage I (36% vs. 29.2%), stage II (10% vs. 20.8%); stage III (32% vs.31.2%); stage IV (12% vs.12.5%) and stage V (10% vs. 6.3%) and the nutritional support given was: oral supplements (62% vs. 29.2%); EN (34% vs, 56.3%) and PN (4% vs 14.5%).Stunting and underweight at diagnosis were more pronounced in first group when compared to the second: 40% vs. 16.7% and 22.9% vs. 10.4% respectively. The fat and muscle stores showed no difference according to WHO standards (33.3% vs. 34.3%), however, the Frisancho tables indicated increased malnutrition in second group (38.3 vs. 56.3%). The overall survival rate increased in second period (60% vs. 75%).
Conclusion: Patients with depleted fat-and muscle stores and high risk disease at diagnosis had a higher mortality. The superior outcome in the second group may be attributed to better equipped and funded facility and more intensive nutritional support.

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DISTORTION PRODUCT OTOACOUSTIC EMISSIONS (DPOAES) MAY SERVE AS PREDICTORS OF INTERNATIONAL SOCIETY OF PEDIATRIC ONCOLOGY (SIOP)-GRADED HEARING LOSS IN PEDIATRIC PATIENTS WITH BRAIN TUMORS

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Background/Objectives: Cisplatin is an effective chemotherapeutic agent which carries a significant risk of dose-dependent cochlear damage resulting in progressive high-frequency hearing loss (HL). Various clinical ototoxicity grading scales are used to detect HL and modify therapy. Distortion product otoacoustic emissions (DPOAEs) are used to evaluate the function of individual cochlear hair cells independent of patient participation, making it a reproducible assessment.
Design/Methods: A retrospective review of 8 pediatric brain tumor patients (6 medulloblastoma, 2 germ cell tumors) treated at our institution between 2007 and 2014 with radiation and cisplatin containing therapy was conducted. Audiograms and DPOAEs for each ear (n= 16) at baseline (pre-cisplatin administration), at mid-therapy, and near the end of therapy (375-400 mg/m^2 cumulative dose) were reviewed. Hearing loss in decibels was graded as per the International Society of Pediatric Oncology (SIOP) grading scale.
Results: At baseline, five (31%) ears had absent DPOAEs at 8 kHz and DPOAEs were present in all ears at 4 kHz. Grade 1 HL was noted in 1 ear. There was no correlation between absent DPOAEs and HL by pure tone audiometry at baseline (p=0.31). Near the end of therapy, 56% of ears were noted to have ≥ Grade 1 HL (6 grade 1, 1 grade 2, 2 grade 3) and DPOAEs were absent at 4 kHz and 8 kHz in 23% and 62% of ears. Absence of DPOAEs at 4 kHz correlated with a ≥ Grade 2 HL (p=0.004) and absence of DPOAEs at 8 kHz correlated with ≥ Grade 1 HL (p=0.005). Moreover, absence of DPOAEs at 8 kHz at baseline was predictive of ≥ grade 1 HL near the end of therapy (p=0.03).
Conclusion: By assessing individual cochlear hair cell function, DPOAEs can serve as a predictor of progression to clinically-graded HL with time. Larger studies are required to further define their clinical functionality.

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IMPROVING QUALITY OF SEXUAL LIFE IN CHILDREN WITH LYMPHOMA IN DEVELOPING COUNTRIES: DISCUSSING THE UNDISCUSSED!

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Background/Objectives: Sex and cancer are two words that do not seem to belong in the same sentence. Success in pediatric oncology requires attention to the psychosocial consequences and quality of life. It is incumbent upon oncologists to conceive of Lymphomas as more than just a disease that begins with diagnosis and ends when the treatment protocol ends instead, it initiates a life-long trajectory of survival having long-term implications for quality of life.
Design/Methods: Emotional needs are deeply frustrated in children, due to long hospitalization, separation from parents, friends, painful tests, anxiety and anguish, hours of loneliness without tenderness, this critical suspension from normal life and shift to emergency survival delays growth of autonomy and independence and further complicates e attainment of satisfying sexual identity and disrupts basic psychosexual maturity process. Adolescent sexuality is very complex, and even more when serious adverse event like cancer affects the individual well-being - sexual and non-sexual - in all its dimensions.
Results: Young survivors are significantly different in specific domains to healthy, they are less feminine in sexual identity have more restrictive and submissive images of sexuality, lower confidence with masturbation. They have less experience of intercourse. These effects can be better understood if put in perspectives with many changes and challenges young cancer survivors have to face and cope with in different emotional, affective, relational, cultural and existential domains. Cultural issues in our society, such as the myth that children are too young to be interested in sexuality and presumption that issues of survival overshadow sexuality, provide barriers to open communication about sexuality.
Conclusion: Sexual function and fertility should no longer be regarded by oncologists as frivolous or irrelevant issues, the very privileged relationship that oncologist have with their patients should permit them to assist children in their journey of lymphoma.

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SERUM LEVELS OF GALACTOMAMMAM, BETA GLUCAN AND UTILITY OF PCR FOR THE DIAGNOSIS OF INVASIVE FUNGUS INFECTION IN PEDIATRIC PATIENTS WITH CANCER

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Background/Objectives: Invasive fungal infections (IFIs) are being increasingly recognized in children with cancer, and delayed diagnosis can lead to death. Our objective was to detect early Invasive fungal infections in immunocompromised children with cancer using noninvasive tests including serum galactomannan(GM), serum 1,3 beta glucan and Conventional PCR for pan fungal infection as recent diagnostic method.
Design/Methods: we studied 50 febrile neutropenic cancer patient (54% with acute lymphoblastic leukemia , 18% with acute non lymphoblastic leukemia, 16% with lymphoma and 12% with neuroblastoma) treated at oncology unit in pediatric department, zagazig university between November 2012 and April 2014. They were 34 female and 16 male, their age range from 2.5 to 15 year, blood samples were collected, cultured for fungal infection and evaluated for noninvasive tests.
Results: :*Eleven patients (22%) proved to have IFI, as defined by the 2008* European Organization for Research and Treatment of Cancer/ Mycoses Study Group (EORTC/MSG) criteria for IFI. Blood culture were positive in 12 patients; (11 with candida and 1 *aspergillus*), the sensitivity, specificity, positive and negative predictive values for positive and negative results of GM in patients with proven and probable IFI were 75.9%, 85.7%, 58%, 88%; for 1,3 beta glucan they were 88.6%, 80.9%, 88.6%, 85%; and for PCR they were 93.1%, 76.1%, 84.3%, 88.8%, respectively.
Conclusion: Invasive fungal infection is relatively frequent among febrile neutropenic children with cancer. PCR is promising for early detection of fungal infection and superior to other noninvasive tests in early diagnosis of IFI.

