

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 (ALLO SCT) 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/m²) ± ATG (8mg/m²) ($n = 45$); Cyclophosphamide (60mg/kg) + Fludarabine (150mg/m²) ± ATG (8mg/m²) ($n = 20$); and Busulfan (12.8-16mg/kg) + Fludarabine (150mg/m²) + Alemtuzumab (54mg/m²) ($n = 35$). 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 $24.7 \pm 4.8\%$ and $18.6 \pm 4.7\%$, respectively. Day 100 and 5 year NRM was $4.1 \pm 2.01\%$ and $15 \pm 3.9\%$, respectively. Overall incidence of primary graft failure (PGF) was $16.5 \pm 3.7\%$. Incidence of PGF with UCB was $33.3 \pm 6.8\%$ vs. 0% for MUD and MSD ($p < 0.0001$). Incidence of PGF with UCB in chemo-naïve vs. non-chemo-naïve patients was $48.3 \pm 9.3\%$ vs. $10.5 \pm 7\%$ ($p < 0.0072$). The 5 year probability of OS and EFS was $69 \pm 5\%$ and $56.4 \pm 5.4\%$, respectively. On univariate analysis, age ($p = 0.12$), malignant disease ($p = 0.1$), UCB ($p = 0.02$), poor risk disease ($p = 0.001$), chemo-naïve 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-naïve 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/m²,