absorption . A simple method to assess PK AUC of single dose/24hrs of IV BU in pediatric patients is described. Patients who signed informed consent were enrolled. The regimen consisted of test dose of IV BU (0.8mg/kg) as a single dose day -10, Fludarabine 30mg/m^2/day on days –10 to –6, followed by BU 3.2 mg per Kg/day on days –5 and –4 and rabbit ATG 2mg/kg on days –4 to –1. Phenytoin prophylaxis was given for 4 days. Cells were infused on day 0. There were 5 patients with a median age 8.0 (0.5-16 years);. The median weight was 22.6 (range 4.3-45.4) Kg. Patients diagnoses include: Omenn's syndrome, Neuroblastoma, ALL, CML, and X linked lymphoproliferative disease. Samples were obtained at 2, 4, 8 and 12 hrs and submitted to the Fred Hutchinson Cancer Center for determination of the AUC. An AUC of 800-1200 was targeted for the test dose. The median measured AUC was 1034 (816-1315) uMol*min; the clearance was 3.1 (2.4-3.9) (ml/min) kg. The target AUC equals the AUC of the test dose multiplied by 4. The dose of 3.2mg/Kg/q24 hrs was administered and the target AUC was 3800-4200. The measured AUC median was 3590 (2307-4097) uMol*min and the clearance 3.4 (3-4.2)(ml/min)/kg, Dose adjustment of 10% lower dose on days –5, –4 was made on one patient who had a high AUC, the modification resulted in a lower AUC. No instances of hepatic veno-occlusive disease or seizures developed. Neutrophil and platelet engraftment was prompt in 3/3 evaluable patients. Three of the patients have achieved full chimerism. In conclusion, PK of a test dose of 0.8 mg/Kg of IV BU multiplied by 4 appears to be predictive of the PK for a single daily dose of IV BU in pediatric patients undergoing a RI HSCT.

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OUTCOME OF TRANSPLANTATION WITH UNRELATED DONOR BONE MARROW IN CHILDREN WITH SEVERE THALASSEMIA

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About 70% of thalassemic patients lack HLA-identical family members to be suitable donors for bone marrow transplantation (BMT). To increase therapeutic opportunity for these patients, we have performed BMT from unrelated donors to children with severe beta-thalassemia at our institute. The objective of this study is to determine the outcomes of patients who underwent unrelated BMT for severe beta-thalassemia. There were 11 patients; 6 homozygous beta-thalassemia, and 5 severe beta-thalassemia/Hb E disease. The median age was 3 years (range, 1-11 years). Preparative regimen consisted of busulfan, cyclophosphamide, and rabbit anti-thymocyte globulin. The patients received bone marrow from unrelated donor (6/6 HLA-matched = 10, 5/6 = 1) with a median CD 34+ cell dose of 3.3 $\times$ 10^6 cells/kg (range, 0.8-6.9 $\times$ 10^6 cells/kg). GVHD prophylaxis was cyclosporin (CSA) and mycophenolate motefil (MMF) (n = 7), or tacrolimus (FK 506) and MMF (n = 1), or FK 506 and methotrexate (n = 3). The median day of neutrophil and platelate engraftment was 16 and 26, respectively. Ten patients engrafted with full donor chimerism, one with mixed chimerism. Six patients (55%) had acute GVHD (gr I = 1, gr II-IV = 5). Limited chronic GVHD appeared in 5 patients (45%). CMV reactivation was detected in 3 patients, no CMV disease. All patients were alive and well with a median follow-up time of 16 months (range, 9-30 months). Our data demonstrate that unrelated BMT could be considered as an optional therapy for children with severe beta-thalassemia.

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REDUCED INTENSITY CONDITIONING AND ALLOGENEIC STEM CELL TRANSPLANTATION (RIALLOSCT) FROM UNRELATED CORD BLOOD AND MATCHED FAMILY DONORS IN CHILDREN AND ADOLESCENT RECIPIENTS RESULTS IN SUSTAINED DONOR CHIMERISM