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HEPATITIS B AND C VIRUSES AMONG EGYPTIAN CHILDREN WITH CANCER

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Background/Objectives: Hepatitis B and C virus infections are major public health problems in Egypt, both are hyperendemic. Egypt has the highest worldwide prevalence of Hepatitis C virus infection, with 9% countrywide rate; and up to 50% rates in certain rural areas. Children with cancer receiving repeated blood transfusions and chemotherapy are at high risk for these infections. The present work aimed to study the prevalence of hepatitis B and C viruses among children with cancer at the oncology department of Zagazig University in Egypt during the period February 2014 to February 2015.
Design/Methods: Sixty Five Egyptian children with cancer (mean age= 5.487+/-2.348) and 30 healthy children age and sex matched as a control group were screened for HBV and HCV. For all children, full clinical evaluation, Liver function tests, the number of transfusions, HBV and HCV serology using the enzyme-linked immunosorbent assay (ELISA) and polymerase chain reaction (PCR) were checked. In seropositive children, HBV-DNA and HCV-RNA were measured. The relationships with study parameters were statistically analyzed.
Results: HBV serology was negative in all patients and control group. HCV specific antibody (anti-HCV) was detected in 31 (47.7%) patients but none had in the control group. We find a statistical significant relation between socio-economic level, education level, residence, longer hospitalization, surgical procedures and frequency of blood transfusion and HCV infection.
Conclusion: In conclusion HBV infection is not common in Egyptian population and; this may denote the success of the national vaccination programme. On the other hand we observed an increased incidence of HCV infections among children with cancer. This can be a serious cause of failure of treatment, morbidity and mortality, and point to the importance of checking the anti-HCV status of the child at presentation, strict HCV screening of blood donors and usage of disposable equipment.

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ADVANCE CARE PLANNING FOR PEDIATRIC CANCER ; A LITERATURE REVIEW

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Background/Objectives: Advance care planning (ACP) is increasingly regarded as the standard in the care of patients with life-limiting illnesses. ACP use has been gradually increasing with Japanese adult cancer patients.ACP is necessary for children with cancer, but there is little research regarding pediatrics in the world, and nothing in Japanese that I could find. I conducted a review on empirical literature on ACP

pediatric cancer patients and families to assess current practices, effects, and perspectives of pediatric ACP (pACP) regarding cancer.
Design/Methods: I searched PubMed for empirical literature on pACP concerning cancer, published January 2000 through December 2014. Key words were "pediatric cancer", "advance care planning", and "advance directive".
Results: I examined 23 studies. Of those, only 6 were identified as pACP related to cancer. These 6 studies focused exclusively on teens or adolescents. Of the 6 studies, 3 included family, 2 included end of life care, 2 referred to a way of providing pACP, and 4 referred to effectiveness. Preliminary data suggests that pACP, with cancer patients and families, can successfully be implemented and is perceived as helpful. It may be emotionally relieving, facilitate communication, and help to improve decision-making.
Conclusion: I think ACP process is helpfull for children with cancer as well as for teens and adolescents. Research with children under 15 years of age is very difficult to find. In most cases for children, basic conversation is all that is done. Of course there is a difference in comprehension for children at different ages, and so we adjust our support accordingly. In order to adopt ACP for children, building a trusting relationship and starting from an early stage are needed. Therefore, I would like to conduct research within that younger age bracket and find ways to apply pACP effectively.

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STEP DOWN ORAL ANTIBIOTIC AS OUTPATIENT FOR LOW RISK FEBRILE NEUTROPENIA : AUDIT OF A SINGLE INSTITUTION PROTOCOL

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Background/Objectives: While febrile neutropenia(F/N) is a potentially serious event in pediatric oncology, prolonged admission for IV antibiotics represents a significant burden for the family and the health care system. Recent efforts have been directed toward identifying patients at lower risk of complication who can safely be managed as outpatient. We describe our preliminary experience of using a consensus-based low risk F/N definition for outpatient management using our Hospital at Home program(H@H).
Design/Methods: Patients, fulfilling medical, social and geographic low risk F/N criteria were started on IV piperacillin-tazobactam, and discharged within 24 hr on oral antibiotics(levofloxacin or ciprofloxacin/clavulin). Daily monitoring alternated between nursing phone call, outpatient physician evaluation and nursing home visit. CBC was performed every other day until ANC ≥ 100 and blood culture(BC) repeated if persistent fever. Antibiotics were stopped when apyrexia >24 hr, BC negative and ANC ≥100. Readmission criteria included intolerance or non adherence to treatment/monitoring, positive BC, clinical deterioration, fever > 5 days.
Results: From 2014-2015, 13 patients met the low risk F/N criteria, accounting for 22 episodes of F/N(10% of all F/N admission). Underlying diagnosis included Acute lymphoblastic leukemia(30%) and solid tumors(70%). The median duration of fever and neutropenia were respectively 2 days(range 1-4 days) and 4 days(range 1-7 days). No adverse event(death, bacteraemia, modification of antibiotics, readmission) was reported. For each F/N episode, the median number of H@H visit and outpatient clinic visit were respectively 1(range 1-2) and 1(range 1-2) compared to 5 days of inpatient admission with previous management.
Conclusion: Our preliminary experience of careful stepdown approach for low risk F/N patients was associates with no adverse event. The support of our H@H program allows for only one outpatient visit per F/N episode/patient. This strategy spared 4 days of inpatient admission. Larger numbers of patients need to be evaluated to confirm the safety of this approach.

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HEALTH-CARE PROVIDERS' PERSPECTIVES ON COMPLEMENTARY ALTERNATIVE MEDICINE IN CHILDHOOD CANCER IN INDONESIA

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Background/Objectives: The use of complementary and alternative medicine (CAM) is prevalent among pediatric cancer patients. However, few studies on health belief and perception on CAM among health care providers (HCP) have been studied. The aim of this study is to investigate perspectives on CAM of HCP involved in the care of children with cancer at Dr Sardjito Hospital in Yogyakarta, Indonesia.
Design/Methods: A cross-sectional study using a self-administered structured questionnaire was conducted in Dr Sardjito Hospital from January to December 2014. All HCPs: pediatric oncologist, pediatric resident, nurse, dietician, and psychologist who work in Pediatric word were invited to participate the study.
Results: One hundred and seventy two HCP (response rate was 80%) completed the questioner. Thirty six percent and 49%of HCP belief that CAM is helpful in childhood cancer treatment and a combination of chemotherapy and CAM is the best way to cure cancer.The most common CAM recommended by HCP was self-prayer (95%), support group (82%) and vitamin-nutritional supplement (56%). The main concern raised from HCP was lack of scientific evidence. Almost all (98%) of HCP agreed that parents should receive guidance about beneficial or harmful effects of CAM, however most of them (74%) stated that their knowledge about the safety and efficacy of CAM is inadequate. Most HCP (80%) stated they discuss openly with parents the use of CAM, and 61% HCP stated that discussion was initiated by the family.
Conclusion: This study found that most HCP accept common practices of CAMs in Indonesia such as self-prayer, support group and vitamin-nutritional supplement. Despite of inadequate knowledge of the safety and efficacy of CAM, they agreed that parents should receive guidance about beneficial or harmful effects of CAM. CAM should be included in the curriculum of health professional education.

