

### SCT-1\_V1.10 OUTCOME IN ALLOGENEIC T CELL DEPLETED HAPLO-IDENTICAL TRANSPLANTATION WITH TCR $\alpha/\beta$ AND CD 19 DEPLETION IN PEDIATRIC PATIENTS: A SINGLE-CENTER EXPERIENCE FROM SOUTH INDIA

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**Introduction:** One of the methods of T cell depletion has been developed which provides efficient depletion of  $\alpha/\beta$  T cells from the graft while retaining large number of effector cells including  $\gamma/\delta$  T cells.

**Methods:** We reviewed outcomes and immune reconstitution of pediatric patients who underwent a haplo-identical HSCT with TCR  $\alpha/\beta$  and CD 19 depleted graft.

**Results:** 19 patients with a median age of 62 months underwent 20 Haplo-HSCT with this technique over two years. Indications of transplant were acute leukemia (ALL 7 and AML 1), thalassemia (n=4), one each for osteopetrosis, primary hemophagocytic lymphohistiocytosis, chronic granulomatous disease, amegakaryocytic thrombocytopenia, juvenile myelo-monocytic leukemia, sickle cell disease, and unstable hemoglobin disease. The conditioning regimens were myeloablative using TBI (n=9) or chemotherapy (n=10). The median infused doses of CD34+ cell,  $\alpha/\beta^+$  T cells,  $\gamma/\delta^+$  T cells and CD19+ cells were  $16.6 \times 10^6/\text{kg}$ ,  $0.055 \times 10^6/\text{kg}$ ,  $9.89 \times 10^6/\text{kg}$  and  $0.22 \times 10^6/\text{kg}$  respectively. All except a salvage transplant achieved neutrophil engraftment, at median of 12 days (range 9 – 20) and platelet engraftment at 11 days (range 7 – 27). Only one patient experienced graft failure and was retransplanted. Four patients (21%) developed acute GVHD grade II-IV (three with gut stage 1 and one with skin stage 3). None of the patients developed chronic GVHD. Viral infection/reactivation was seen with CMV (n=7), EBV (n=2) and adenovirus (n=1). Five patients died due to relapse (n=2), sepsis (n=1), CMV (n=1) and adenoviral infection (n=1). With a median follow-up of 379 days (range 53 – 756), the probability of event-free survival for the whole cohort was 73 % (SE 12.1). Immune reconstitution kinetics showed a robust NK cells recovery in the immediate post-transplant period.

**Conclusions:** Haplo-identical transplantation using TCR  $\alpha/\beta$  and CD 19 depleted graft may be associated with reduced risk of acute GVHD. Infectious complications especially viral infections are common.

### SCT-1\_V1.11 REDUCED TOXICITY AND EXCELLENT OUTCOMES USING A TREOSULPHAN BASED CONDITIONING REGIMEN AND UNRELATED HAEMATOPOIETIC STEM CELL TRANSPLANTATION IN CHILDREN WITH THALASSAEMIA MAJOR

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**Aim:** Thalassaemia major affects 10,000 new babies each year in our country and these children need to be treated with lifelong monthly blood transfusion and chelation. Haematopoietic stem cell transplantation is the only curative option for these patients. Unfortunately, only 35% of our patients have a fully matched family donor. With increasing awareness and access to donor registries with Indian donor databases, we have been able to find optimally matched donors for our patients. We have analysed the outcome in children with thalassaemia major who underwent fully matched unrelated haematopoietic stem cell transplantation with a treosulfan based conditioning regimen at our centre.

**Patients and methods:** We conducted a retrospective study of children with thalassaemia major who underwent fully matched unrelated bone marrow transplantation in our centre from 2012 to 2016. The match level accepted was 10/10 for an adult donor and 8/8 for cord blood stem cells. Acute events like sepsis graft versus host disease, bleeding and sinusoidal obstruction syndrome and chronic complications like graft versus host

disease, graft rejection and mortality were recorded. The children were treated using a uniform protocol of thiotepea, treosulphan, fludarabine and antithymocyte globulin with tacrolimus as the drug of choice for immunosuppression.

**Results:** A total of 21 children have undergone an unrelated fully matched haematopoietic stem cell transplantation at our centre using cord blood as a source in 3 children and adult peripheral blood stem cells in 18 children. Twelve were boys and 9 were girls ranging from 1 year to 14 years of age. There was one death due to gram negative sepsis in a child undergoing cord blood stem cell transplantation resulting in a mortality rate of 4.7%. Acute skin graft versus host disease (GVHD) occurred in 30% children, acute gut GVHD in 35% and mild chronic skin and mouth GVHD in 45% patients. Posterior reversible encephalopathy syndrome due to a combination of steroids and tacrolimus was seen in 24% children and steroid induced diabetes in 5% children. Reactivation of cytomegalovirus was seen in 38% children and routine CMV PCR monitoring and pre-emptive therapy helped prevent CMV disease in these children. Rare manifestation of GVHD in the form of immune cytopenia was seen in 20% children. There were no graft rejection or sinusoidal obstruction syndrome seen.

