0.73). All patients underwent HSCT for malignancies and none who received a reduced intensity HSCT have developed a SMN to date. Of those with exostoses, 1 patient had received autologous HSCT and underwent allogeneic HSCT for myelodysplastic syndrome. The other SMNs in this group include thyroid papillary carcinoma, osteogenic sarcoma, GIST, PNET. 3 of 4 SMNs in the control group had received allogeneic HSCT and all 4 had thyroid papillary carcinoma. Matched data analysis showed that exostosis cases were less likely to have been treated with steroids for acute GVHD (McNemar test p = 0.022) but no differences existed in other clinical variables examined. However, cases were younger at HSCT (3.9 vs 6.3 yrs, paired t-test p = 0.004) and had longer F/U than controls (11.7 vs 8.8 yrs, p = 0.003). There was no difference in time from HSCT to SMN (or latest F/U) by Kaplan-Meier (cases = 14.9, control = 12.7 yrs, log rank p = 0.35). Among all 52 patients without considering exostosis, the age at HSCT was not different for those with SMN than without (p = 0.87). Descriptive analyses comparing SMN occurrence in exostosis cases and controls appears in the attached table. In conclusion, for occurrence of exostoses our study showed only acute GVHD to be different between the groups, and the likelihood of SMN was similar for cases and controls. Of the 10 SMNs, 50% were thyroid carcinomas, which are common after low dose radiation exposure to the thyroid. Of note, 43% of the other solid SMNs among this group occurred in the field of focal radiation for the primary tumor, highlighting the importance of high dose focal radiation as a SMN risk.

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REDUCED TOXICITY CONDITIONING (RTC) AND ALLOGENEIC STEM CELL TRANSPLANTATION (ALLOSCT) IN 100 CONSECUTIVE PEDIATRIC RECIPIENTS: VERY LOW INCIDENCE OF DAY 100 TRANSPLANT RELATED MORTALITY (TRM)

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Myeloablative AlloSCT is associated with 20-40% non-relapse mortality (NRM) in the first 100 days. NRM depends in large part on graft source, disease and disease status and possibly intensity of conditioning. RTC may decrease NRM but pediatric data are limited (Satwani/Cairo BBMT, 2005). We evaluated the feasibility and toxicity of RTC-AlloSCT in 100 consecutive children (median age 9.23±6.79 yrs) with malignant disease (50) or non-malignant disease (50) undergoing UCB (n = 51), MFD (n = 41), or MUD (n = 8) AlloSCT (89 average risk, 11 high risk). Regimens included Busulfan (6.4-8mg/kg) + Fludarabine (150-180mg/m^2) ± ATG (8mg/m^2) (n = 45); Cyclophosphamide (60mg/kg) + Fludarabine (150mg/m^2) ± ATG (8mg/m^2) (n = 20); and Busulfan (12.8-16mg/kg) + Fludarabine (150mg/m^2) + Alemtuzumab (54mg/m^2) (n = 35). Mean follow-up is 1277 ±1041 days. Time to neutrophil and platelet engraftment was 19 ±10 days and 35 ± 26.6 days, respectively. Donor chimerism on day 30, 100 and 365 was 86 ±27, 92.6 ±15.8 and 93±16, respectively. Cumulative incidence of aGVHD and cGVHD was 24.7%±4.8% and 18.6%±4.7%, respectively. Day 100 and 5 year NRM was 4.1%±2.01% and 15±3.9 %, respectively. Overall incidence of primary graft failure (PGF) was 16.5%±3.7%. Incidence of PGF with UCB was 33.3%±6.8% vs. 0% for MUD and MSD (p < 0.0001). Incidence of PGF with UCB in chemo-naive vs. non-chemo-naive patients was 48.3%± 9.3% vs. 10.5%±7 % (p < 0.0072). The 5 year probability of OS and EFS was 69%±5% and 56.4%±5.4%, respectively. On univariate analysis, age (p = 0.12), malignant disease (p = 0.1), UCB (p = 0.02), poor risk disease (p = 0.001), chemo-naive patients (p = 0.1), fungal infection (p = 0.01), alemtuzumab based RTC (p = 0.03) and PGF (p = 0.03) were associated with poor OS. However, on Cox proportional hazard model based multivariate analysis only graft failure (p = 0.028) and poor risk disease (p = 0.03) were associated with poor OS. In summary, in this largest reported pediatric series, RTC-AlloSCT demonstrated substantially reduced day 100 NRM and sustained donor chimerism. However, chemo-naive children undergoing RTC-AlloSCT with UCB grafts have a higher incidence of PGF, and poor OS.

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DACLIZUMAB AS A SECOND-LINE TREATMENT OF GI GRAFT-VERSUS-HOST DISEASE IN PEDIATRICS

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Background: Steroid-refractory acute gastrointestinal graft-versus-host disease (GvHD) remains major cause of mortality in pediatric patients undergoing hematopoietic stem cell transplantation (HSCT). Among newly developed agents suitable for the treatment of GvHD, monoclonal antibodies hold much promise.