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ADOPTIVE CELLULAR THERAPY IN PERSISTENT ADENOVIRAEMIA

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Background/Objectives: Adenoviraemia (AdV) is a significant complication of haematopoietic stem cell transplant (HSCT). Antivirals control viraemia but T-cell reconstitution is often required for viral clearance.
Design/Methods: We describe a patient with high level AdV post-transplant who failed antivirals but responded to administration of expanded adenovirus-specific T-cells (ADVT). A 12 year old boy in CR3 following extramedullary relapse of precursor-B cell acute lymphoblastic leukaemia underwent a 9/10 A-antigenic mismatched sibling donor HSCT (3.55×10^6/kg CD34) following Cyclophosphamide/ Total Body Irradiation/ Alemtuzumab/ CNS boost conditioning. His transplant was complicated by poor graft function with lymphopenia of $<0.1 \times 10^9$/L. He developed AdV from D+33 with progressively worsening adenoviral levels (460 to 480,000 copies/ml) despite antivirals (ribavirin and cidofovir) and stopping Ciclosporin by D+68. He remained symptomatic with fever, nausea, diarrhoea and significant weight loss (>10%). Chimerism was 100% donor in whole blood but with no signal in T-cells.
Results: 100ml of whole blood was collected from his donor after written informed consent. Product was transported to the Centre for Cell, Gene and Tissue Therapeutics, Royal Free Hospital, London. A one-touch rapid expansion process by exposing T cells to overlapping peptides covering the entire adenoviral hexon V protein and a 10-day expansion in the presence of cytokines without further intervention until ADVT were harvested and cryopreserved. 10^4/kg ADVT with 95% purity was administered on D+117. Patient became afebrile, tolerated oral feeds with AdV of 95 copies/ml by D+135 allowing cessation of Cidofovir. Lymphopenia improved to $>0.8 \times 10^9$/L; graft function improved with 100% donor T-cell chimerism and no evidence of graft versus host disease.
Conclusion: Adoptive anti-adenoviral cellular therapy has proven to be safe and effective in this patient.

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THE USE OF COMPLEMENTARY AND ALTERNATIVE MEDICINE AMONG CHILDREN WITH CANCER IN INDONESIA

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Background/Objectives: The rate to use complementary and alternative medicine (CAM) among children with cancer become increasingly. Little is known about the use of CAM in Indonesia like another developed countries. The aim of the study was to investigate the type, frequency, reason, component and expectations on use of CAM.
Design/Methods: A cross-sectional design was conducted using a semi-structured questionnaire developed by the researchers. Parents of childhood cancer patients who were requested to participate in the study between September 2013 to October 2014 in Sardjito as one of tertiary hospital in Indonesia.
Results: One hundred and seventy-six of parents obtained in this study (respond rate = 85 %), women (73 %) more higher than men (27 %). Commonly use of type of CAM before and during childhood cancer treatment were praying (91 %), vitamin-supplement (48 %), and acupuncture (30 %). Some CAM become decreased during treatment, such as acupuncture(30 % to 1 %), massage (29 % to 9 %), old-smart people (29 % to 14 %).The most reasons using CAM were hope for improvement of child's condition (74 %) and hope for cure (70 %). Only 20 % doctor had ever asked

parents to use of CAM. More half parent`s expectation include listen if they interested to use of CAM (75 %), ask them whether interested to CAM (61 %), and doctor have update information about CAM (60 %).
Conclusion: CAM is frequently used by parents of childhood cancer patient and the most commonly CAM include praying, vitamin-supplement, and acupuncture. Health-care provider should consider about parent`s perspectives toward CAM use.

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IMPROVING PEDIATRIC ONCOLOGY SERVICES IN A UNIVERSITY HOSPITAL IN NORTH INDIA

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[1] Postgraduate Institute of Medical Education & Research, Pediatrics, Chandigarh, India; [2] Jiv Daya Foundation, Medical Oncology, Dallas-Texas, USA Background/Objectives: Treatment of childhood cancer in developing countries is fraught with challenges. The major challenges are accessibility to medical services and affordability. Consequently the incidence of refusal and default of therapy is high. How do we improve?

Design/Methods: Three full time trainee fellows were added to the 3 consultants and 1 registrar running the unit towards end of 2009. In addition, a full time social worker was assigned to counsel and assist patients in applying from governmental agencies for financial support. Unit data was analyzed to evaluate improvement in patient care.
Results: We registered 3568 children with cancer from January 2004 – June 2014. Refusal of Therapy: Twenty six percent patients refused therapy. Refusal was 29% till 2010 and 24% after 2010. Maximal refusal was seen in patients with Acute Myeloid Leukemia and Neuroblastoma (NBL) (50 & 40%). Refusal in Acute Lymphoblastic Leukemia (ALL) and Non-Hodgkin Lymphoma (NHL) decreased from 34% to 23%. Wilms Tumour (WT), Germ Cell Tumour (GCT), Hodgkin Lymphoma have a refusal rate of around 10%.Default of therapy: Twenty eight percent defaulted therapy before 2010; 17% defaulted after 2010 ($p<0.05$). Default diminished from 14 to 6.5 % in children with ALL, and from 25% to 11.5% in AML. Nearly 30% of solid tumors would lapse therapy, which decreased to 15-20%. Default in Retinoblastoma (RBL), NBL and rhabdomyosarcoma remains high, decreasing from 50-60% to 30%-40%. Most (80%) patients defaulted after 1-2 courses of chemotherapy. Three fourth of defaulters had advanced stage disease. Patients with RBL, sarcomas & WT abandoned therapy before surgery.
Conclusion: With the help of dedicated medical staff and social workers, we have significantly decreased attrition and increased the number of patients taking therapy. Developing a model for improving care requires enhancement of medical & ancillary staff services and developing shared care with peripheral pediatricians in resource-crunched countries.

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FERTILITY PRESERVATION IN PREPUBERTAL BOYS DIAGNOSED WITH CANCER

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Background/Objectives: There is a high risk of infertility after successful childhood cancer treatment. In prepubertal boys fertility preservation might be possible by freezing a testicular biopsy before chemotherapy. Thanks to still ongoing research spermatogonial stem cells (SSCs) can be isolated from the cryopreserved tissue, propagated and autotransplanted in the adult patient to facilitate natural conception.Although basic research is still needed the interval between biopsy and autotransplantation legitimates starting cryopreservation in a research setting now with approval of the Dutch Central Ethical Commission.
Design/Methods: Every prepubertal boy presenting to our children's oncology department because of a malignancy requiring chemotherapy with increased risk of infertility will be considered for fertility preservation. Under general anesthesia a unilateral testicular biopsy is taken using microsurgical technique .This is linked to central line placement for chemotherapy, so that no separate anaesthesia is necessary. Follow up of these patients includes postoperative examination for surgery related complications and ultrasonography of the testis at predetermined time intervals. At 1 , 6 and 12 months post-surgery the testes were evaluated for abnormalities in testis parenchyma and testicular perfusion.
Results: From 18-03-2011 until 01-01-2015 the parents of 74 boys were asked to participate, of which 24 declined. After signing informed consent in 50 of them a testicular biopsy was performed without any complications. Spermatogonia were preserved in all patients but one, in which no spermatogonia were found in the biopsy.35 patients have been evaluated 1 year after surgery. 3 patients had minor disturbances in testis parenchyma. All other 32 patients had normal testis parenchyma with normal perfusion.
Conclusion: Fertility preservation by performing testicular biopsies prior to chemotherapy in prepubertal boys with cancer is a safe procedure and should therefore be routinely offered.