**Conclusion:** Unrelated donor transplantation is now a realistic therapy for children with thalassemia major in India. Treosulfan based conditioning therapy, optimal donor selection and early transplantation before the onset of iron overload has resulted in outcomes on par with sibling donor transplantation with over 90% cure rates. We need to create greater awareness to increase our donor databases and we also need to work with NGOs and government to expand access to care to cover the cost of 25 lakhs needed for each of these procedures.

### Solid Tumors

#### ST-1\_V1.1 PEDIATRIC EWING SARCOMA: EXPERIENCE FROM TATA MEDICAL CENTER, KOLKATA

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**Aim:** Survival in children with localized Ewing sarcoma is ~70% in Western studies. Our aim was to evaluate the clinical profile and outcome in a new tertiary non-profit cancer hospital in Eastern India.

**Material & Methods:** Children (<18-years) with Ewing's sarcoma were enrolled between January 2011 and May 2016. Information was collected retrospectively from hospital records. Demographic profile, clinical features, pathology, treatment and outcome were analyzed. Kaplan-Meier method was used for survival analysis. Multivariate logistic regression analysis was used to evaluate risk factors for relapse/progression.

**Results:** Thirty-four children were enrolled. Median age was 10.5-years (Range:1.4–16.9). Male:female was 2:1. Presenting complaints included: swelling (21;61%), pain (19;55%), restriction of movement (7;20%), fever (6;17%), neuropathy (6;17%), and, respiratory distress (1). Diagnosis was confirmed by histopathology in all. EWSR1 gene rearrangement was performed in 7 patients and was positive in 6. Disease in localized in 21 (70%) and metastatic in 9 (30%); data was missing in 4 patients. Six (20%) had presented with relapse/refractory disease. Origin was skeletal in 26 (76%) and extra-skeletal in 8 (23%). Nineteen (55%) had axial tumor, while 15 (44%) had non-axial disease. Sites of axial disease included the pelvis (7;36%), spine and vertebra (5;26%), chest-wall (5;26%), abdomen (1;0.05%), and, head and neck (1;0.05%). Sites of non-axial disease included the upper extremity (7;46%) and lower extremity (8;53%). The most frequently involved bone was the tibia. Metastatic sites included: isolated lung (4;44%), isolated bone (2;22%), lymph nodes (2;22%), disseminated disease (lung, bone, bone marrow: 1;0.1%).

Twenty-seven (79%) children received treatment, including 4 who received palliative chemotherapy. There was heterogeneity in the

protocols used: EuroEwing-99 (10;43%), MSKCC-P6 (9;39%), others (4;17%).

Multimodal treatment was used in 23 (85%): chemotherapy and radiation in 8 (34%), chemotherapy and surgery in 5 (21%), chemotherapy, surgery and radiation in 10 (43%). Nine patients with non-axial disease and 5 patients with axial disease had surgery ( $p=0.03$ ). Median follow-up for the treated patients was 27.5-months (Range:1-90). Out of 23 children who received curative treatment-11(47%) were alive & well, 5 (21%) were on treatment, 2 (0.08%) abandoned treatment & 4 (0.17%) had relapse/refractory disease; one (0.04%) patient died from treatment related toxicity. Five-year overall survival and event-free survival were 40% & 52%, respectively. Axial location ( $p=0.27$ ), metastatic disease ( $p=0.74$ ), and lack of surgery ( $p=0.34$ ) were not statistically predictive of relapse/progression, probably due to low numbers of patient and limited duration of follow up.

**Conclusions:** In spite of a similar clinical profile and disease stage, the outcome of Ewings sarcoma in our patients simulates that reported in Indian studies, however lags behind Western statistics. Reducing abandonment by tracking defaulters and providing support, using a uniform protocol, and improving supportive care, were identified as plausible steps to improve outcomes.

### ST-1\_V1.2

#### CLINICAL EXPERIENCE AND OUTCOME OF HEPATOBLASTOMA IN CHILDREN: A 9-YEAR RETROSPECTIVE STUDY

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**Background:** Hepatoblastoma (HBL) is the most common primary liver tumor in children. Metastatic disease at presentation, alphafetoprotein (AFP) less than 100 ng/ml, PRETEXT IV, undifferentiated histology are usual poor prognostic markers. Neoadjuvant chemotherapy with surgical resection has led to increased survival of these patients

**Aim:** This single centre study assesses the outcome and the factors affecting prognosis of children treated as per guidelines of SIOPEL3 in a low middle income country (LMIC).

**Materials & Methods:** Forty children with HBL treated as per protocol from Jan 2007 to Dec 2015 were analyzed. The diagnosis was established by imaging, AFP and histology/cytology.