Methods: we report a series of 10 children who underwent allogeneic transplant from June 2007 through June 2009 and were treated with daclizumab for steroid-refractory acute GI GvHD (grade III-IV). Median of patients' age was 6.27 years (range 1-11) and 8 of patients were male. 8 of 10 patients underwent myeloablative and 2 of them nonmyeloablative stem cell transplant. Bone marrow (BM), peripheral blood (PB), and cord blood were stem cell sources in 4 patients, 3 patients and one patient respectively. Additionally, double cord blood in one patient and BM and PB concurrently in another one were used. Patients were transplanted from full match related (n = 6), one locus mismatch related (n = 1), two locus mismatch unrelated (n = 2) and haploidentical related (n = 1) donor because of Thalassemia (n = 4), Acute Lymphoblastic Leukemia (n = 2), Aplastic Anemia (n = 1), Fanconi Anemia (n = 1), Leukocyte Adhesion Deficiency (n = 1), and Wiskott-Aldrich Syndrome (n = 1). After first line therapy failed to control GvHD, Daclizumab added at a dose of 1 mg/kg every 10-14 days until response achieved and/or maximum 5 doses administered.

Results: 9 of 10 patients (90%) responded to Daclizumab therapy completely, but one patient failed. There were no infusion-related reactions. 8 patients developed CMV infection during Daclizumab therapy. Invasive fungal and bacterial infections occurred in 6 patients following Daclizumab therapy. Seizure and Guillain-Barre were important complications after daclizumab therapy in two patients which may be attributable to this monoclonal antibody. At a median follow-up of 460 days, 8 patients (80%) are alive and free of GvHD, severe infections and underlying disease. The remaining two patients died because of bacterial meningitis and severe non-responding acute GI GvHD. Limited Chronic GvHD, occurred in 2 patients.

Conclusions: Daclizumab was able to induce complete responses in pediatric patients with refractory acute gastrointestinal GvHD, but is associated with morbidity and mortality due to infectious complications. Aggressive prophylaxis against viral and fungal infections is recommended.

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A PROSPECTIVE STUDY OF REDUCED INTENSITY CONDITIONING (RIC) IN CHILDREN UNDERGOING UNRELATED UMBILICAL CORD BLOOD TRANSPLANTATION (UCBT) FOR NON-MALIGNANT DISEASES: PRELIMINARY RESULTS DEMONSTRATE A HIGH RATE OF ENGRAFTMENT AND LOW INCIDENCE OF GVHD

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Reduced intensity conditioning (RIC) reduces transplant related morbidity and mortality. However, engraftment remains a challenge after RIC in children with non-malignant disorders undergoing UCBT. We designed a novel RIC regimen for such children to study its efficacy to promote durable engraftment. Outcomes of 8 such children enrolled between Dec 2008 and July 2010 are presented in this preliminary analysis. RIC regimen consisted of alemtuzumab (3.2mg/kg), hydroxyurea (HU), fludarabine (FLU) 150 mg/m^2,

Table 1. Demographic and transplant details

No./Sex/Age (y)	Diagnosis/Co-morbidities	HLA match	TNC $\times 10^7$/kg (cryopreserved)	Days to ANC>500	Whole blood chimerism/day post-tx	Event	Follow-up
1/M/2.03	MPS II / Cardiomyopathy	4/6	9.64	19	>98%/+623	A/W	655+
2/M/3.35	MPS IIIB	6/6	6.09	15	92%/+384	A/W	433+
3/F/3.32	MPS IIIB	5/6	6.08	28	63%/+112	Death	170
4/M/1.3	CHH	6/6	17.68	NE	0/+30	Graft failure	368+
5/M/6.76	MLD	5/6	5.88	24	>98%/+268	A/W	280+
6/F/3.32	Zap 70 def./Enteroviral meningitis, Resp. MAI, Pseudomonas, Candida, Paraflu	5/6	8.3	21	>98%/+97	A/W	131+
7/F/0.45	HLH	5/6	22.27	19	>98%/+61	A/W	111+
8/F/0.58	HLH/Adenoviremia	4/6	14.19	20	>98%/+57	A/W	76+
Median: Age 2.67			8.97	20			280

MPS = mucopolysaccharidosis; CHH=Cartilage Hair Hypoplasia; MLD=Metachromatic Leukodystrophy; HLH=Hemophagocytic Lymphohistiocytosis; NE=not evaluable; A/W=alive and well