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CHILD BURDEN OF PARTICIPATION IN A CLINICAL TRIAL DURING THE PALLIATIVE PHASE

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Background/Objectives: To test the value of novel, promising anti-cancer medication, clinical trials in children are essential. Parents' perspectives regarding clinical trial participation of their child with incurable cancer, specifically the child's burden, is an important topic that warrants more attention. The aim of this study is to explore parents' perspectives of participation of their child with incurable cancer in a clinical trial.
Design/Methods: A retrospective questionnaire was send to parents who lost a child to cancer. Parents were requested whether their child with incurable cancer participated in a clinical trial during the palliative phase, their motives for participation, the child's perceived burden (5-point Likert scale), and whether they would enrol again. Median follow-up time was 5 years[3-8 years].
Results: Twenty-four/74 parents of 16/49 deceased children(33%) indicated that their child participated in a clinical trial during the palliative phase. Parents' reasoning for their child's participation was(more than one answers possible): treatment for future patients(n=16); followed by hope for a cure(n=9); prolonging their child's life(n=6) and other reasons(n=5). To the question about the child's burden of participation, 8 parents marked '1'(not burdensome) and 4 parents '5'(very burdensome). Remaining parents scored between '2' and '4'. None of the parents would decline participation if they would be in the same situation again.
Conclusion: Performing clinical trials, even in a vulnerable population as children with cancer at the end of life, may not always lead to increased burden. None of the parents would in future, given the same circumstances, decline participation in a clinical trial.

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PSYCHOSOCIAL OUTCOMES AMONG BEREAVED SIBLINGS OF CHILDREN WITH CANCER

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Background/Objectives: The number of studies exploring long-term adjustment of bereaved siblings are limited and lack conclusive evidence about the psychosocial adjustment of siblings after the death of a brother or sister with cancer. Gaining knowledge about long-term adjustment of siblings is important to be able to adequately meet the needs of siblings.
Design/Methods: Parents who lost a child to cancer between 2000 and 2004 were asked to retrospectively complete two statements about the well-being of siblings, which was embedded in a larger study exploring parents' perspectives on paediatric palliative care. Parents were asked to rate both statements on a five-point Likert scale, ranging from '1' (disagree) to '5' (agree).
Results: Sixty-eight parents completed both questions about siblings' well-being. In total, 29/68 parents (43%) (somewhat) agreed with the statement that their other children had experienced a lot of problems in the period before and after the death of their brother/sister. Interestingly, most parents mentioned that the siblings still experienced negative consequences as a result of the death of their brother/sister after a median follow-up time of 5 years (31/68 parents (46%)).
Conclusion: Negative consequences of the child's loss still occur in bereaved siblings, even many years later. Though we here report findings of a small evaluation and we did not use validated instruments to measure the siblings' well-being, findings are valuable in stressing the need to support siblings, which could improve future paediatric palliative care. Considering the impact of a siblings' loss, upcoming studies should focus on developing supportive intervention strategies for siblings, and exploring whether a potential effect of intervention strategies sustains over time.

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HOME-BASED PAEDIATRIC PALLIATIVE CARE FOR CHILDREN WITH INCURABLE CANCER: PERSPECTIVES AND IMPACT ON GENERAL PRACTITIONERS

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Background/Objectives: A substantial number of children with advanced cancer die at home, implicating that the direct burden of care is delegated to general health care professionals. So far, hardly any information is available on the quality of home-based paediatric palliative care, and the impact of providing palliative care for children on general practitioners (GPs) has never been established.
Design/Methods: Between 2001 and 2010, 150/264 (57%) children with cancer treated at our hospital died at home. GPs of these children were approached to retrospectively complete a questionnaire about their experiences with the quality of care, and the impact of providing paediatric palliative care in a home-based setting.
Results: 91/112 GPs (81%) returned 93 questionnaires. GPs recognized the child's fatigue (n=60, 65%) and pain (n=54, 58%) as the most prevalent symptoms. Difficulties with communication (14%), coordination (11%), collaboration (11%) and accessibility (2%) were uncommon. The moment the child has passed away, as well as the atmosphere around the child's death were positively experienced. Hectic (7%) and shocking (4%) situations were rare, even as panic (2%) around the child's death. During the terminal phase, GPs rated a median score on the distress thermometer of 6 [range 0-9.5]. Almost all GPs were able to come to terms with the child's death. Being a female GP ($p=0.05$), having observed the child's nausea ($p=0.04$) or dyspnoea ($p=0.04$), and a restless death ($p<0.01$) were associated with higher levels of distress in GPs during the terminal phase.
Conclusion: In general, GPs were satisfied with the quality of paediatric palliative care. The death of a child highly impacts GPs. The child's suffering and the atmosphere around the child's death partly account for the impact on GPs during the terminal phase.

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OUTBREAK OF INFLUENZA A/H1N1 IN AN OVERCROWDED PEDIATRIC ONCOLOGY WARD

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Background/Objectives: Outbreaks of Influenza A/H1N1 in pediatric oncology patients have been reported from many countries in the world, but the data from India and other South-east Asian countries is deficient. We carried out a prospective observational study in an overcrowded 30-bedded pediatric oncology ward in Northern India during the H1N1 epidemic from January 2015 – March 2015. The clinical characteristics and outcome of laboratory-proven H1N1 in children with cancer was studied.
Design/Methods: During the epidemic of H1N1 in India from January 2015 – March 2015, all the children in the pediatric cancer ward who had suspected influenza (respiratory symptoms with or without fever) were tested for H1N1 by polymerase chain reaction (PCR) in the nasopharyngeal swab. Clinical and laboratory data and outcomes were recorded for all the laboratory confirmed H1N1 cases. A repeat PCR was performed in all the cases to document viral clearance.
Results: We identified 75 episodes of suspected influenza in 65 children. Of all these episodes, 8 (10%) tested positive for H1N1 (3 ALL, 2 Neuroblastoma, 1 Wilms tumor, 1 Ewings sarcoma, 1 Germ cell tumor). The common clinical features recorded were fever (6/8), cough (6/8) and rhinorrhea (4/8). Three of these 8 H1N1 positive children required hospitalization due to severe symptoms. One child developed pneumomediastinum and subcutaneous emphysema and one developed severe upper airway obstruction. Systemic antibiotics were given to 4 children. There was a delay in planned chemotherapy in 2 children. Seven children improved on treatment, while one with upper airway obstruction died after 10 days. Two children had persistent H1N1 positivity on repeat testing and required oseltamavir for 14 days and 18 days respectively to clear the virus.
Conclusion: Influenza A/H1N1 results in increased hospitalization and antibiotic usage in immunocompromised childhood cancer patients. These children can also have unusual clinical manifestations and delayed viral clearance.