**Results:** 27 boys & 13 girls; median age 12 months (2-120) with a mean symptom diagnosis interval (SDI) of 5.3 weeks (1-24) were diagnosed. Multifocal involvement was seen in 7/40. Median AFP at diagnosis: 16500 ng/ml (3-406198). 2 had AFP less than 100 ng/ml. Mean platelet count at diagnosis was 701375/cmm (95% CI 595510.80 to 807239.20). 7 (17.5%) had metastatic disease (6 lungs; 1 adrenal). PRETEXT: I-IV: 6, 13, 11 & 9. Nineteen: high risk (HR) disease (7 with SDI more than 8 weeks) 13/40 defaulted/refused therapy. All cases received neoadjuvant chemotherapy. 3 deaths occurred prior to surgery. 25 underwent surgery; complete resection (CR): 18/25 [14 : well; 3 relapsed, 1 died]. 7 cases subtotal resection : 2 : well, 4 had persistent disease and 1 death. 2/3 children who received salvage chemotherapy with Docetaxel had no response. HR patients had a poorer outcome ( $p=.012$ ), more multifocal disease ( $p=.0395$ ) and significantly lower CR ( $p=.0016$ ) as compared to standard risk patients. On comparing well Vs relapsed/residual disease cases; there was no difference in AFP levels, volume reduction after neoadjuvant therapy, metastasis, & histopathology ( $p=ns$ ). Relapsed/residual disease was significantly higher in those with higher mean age (24 mth Vs 12 mth); PRETEXT IV & multifocal disease ( $p=0.02$  &  $0.04$ ). 16 of 27 patients are presently well; median follow up being 48.3 months (7-101).

**Conclusion:** 59% (16/27) of cases who were treated are well. 86% of SR HBL had good outcome. Higher age at presentation, multifocality and high PRETEXT was associated with poor outcome. HR patients had a longer SDI. Docetaxel as a salvage therapy was not effective. Liver transplant, not available at our centre, would have helped the children with incomplete resection. Delayed referral and diagnosis remains a problem in LMICs as evident by greater SDI in those with HR disease.

### ST-1\_V1.3

#### MULTIDISCIPLINARY MANAGEMENT OF HEPATOBLASTOMA WITH INCORPORATION OF LIVER TRANSPLANTATION IN CHILDREN

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#### Abstract

**Background:** Advances in chemotherapy, liver resection techniques and pediatric liver transplantation have vastly improved survival in children with hepatoblastoma (HB). These are best managed by a multidisciplinary team in a setting where all treatment options are available. Until recently this was difficult to achieve in India.

**Methods:** Review of all children (< 16yrs) with HB treated in a pediatric liver surgery & transplantation unit between Jan 2011 and July 2016. Data regarding the clinical presentation, pre-operative management, surgical treatment, postoperative course and outcomes was extracted from a prospectively managed database.

**Results:** Thirty children were treated for HB during the study period. Nine children were PRETEXT 4, 7 were PRETEXT 3, 13 were PRETEXT 2 and one was PRETEXT 1. All children received neoadjuvant chemotherapy before surgery followed by adjuvant chemotherapy. Nineteen children had complete resection, while six underwent primary living donor liver transplantation. There were 6 mortalities including 5 children who poorly responded to chemotherapy with progressive tumor extension. At a median follow-up of 30 months, two children who underwent resection and one child who underwent liver transplant had disease recurrence.

**Conclusion:** Improved outcomes can be achieved in children with HB even in countries with limited resources when they are managed by multidisciplinary teams with expertise in pediatric oncology, liver resection and liver transplantation.

### ST-1\_V1.4

#### CLINICOPATHOLOGICAL PROFILE OF PEDIATRIC MEDULLOBLASTOMA

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**Introduction:** Medulloblastoma is the second most common primary malignant brain tumour in children. We present the clinic-pathological profile of children seen in a pediatric hematology/Oncology unit over a ten-year period.

**Method:** Clinical and laboratory data of children with medulloblastoma who attended the pediatric hematology/oncology unit of CMC, Vellore from 2004 to 2014 were retrieved from the medical records and reviewed.

**Results:** 76 children, 49 boys and 27 girls, with mean age at presentation  $8.5 \pm 3.45$  years. 7 were < 3 years and 22 were >10 years. Headache (86%) vomiting (79%) and ataxia (58%) were the common symptoms. The mean duration from onset of symptoms to diagnosis was  $2.7 \pm 2.2$  months with 78% diagnosed within 3 months. All children presented to the neurosurgical team at first visit. 30% required emergency CSF diversion procedure. All children underwent upfront surgical excision; 30 had residual tumour  $>1.5\text{cm}^2$ . Risk stratification based on age at presentation, volume of residual tumour and presence of metastatic disease, showed 43/76 to be in the high risk category.

Histological classification showed the following: classic 22 (37%), desmoplastic 19 (33%), medulloblastoma with extensive nodularity 9 (16%), large