melphalan (MEL) 140 mg/m^2 and thiotepa (TT) 200mg/m^2. GVHD prophylaxis consisted of tacrolimus and MMF. All patients received single UCBT; median age and weight at the time of transplant were 3.3yrs and 15.1kg respectively; cryopreserved median cell dose was 8.97x10^7 TNC/kg (range 5.9–22.3). HLA match was 4/6, 5/6 and 6/6 in 2, 4 and 2 patients respectively. Preparative regimen was well tolerated. Maximum mucositis was grade 3. To date, no patient has experienced CNS, cardiac, pulmonary or hepatorenal toxicity attributable to conditioning. Patient with Cartilage Hair Hypoplasia (CHH) with no post-thaw CFU growth had autologous recovery on day +30. He was successfully retransplanted with RIC conditioning. The remaining patients (7 of 8) engrafted at a median of 20 days post-transplant. At the last evaluation, whole blood donor chimerism in engrafted patients ranged from 63% to > 98% with 6 of 7 engrafted patients > 90% donor. None of the patients have had Grade 3-4 acute GVHD or extensive chronic GVHD thus far, although follow-up for chronic GVHD is short. Untransfused platelet count > 50K was achieved in all engrafted patients at a median of 39 days. Viral reactivation and/or de novo viral infections were seen commonly but without appreciable end organ disease. Adenovirus infection was noted in 5 patients (1 patient had adenoviremia that resolved with cidofovir and adoptive immunotherapy); the patient with autologous recovery had prolonged CMV viremia. Seven of 8 patients are alive with a median follow-up of 280 days. One patient with mixed chimerism died on day +170 of an acute hemolytic transfusion reaction. The first two patients are off immunosuppression with age appropriate immune profiles.

Conclusions: RIC with alemtuzumab, HU, FLU, MEL, TT is well tolerated and results in a high rate of donor engraftment with a low risk of GVHD and regimen related toxicity in children with chemotherapy naïve non-malignant diseases undergoing UCBT.

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IMPACT OF A PRUDENT© CONSERVATIVE RED BLOOD CELL TRANSFUSION STRATEGY IN CHILDREN UNDERGOING HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Prior to 2009, stable patients in our hematopoietic stem cell transplant (HSCT) unit received routine transfusions for hemoglobin < 9 g/dL. In February 2009, we changed this transfusion threshold to Hgb < 7 g/dL based on published data in critically ill but stable pediatric intensive care unit patients. AIM: The aim of our study was to assess the impact of changing to a conservative transfusion strategy in children undergoing HSCT at our institution.

Methods: We compared census and transfusion data obtained during primary admissions for HSCT using the prior transfusion threshold (1/1/08-12/31/08) and after implementation of the conservative transfusion threshold (3/1/09-2/28/10). All transfusion decisions in both study periods were made at the discretion of physician attendings. Data was analyzed with help from the PRUDENT© quality improvement team, which focuses on Pediatric Resource Use and the Determination of Effective and Necessary Targets at our hospital.

Results: 66 patients admitted for HSCT pre-intervention were compared with 75 post-intervention. Pre-and post- patients were of similar ages (median 6 (IQR 2, 12.5) vs. 6 (3, 13) yrs old, p = .8), and underwent similar types of transplant (22 (33%) vs. 26 (35%) autologous, p = .9), for similar diagnoses. Similar numbers of patients received at least one transfusion in the two periods (65 (98.5%) vs. 72 (96%), p = .4). Post-intervention patients, however, received significantly fewer RBC units (median 4 (IQR 3, 8) vs. 3 (2,5), p = .002) and had fewer transfusion days (median 4 (IQR 2, 5) vs. 3 (2, 5), p = .01). In addition, median Hgb pre-transfusion significantly decreased from 8.8 g/dL to 6.8 g/dL (p < .0001). Patient outcomes appeared similar, with no differences in median length of stay in days (37 (IQR 30, 46) vs. 37 (29, 52), p = .7), median days to engraftment (20 (IQR 12, 25) vs. 18 (12, 24), p = .7) or 100 Day Mortality (26% vs. 18%, p = .2). Finally, median blood product related charges were significantly less post-intervention ($3624 (IQR $2265, $6040) vs. $2185 ($1812, $3997), p = .004).

Discussion: A review of our institutional experience suggests a conservative transfusion target of a Hgb of < 7 g/dL in otherwise stable children undergoing HSCT results in fewer transfusions without increasing adverse outcomes. Further study is required to fully evaluate the safety of this practice as well as to comprehensively assess its impact on the provision of high-value, high-quality care in pediatric HSCT units.

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CLONAL EVOLUTION IS A STRONGER PREDICTOR THAN DISEASE STATUS OF DISEASE-FREE SURVIVAL AFTER PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: Clonal evolution as a model of tumor development and progression was first proposed by Nowell in 1976. Genetic instability of tumor cells leads to subpopulations with additional cytogenetic abnormalities. Subpopulations with cytogenetic abnormalities that confer a survival advantage become the dominant population leading to progression. Although clonal evolution has been generally viewed as an adverse event, there is limited data regarding the effect on outcome after HSCT.

Methods: We conducted a retrospective chart review of pediatric patients who underwent HSCT for leukemia beyond CR1/CP1 or with refractory disease from 2005-2010. Three patients with isolated CNS relapse and two patients with JMML were excluded. Cytogenetic analyses from diagnosis and relapse were compared for 16 patients. Ten of these patients had clonal evolution, defined as an additional cytogenetic abnormality from diagnosis. Relapse-free survival was analyzed using the Kaplan-Meier method and the differences between survival curves were tested using a log rank test at a 0.05 significance level.