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DEVELOPMENT OF A ROLE-PLAYING WORKSHOP TO TEACH MEDICAL STUDENTS IN BOTSWANA HOW TO COMMUNICATE EFFECTIVELY AND DELIVER BAD NEWS

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Background/Objectives: Delivering bad news is a task that doctors encounter often, especially in low- and middle-income countries (LMIC) where morbidity and mortality are high. Existing reports show doctors lack confidence and skill in performing this task and most have never received formal training. This is the first report describing a workshop teaching communication skills to medical students in a LMIC on delivering bad news.
Design/Methods: We conducted 2-hour small group workshops to final year medical students at the University of Botswana rotating through their pediatric clinical rotation. The curriculum developed for this workshop included: overview of communication basics with pediatric patients and families, end of life, HIV disclosure, and introduction of the validated SPIKES protocol for delivering bad news. Education strategies included didactic lecture, role-playing case sessions, open forum discussion, and handouts. Pre- and post-training surveys were completed by participants using a 5-point Likert scale to determine 1) previous experience, 2) perception of skill and confidence to deliver bad news, and 3) overall workshop effectiveness.
Results: 33 medical students attended the workshop and 82% (27/33) completed the pre- and post-training survey. Medical students reported exposure to delivering bad news on average 22 times monthly with 63% having delivered bad news themselves. The preparedness to deliver bad news using a specific strategy increased from 29% to 100%, and self perceived skill and confidence increased from 18% to 85%. Feedback after the workshop demonstrated that 100% found the SPIKES approach helpful and plan to use it in clinical practice, found role-playing helpful, and requested more sessions.
Conclusion: This workshop was effective in increasing medical student skill and confidence in delivering bad news and has been successfully implemented into our ongoing curriculum. Standardized role-playing communication workshops integrated into medical school curriculum could be a low-cost, effective, and easily implemented strategy to improve doctors' communication skills in LMIC.

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DEVELOPMENT OF A PAEDIATRIC PALLIATIVE CARE OUTREACH SERVICE IN N.W.CAMEROON

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Background/Objectives: We have treated over 1,000 patients with Burkitt lymphoma (BL). Approximately 40% of children treated are in need of palliative care(PC). A survey in late 2012 showed that the majority of these children live beyond the range of the 4-wheel drive vehicles used by the existing hospital palliative care team. Our objective was to establish an effective outreach PC service to these children.
Design/Methods: A motorbike was purchased in 2012 and a male nurse with paediatric nursing experience was appointed. Our nurse is undertaking further training in paediatric palliative care. The outreach PC nurse spends over 50% of his time on the ward getting to know patients and their guardians: he is an integral part of the hospital team. The service has now extended to outreach from Mbingo Baptist Hospital.
Results: We abandoned the motorbike as a mode of transport in 2013 but the service continues using public transport and lifts with other outreach hospital teams. For each home visit the PC nurse completes a report of care given and details of sociological information (carers, traditional medicine). In 2013 a visiting paediatric oncologist (Dr Mona Tamannai) set out to assess quality of life issues for both children and guardians in an attempt to find out how the new service affected these. We now have 2 years' statistics covering home visits.
Conclusion: PC home visits have improved quality of life for children and their guardians. Increasing numbers of children with other cancers, mostly Wilms tumour and retinoblastoma, are now treated under established programmes at Mbingo Baptist Hospital. The need for PC home visits is ever greater.

Posters: Surgery (IPSO)

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HUGE CERVICO-THORACIC MALIGNANT NERVE SHEATH TUMOR (MPNST) IN A 10 YEAR GIRL - A RARE CLINICAL ENTITY

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Background/Objectives: Malignant peripheral nerve sheath tumors (MPNST) account for 5-10% of soft tissue sarcomas and are more common in patients of Neurofibromatosis type 1. Only 18 cases of intra thoracic MPNST have been reported so far and that too mostly in adults. Herein, we report an unusual case of a 10 years old girl with a huge dumbbell shaped intra-thoracic MPNST that proved to be a diagnostic and therapeutic challenge.
Design/Methods: Retrospective review of case records.
Results: A 10 year old girl presented to us with a progressively increasing left axillary and neck swelling for the last 9 months which was being treated with anti-tubercular medications. The child had developed weakness of the left upper limb with Erb's palsy and progressive dyspnea and cough for the last 3 months. Further evaluation suggested a large 15x 8 x7cm lobulated tumor in the left upper neck and thoracic region, encasing the major vessels in the neck and superior mediastinum. Biopsy proved it to be a MPNST. After 8 cycles of chemotherapy (Vincristine, Ifosfamide, Actinomycin D), the tumor was deemed to be resectable, radiologically extending from the angle of the base of the skull to the anterior mediastinum upto the pulmonary artery with intraspinal extension. The child underwent median sternotomy and removal of a large dumbbell shaped tumor measuring 18x 9cm (intra-thoracic component) and 5cmx8cm (neck component). The neurological deficits drastically improved after resection and proper physiotherapy of the left arm and hand. The patient was not given any post operative chemotherapy or radiotherapy. The child presented with multiple local recurrences after 4 months.
Conclusion: This is one of the largest reported intra-thoracic MPNST in children. The poor outcome and early recurrence despite chemotherapy and complete surgical resection highlights the need for the role of post-operative adjuvant chemotherapy and possibly radiotherapy.

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AMELOBLASTOMA - MANAGEMENT AND REVIEW OF LITERATURE

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Background/Objectives: The purpose of this report is 1] To report the experience of the department of Pediatric Surgery in the management of Ameloblastoma of the mandible in children treated 2] To do a systematic review of the literature of last 10 years regarding the outcome of treatment of ameloblastoma in children.
Design/Methods: For the first part of the study, a retrospective review from the case reports of the children treated in a single hospital in last 10 years from Jan 2005 till December 2014 was done. The second part of the study was systematic review of treatment of ameloblastoma in the developing and developed nations during the same period.
Results: Three children (1 boy, 2 girls) < 16 years age with ameloblastoma were treated. All 3 had unicystic lesions of the mandible, 2 on the left with loss of teeth at the siteof the lesion and one on the right side. As primary treatment, all 3 children underwent upfront enucleation. One child had remodeled bone graft filled after enulceation. One child developed recurrence after about 1 year for which mandibular resection and reconstruction was done. Literature review showed approximately 250 children and adolescents with ameloblastoma, solid variant predominating.
Conclusion: Ameloblastoma in children has to be evaluated for the type, the extent and the histology of the lesion which will dictate the treatment. While enucleation is a much simpler procedure, it must be borne in mind that recurrence rate is high and the child might require an extensive surgical reconstruction. Large series of long term results in unicystic ameloblastoma are yet awaited. Enucleation is done in many centers upfront, causing higher rate of recurrence variable from center to center ranging from 40% to 70%. Most have recommended bony excision and reconstruction with the disadvantage of disfigurement and complex surgical intervention.