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Mixed and ultimately complete donor chimerism have been achieved in adults following RIAlloSCT from matched related and unrelated donors (Slavin et al, Blood:99:1071, 2002). However, there is little data regarding the use of a RIAlloSCT approach in pediatric recipients. We determined the degree of chimerism by unique VNTR and STR alleles after RIAlloSCT in children following matched family donor (MFD) stem cell & unrelated umbilical cord blood (UCB) transplants. Donors: 14 UCB, 2 BM, 4 PBSC, and 1 BM + PBSC. RIC: Busulfan (Bu)/Fludarabine (Flu)/r-ATG (N = 11); Bu/Flu (N = 1); Bu/Flu/Alemtuzumab (N = 2); Flu/Cyclophosphamide (Cy)/r-ATG (N = 4); Flu/Melphalan/h-ATG (N = 1); 200 cGy TBI/Flu/Cy/h-ATG (N = 1); and Flu/Cy/etoposide/r-ATG (N = 1); GVHD prophylaxis: FK-506 and MMF. Demographics: median age 13 (0.5-21) yrs; HD (6), NHL (1), neuroblastoma (2), Wilms' tumor (1), CML (1), AML (1), MDS (1), Wiskott-Aldrich syndrome (1), -thal (2), aplastic anemia (2), Fanconi anemia (1), HLH (1). The UCB median cell dose was 4.3 (0.9-10.8) $\times$ 10^7 nc/kg and 1.9 (0.3-6.9) $\times$ 10^5 CD34/kg. The BM/PBSC cell dose was 8.3 (4.7-18.9) $\times$ 10^8 nc/kg and 5.0 (4.6-6.4) $\times$ 10^6 CD34/kg. MFD vs. UCB median time to ANC $\geq$500 $\times$ 2d was 14 (8-22) days vs.18 (2-45) days and platelet count $\geq$20,000 untransfused $\times$ 7d was 11 (8-22) days vs. 21 (6-170) days. Maximal donor chimerism (MDC) for UCB was 100% for 8 pts, 98% for 1 pt, 95% for 1 pt, 55% for 1 pt (died of PD on day+79), and 0% for 3 pts. For related MFD, MDC was 100% for 6 pts, 65% for 1 pt and 55% for 1 pt. Primary graft failure occurred in 3 patients (-Thal, MDS, HLH). Secondary graft failure occurred in 2 patients (AA and -Thal). Grade 4 toxicities were: 1 transaminitis, 1 hyperglycemia, and 1 leukoencephalopathy. Opportunistic infectious complications included: candidemia (N = 3), aspergillosis (N = 1), adenovirus (N = 4), *Mycobacterium spp.* (N = 2) and one subclinical CMV infection. The probability of AGVHD grade II-IV in UCB vs. MFD was 30.1% vs. 46.5%. The overall probability of CGVHD was 10% at day 200. The probability of 1-yr OS is 69%. RIAlloSCT in children and adolescents appears feasible and tolerable and results in $\geq$70% achieving $\geq$90% sustained mixed donor chimerism within 2 months. The risk of graft failure following RIAlloSCT in children and adolescents is similar to adults (Maris et al, Blood 102:2021, 2003) and occurs mainly in non-malignant diseases (-Thal, MDS, AA, HLH).

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NONMYELOABLATIVE TRANSPLANT IN CHILDHOOD DISEASES

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Nonmyeloablative transplant provides a cure for seriously ill children with lesser degree of toxicity. We report our experience on fludarabine based preparatory regimen in 12 subjects (M:F = 5:7, median age 95 months) from September 1999 to June 2002. There were acute lymphoblastic leukemia(1), acute myeloid leukemia(1), chronic myeloid leukemia(1), severe aplastic anemia(5), Fanconi anemia(1), Wiskott Aldrich syndrome(1), Omenn syndrome(1) and I cell disease(1). They were either with complications from prior intensive chemotherapy, second transplant, mismatched related donors/cord blood or matched unrelated donors. The conditioning regimen consists of fludarabine 30mg/m^2 for 5 days from day-8, cyclophosphamide 60mg/kg for 2 days from day-3 and anti-thymocyte globulin 30mg/kg (10mg/kg for HLA-identical related transplant) for 3 days from day-3. The donor graft was not T cell depleted with median CD34 count of 4.12 $\times$ 10^6/kg. The neutrophil engraftment occurred at median of 16 days (9-29), platelet transfusion independence at median of 21 days and red blood cell transfusion independence at median of 23 days. No confirmed septicemia was noted. One patient had herpes simplex encephalitis on day 32 with significant physical handicap. No other major toxicity was noted. Three developed mixed chimerism with subsequent conversion to complete chimerism by either withdrawal of immunosuppressives or donor leucocyte infusion. The patient with I cell disease had stable mixed chimerism and remained clinically stable. Two had mixed chimerism and then rejection of the donor graft. The remaining 6 remained in complete