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ANTERIOR APPROACH IN RETROPERITONEOSCOPIC REMOVAL OF A NEUROBLASTIC TUMOR IN INFANCY

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Background/Objectives: Minimally invasive surgery (MIS) is an accepted approach for neuroblastic tumors. The transperitoneal approach has been described in recent pediatric literature, while no report concerning the retroperitoneoscopic anterior approach in infants exists.
Design/Methods: We retrospectively reviewed the clinical records of a 5-month-old infant operated on for a neuroblastic tumor.
Results: A newborn was delivered at term by caesarean section due to gestational diabetes (birth weight 3080g). After two weeks she was readmitted with massive abdominal distension and hepatomegaly. Abdominal ultrasound revealed a hyperhecoic mass (49 × 34 mm) in left hypocondrium with multiple hepatic nodules, confirmed by CT-scan, suggestive for aggressive metastatic neuroblastoma. Low haemoglobin and platelet values, increased LDH, transaminases, NSE and pathologic urinary cathecolamines were found.Considering the high bioptic risk we immediately started chemotherapy (Carboplatin, Etoposide 1st cycle).Twenty days later open biopsy of the adrenal mass and bone marrow aspirate were performed, and the 2nd chemotherapy cycle was started. Based on histological/biological features the European Neuroblastoma High-risk Protocol was adopted for two cycles. The lesion size was reduced to 25 mm, so anterior approach retroperitoneoscopic adrenalectomy was performed with 3-port 5 mm. The retroperitoneal space was created with a 10 mmHg pressure. Adrenalectomy was performed and the mass was removed with an endobag. No complications occurred. The baby, two months after surgery, is doing well, completing the therapy protocol.
Conclusion: In carefully selected cases, MIS is a safe and effective method to resect neuroblastic tumors. Retroperitoneoscopy provides direct access to the adrenal gland and easy visualization of the adrenal vessels. Despite its limits, like significant small working spaces and reverse orientation of the kidney, it minimizes the risk of injury to other organs, especially liver and spleen, avoids colonic mobilization, and the risk of adhesions.

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LAPAROSCOPIC "PNEUMOVESICUM" IN THE DIAGNOSIS AND TREATMENT OF INTRAVESICAL TUMORS IN CHILDREN

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Background/Objectives: In children, the diagnosis and treatment of the intravesical tumors, sometimes are very difficult, mostly if they are perimeatal. The main criterion for choice of a "particular" procedure has been the success of this procedure in the hands of a "particular" surgeon. However, "open" surgery is not without its complications. We have evaluated our results with a new method, using laparoscopic pneumovesical approach in the diagnosis and treatment of intravesical tumors of their uncertain "behavior" in children.
Design/Methods: From December 2013 we performed a laparoscopic "pneumovesicum" in 3 male patients of 1, 7 and 14 years respectively. The procedure starts with cystoscopic examination of the bladder.After a short skin incision the first 5 mm diameter trocar is introduced suprapubically. The two laterals trocars (5 mm) are then introduced trough the anterolateral wall of the bladder under cystoscopic or vesicoscopic vision, depending on the surgeons' preference.
Results: In the first case a biopsy of the primary tumor was performed; in the last two cases it was possible the total removal of the papillomas that were "in close" connection with the urethral meatus. There are no intraoperaitive complications. Patients from our group had a mean hospital stay of 3 days.
Conclusion: The advent of minimally invasive surgery has changed the way of surgery is practiced even if there is no consensus about the choice of technique to approach perimeatal intravesical tumors in children. The laparoscopic pneumovesicum represents an alternative to other "open" techniques and the major advantages include less surgical trauma and faster operative recovery. A larger multicenter, prospective randomized study to evaluate this new approach in comparison with the conventional approach is warranted.

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MANAGEMENT OF GIANT HEPATIC HEMANGIOMA IN CHILDREN

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Background/Objectives: Hemangioma is the most common benign tumor of the liver in infancy and the prevalence ranged from 3-20% in autopsy series. Many of these lesions are discovered incidentally and are localized and small enough to be of no clinical significance. Even if, as with their cutaneous counterparts, hepatic hemangiomas exhibit

multiple patterns of presentation and differing biologic behaviors. The severity of these lesions varies widely, ranging from asymptomatic to life-threatening complications.
Design/Methods: The records of 3 infants and children of 3 days, 4 and 7 years old respectively, with giant hepatic hemangioma, between December 2011 to February 2015 were collected. The clinical data including sex, age, symptoms, the size, number, and location of the tumors, preoperative liver function test and complications were retroactively reviewed and follow up information was available for all the patients.
Results: All three patients underwent therapy with propranolol (2 mg/Kg/die). In the newborn, a repeat ultrasonography after 6 months, showed almost complete clearance of hepatic focal lesion. There were no adverse events of the therapy during the entire duration of treatment and the child now is off treatment for past two years and has no evidence of disease recurrence. In the patient of 4 years old, indications for surgical intervention, a left hepatic lobectomy, were abdominal pain and increased hemangioma size after two months. In the third patient we are waiting for the results after one month of therapy.
Conclusion: Many treatment options are available for hepatic hemangiomas. Close observation should be reserved for a symptomatic tumors, and surgical resection is offered for symptom relief of complicated hemangiomas or lesions in which the diagnosis is uncertain. In our experience, hepatic hemangioma associated with prenatal cardiac disorders, large volume and more than one enlarged hepatic vessel, have poorer outcome and require specific perinatal multidisciplinary management.

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BILATERAL WILMS' TUMOR (WT) IN A HORSE SHOE KIDNEY WITH WAGR SYNDROME: A RARE ASSOCIATION

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Background/Objectives: In pediatric surgical practice the diagnosis of either horse shoe kidney or bilateral WT is not uncommon, but their combination is extremely rare. We here in share a rare association of bilateral WT in a horse shoe kidney associated with WAGR syndrome (11p deletion syndrome) and its challenge in the course of management.
Design/Methods: The child presented at 5 months of age with hypospadias and right non-palpable undescended testis (UDT). He was also having aniridia with nystagmus and was diagnosed as WAGR syndrome complex and was on regular 6 monthly follow up. At one and half years of age he underwent laparoscopic Fowler's Stephen's I orchidopexy elsewhere. At 2 years he presented with abdominal fullness with pain during defecation and on evaluation was found to have bilateral WT in a horse shoe kidney.
Results: The child received 9 weeks of neoadjuvant chemotherpay (Vincristin+Dactinomycin+Doxorubicin) and then was subjected for surgery. Left nephroureterectomy (for tumor involving the entire left moiety) with partial nephrectomy on right side was performed. Post-operatively the child developed hypertension with renal insufficiency for which he has to put on hemodialysis. While on hemodialysis he was continued on chemotherapy with the plan of continuous ambulatory peritoneal dialysis(CAPD) once chemotherapy was over. The child was later admitted in emergency with loose stool and shock and succumbed to severe unresponsive shock.
Conclusion: A patient with WAGR syndrome carries the higher risk (45%) of developing WT and also the risk of end stage renal disease. This risk increases further when the tumor is bilateral. We recommend frequent follow up of in the first 6 years for early diagnosis, evaluation and surveillance of patients with WAGR syndrome.

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PULMONARY METASTASECTOMY IN PAEDIATRIC SOLID TUMOURS IS FEASIBLE, SAFE AND MAY IMPROVE LONG TERM SURVIVAL

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Background/Objectives: Pulmonary metastases may be identified either at primary diagnosis or relapse. We aimed to determine the feasibility, safety, any effect on treatment decisions and long term outcome of pulmonary metastasectomy.
Design/Methods: All patients who underwent pulmonary metastasectomy were identified from our institution's pathology database and case notes were retrospectively reviewed.
Results: Nineteen patients (12 males; median age 11 years 6 months (IQR: 4-16 years) with solid tumours underwent metastasectomy between 1993 and 2015. Ten patients underwent surgery at the end of first line therapy, 3 during treatment and 6 at relapse. Eleven had metastases identifiable on both CXR and CT and 8 on CT only. At least 37 metastatic nodules were removed from 26 hemi-thoraces (12 patients unilateral, 7 bilateral of which 2 thoracoscopic). No major post-operative complications were observed. In 14 patients excision was complete both pathologically and radiologically (one patient underwent initial thoracoscopy but required subsequent open resection to achieve this). Viable tumour was resected in 16 patients with the remaining 3 having non-viable/necrotic tumour excised; this determined the need for lung radiotherapy or changed chemotherapy in 9 patients. Nine patients, of whom 8 had complete resection, are alive with median follow-up of 24 months (IQR: 6months-6years). Of the 10 patients who died only 5 achieved complete resection of nodules radiologically.
Conclusion: Our experience supports the evidence that pulmonary metastasectomy in paediatric solid tumours is both feasible and safe. If complete excision can be achieved both radiologically and pathologically this aids ongoing management decisions and may contribute to an improved long term outcome. We therefore recommend that careful consideration should be given to surgical resection of pulmonary metastatic disease. The optimal surgical route is dependent on the number and location of metastatic nodules; thoracoscopic excision being reserved for pleural metastases whilst thoracotomy being employed for those within the lung parenchyma.

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EWING SARCOMA OF STERNUM - SURGICAL CHALLENGE IN A CHILD

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Background/Objectives: Achieving R0 resection in Ewing sarcoma (ES) of the chest wall is often challenging in children and reconstruction is even more exigent. We present a child with localized ES arising from the body of sternum; managed with neoadjuvant chemotherapy (NACT) followed by surgical resection and chest wall reconstruction.
Design/Methods: Retrospective case study.
Results: A 7-years-old boy presented with cough and chest pain for 2.5 months and respiratory distress for 25 days. Chest X-ray showed a right sided opacity. CT chest revealed 10 × 17 cms heterogenous anterior-mediastinal mass with necrotic areas, displacing and compressing the mediastinal structures. Image guided biopsy confirmed ES (CD-99 and FLI-1 positive on IHC). Metastatic workup was negative. Bone scan revealed focal abnormal uptake in the sternum suggesting the origin of ES. He was given NACT [Vincristine Doxorubicin and Cyclophosphamide alternating with Etoposide Ifosphamide every 3 weeks (VDC/IE)]. Re-evaluation after week 12 showed >60% reduction in tumor size (good PR). The tumor now measured 6.6 × 3.7 cms and was abutting the great vessels. Resection of the tumor with 5 cms of the sternal body and adjoining 3rd and 4th costal cartilages on either side was done. The sternal defect was reconstruction with prosthetic material "Biopore" after confirming negative margins on frozen section. Histopathology confirmed residual ES with 25% necrosis and wide free margins. He had excellent cosmesis with no paradoxical movements of the chest wall. He is currently on consolidation chemotherapy (week 24). Radiotherapy was deferred since local control had been achieved by surgery alone.
Conclusion: Multimodality treatment of localized ES of chest wall can facilitate R0 resection after cytoreduction. Newer prosthetic materials are promising for sternal reconstruction. However long term follow-up is essential to look for future chest wall deformities.

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UTERINE TUMOR RESEMBLING OVARIAN SEX CORD STROMAL TUMOR - AN UNUSUAL UTERINE TUMOR IN AN ADOLESCENT

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Background/Objectives: Uterine sarcomas are rare in adolescents and have a poor outcome. We present a young girl with a rare variant of uterine tumor which was managed conservatively.
Design/Methods: Retrospective case study.
Results: A 17-years-old girl presented with menorrhagia and dysmennorhoea for 6 months. Evaluation elsewhere showed sonographic evidence of 6.6 × 5.2 cms large fibroid in posterior wall of uterus bulging into endometrial cavity. She underwent laparoscopy at local hospital. However procedure was abandoned after biopsy since incision on the posterior wall of myometrium revealed myxoid material. Histopathology (HPE) showed mesenchymal tumor with extensive myxoid change, IHC was inconclusive. She presented to us one month later. HPE review showed probable smooth muscle tumor with low-to-intermediate aggressiveness. MRI pelvis confirmed the lesion and PET-CT demonstrated non-metastatic disease. After counselling for possible hysterectomy, she was re-explored. At surgery there was a well-defined yellowish lesion in the posterior wall of uterus which was easily enucleated. Frozen section revealed a spindle cell lesion. Giving the benefit of doubt to the young unmarried patient, hysterectomy was deferred; and retroperitoneal with para-aortic lymph node sampling was done. Final HPE showed neoplastic cells in sheets and cords infiltrating the myometrium without tumor necrosis. IHC was positive for CD99, WT1, ER, PR, CD56 and focally for CK and negative for calretinin, inhibin, SMA, caldesmon, SMMH, EMA, S100, HMB-45 & desmin. The features were suggestive of uterine tumor resembling ovarian sex cord stromal tumor (UTROSCT). The institutional tumor board decided to keep her on regular and close follow-up as UTROSCT is locally invasive but usually does not metastasize. She has been followed for 4 months with no recurrence on imaging.
Conclusion: UTROSCT is a rare tumor in adolescents which must be differentiated from uterine endometrial stromal sarcoma. Preservation of the uterus is possible due to the less aggressive behavior of this tumor.

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ROBOTIC ASSISTED RESECTION OF LEFT ADRENAL GANGLIONEUROMA IN A CHILD

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Background/Objectives: The use minimally-invasive-surgery (MIS) for therapeutic resection of solid tumors in children is limited in resource challenged nations. Ours is one of the few institutes in the country where robotic assisted pediatric onco-surgeries are performed. We report a child who underwent successful robotic excision of left adrenal ganglioneuroma. Short video of the procedure is also presented.
Design/Methods: Retrospective case study.
Results: Eleven-years-old boy presented with an incidentally diagnosed left adrenal mass. He was evaluated elsewhere for chest pain and cough of 1-month duration. Imaging revealed a well-defined heterogeneous left adrenal mass measuring 5.5×4.2×6 cms without vascular invasion or calcification. His blood pressure and urinary catecholamines were normal. CT-guided fine needle aspiration cytology (FNAC) showed lipoma. Repeat endoscopic ultrasound (EUS) guided FNAC was suggestive of a tumor of neural crest origin- ? neuroblastoma ? phaeochromocytoma. Metastatic workup was negative. Since there were no image defined risk factors he was taken up for upfront robotic surgery. Four-ports access with 12mm para-umbilical camera port and three 5mm working ports, were used for the child in semi-lateral position. After docking, the robotic arms of the da Vinci Si Surgical System assisted in resecting the tumor. The adrenal mass was well encapsulated and could be easily separated from the upper pole of kidney, pancreas and spleen. The adrenal vessels were clipped while preserving the renal and splenic vessels. The specimen was removed through an extended para-umbilical incision using an endo-bag. The operative time was 50 minutes and blood loss was minimal. The child recovered smoothly and was discharged after 24 hours. Histopathology confirmed mature ganglioneuroma. He has been followed up for 3 months with no problems.
Conclusion: Robotic resection of pediatric tumors is a feasible option in selected cases. The advantages of advanced three-dimensional high-definition magnified visualization; and supra-human dexterity and range of motion of Endo-Wrist instruments cannot be overemphasized.

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MUSCULO-SCELETAL TUMORS DEPARTMENT OF THE INSTITUTE OF PEDIATRIC ONCOLOGY AND HEMATOLOGY: ANALYSIS OF THE WORK IN 2011 - 2013

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Background/Objectives: Bone and soft tissue tumors are one of the most common cancer in children.
Design/Methods: In 2011 – 2013 in the department of tumors of the musculoskeletal system, which has 25 beds, 549 patients were treated at the age of 6 months up to 17 years.
Results: On each bed during the analyzed period were treated 22 people. It was carried out in 1833 hospitalizations, the average time of hospital stay was 18 bed-days. Was performed 408 surgeries, including 132 (32.3%) – arthroplasty replacements and 1 – bladebone arthroplasty. Patients with different localizations osteosarcomas - 246 (44.9%), Ewing's sarcoma family of tumors - 138 (25.1%), soft tissue tumors - 100 (18.2%) melanoma - 7 (1.3%), other tumor - 58 (10.5%).
Conclusion: Patients with osteosarcomas of different locations were dominated. Prolonged hospital stay was due to a course of chemotherapy with high-dose methotrexate. Carrying out of the chemotherapy for patients in the one day clinic can increase the activity of surgical departments and the total number of patients.

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IS GLUTEAL REGION A FAVOURED SITE FOR AGGRESSIVE INFANTILE FIBROMATOSIS?

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Background/Objectives: Infantile aggressive fibromatosis, also known as desmoid type fibromatosis, is a rare tumor of musculoaponeurotic tissue. Though benign, it is a locally aggressive tumor with a high recurrence rate. Head and neck are the most common site affected followed by shoulder, upper arm, chest wall and paraspinal muscles. Gluteal involvement though reported in large series is not a favored site. We present a series of three patients in last four years, all of them had gluteal fibromatosis. Objectives: 1) To report the increasing incidence of aggressive infantile fibromatosis in the gluteal region. 2) Gluteal site associated with high recurrence rate.
Design/Methods: Retrospective analysis of case records of patients with fibromatosis was done. Last 4 years (July 2010 to June 2014) data was collected. All of these patients had tumor in the gluteal region two on the right and one on the left side. Size of the tumor ranged from 8-12 cm at initial presentation. Preoperative biopsy was done in all the cases, and it reported fibromatosis. Excision of tumor was done with one-centimeter rim of normal looking tissue.
Results: There were 3 patients, all boys of 1, 2 and 9 years of age. All the patients had recurrence within one year of excision. One of them was lost to follow up. In other two, one had re-excision of the tumor with postoperative radiotherapy and other had a gross tumor with pelvic extension. The later patient is on chemotherapy for tumor size reduction.
Conclusion: Gluteal region is the favored site for aggressive fibromatosis in children with a very high recurrence rate. In children wherein fibromatoses occurs in this region, the prognostication must be done as per the above observations.

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SURGERY OF NEPHROBLASTOMA EXPERIENCE OF THE DEPARTMENT OF PEDIATRIC SURGERY IN SETIF, ALGERIA

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Background/Objectives: To present the results of our experience in the surgery of nephroblastoma and to analyze peroperative complications.
Design/Methods: A total of 47 children were referred to our departement of pediatric surgery for surgical managment of wilm's tumor between January 2000 and December 2011. All patients underwent total or subtotal ureteronephrectomy.
Results: Twenty girls and 27 boys with a mean age of 38 months were treated surgically in our center. Nephroblastoma was in the right side in 24 cases and in the left side in 23 cases. Twenty five patients have had chimiotherapie wich decreases the tumor volume in 19 patients before surgery. The tumor resection was easier in the left side than in the right side. Because of the huge tumor volume and to avoid tumor rupture in many cases, we were not able to do an initial vessel aproach.
Conclusion: Surgery of nephroblastoma is a big challenge for pediatric surgeons. Perspective 3D virtual tumorectomy will be part of the check list in the management of wilm's tumor.

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NEONATAL SACROCOCCYGEAL TERATOMA- EARLY COMPLICATION AND LONG TERM OUTCOME

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Background/Objectives: To evaluates the presentation, early and long term outcome of neonatal sacrococcygeal teratoma.
Design/Methods: Retrospective analysis of consecutive cases of neonatal sacrococcygeal teratoma presenting at VMMC and Safdarjang Hospital, New Delhi from2003 through 2013 was carried out. The age at presentation, significant pelvic extension (Palpable per abdomen), treatment, histology, early complication, recurrence and long term outcome were reviewed.
Results: Eighteen patients (14female, 4 male) were identified. Median age of presentation was 3 days (range1-30 days). All presented with external mass. Significant pelvic extension was found in two (11%). Posterior sacral approach in fifteen (83%), and combined abdominal and sacral approach in three (17%), were used for excision. Histologically sixteen (89%) were mature teratoma (MT), and two immature teratoma (IMT). All underwent complete excision. Three (17%) developed wound infection (two managed conservatively, one required diverting colostomy). Two (11%) had early urinary dribbling and two (11%) had early fecal incontinence (resolved subsequently). Recurrence (in pelvis and gluteal) developed in two (11%) [1 MT and 1 IMT at initial diagnosis].Histology of recurrences were one [Yolk sac tumor (YST) (normal AFP, histology YST, Given PEB-chemotherapy)] and one IMT (Complete excision). Mean follow-up was 60 months (range 20-122 months). In the long term, one (6%) had persistent urinary dribbling, none had fecal incontinence. one patient died after colostomy closure at 4 month of age.
Conclusion: Neonatal sacrococcygeal teratoma presented with External mass. Overall survival (94.4%) is good with a recurrence rate of 11%. Early complication (22%) and Long term sequelae (6%) are acceptable and manageable.

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