on day +112. One recipient is pregnant 9 months post transplant. In summary, this regimen is well tolerated, without increased TRM or GVHD, and supports engraftment with varied stem cell sources despite risk factors for graft rejection. Lymphopenia in the early post transplant period requires close vigilance and early intervention for infection.

Table.

Disease	Age (years)	Source	Cell dose (TNC/kg)	Engraftment	GVHD
Hurler's	1.5	BM	3.26 × 10 (8)	donor	0
Langerhan's	19	S BM	3.38 × 10 (8)	donor	Gr1-sk
Thalassemia	10	S BM	2.2 × 10 (8)	BM-d;PB-mixed	0
Evan's	12	UCB4/6	1.3 × 10 (7)	donor	0
Aplastic anemia	12	S PB	1.9 × 10 (10)	donor	Gr1-sk
Adrenoleukodystrophy	3	S PB	4.58 × 10 (8)	donor	0
Sickle cell anemia	2	S BM	3.3 × 10 (8)	donor	0
Aplastic anemia	20	S BM 5/6	4.2 × 10 (8)	NA	0
Hemophagocytosis	3	S BM	3.7 × 10 (8)	NA	0
Aplastic anemia	32	UCB5/6	2.02 × 10 (7)	NA	0

sk = skin; s = sibling; d = donor; NA = Not available.

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FREQUENCY AND MAGNITUDE OF DOSE ADJUSTMENT OF IV BUSULFAN IN TARGETED DOSING STRATEGY FOR PEDIATRIC ALLOGENEIC TRANSPLANTATION

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Busulfan is an important therapuetic agent in pediatric allogeneic transplantation. The recent introduction of IV busulfan (IV Busulfex®, ESPpharma) has descreased the intra-and interpatient dose variations associated with oral absorption and allows for targeted therapy. Children have increased drug clearance and varying degrees of hepatic function both developmentally and associated with the underlying disorders for which they are being treated. Because of this variability, first dose pharmacokinetics were perfomed on all of our patients to ensure the targeted AUC was achieved. In a series of 85 consecutive children undergoing allogeneic transplant at Methodist Children's Hospital/Texas Transplant Institute from June 2001 to October 2003, 45 children received myeloablative doses of busulfan (0.8 mg/kg for patients 3-10 kgs; 1 mg/kg for patients > 10 kgs till age 4 yrs; 0.8 mg/kg for patients > 4 yrs given every 6 hours for 16 doses) as part of a busulfan/cyclophosphamide, busulfan/melphalan or busulfan/fludarabine preparative regimen. 42/45 patients had their actual weight used for dosing calculations. Adjusted IBW was used in 3 patients. All patients received dilantin for seizure prophylaxis. First dose pharmcokinetics were performed by the Clinical Pharmokinetics Lab at Seattle Cancer Care Alliance, targetting an AUC of 900-1300 umol.min, with dose adjustments done starting with dose 7, if needed. Donor source was matched sibling donor bone marrow or cord blood in 10 and unrelated donor sources in 35 (2 marrow and 33 mismatched umbilical cord units). The median age was 4.7 yrs (range 1 month to 17 years). Patients underwent transplant for a variety of conditions: 12 AML, 5 CML, 1 JMML, 9 ALL, 1 lymphoma, 3 HLH, 10 primary immunodefiencies, 4 hematology disorders. No patients developed VOD. 32/33 patients of patients who received a fully myeloabalative preparative regimen engrafted. A targeted AUC (900-1300 umoles.min) was achieved with initial dosing in 50% of the patients. However, many children required dose adjustment to achieve the targeted AUC, mostly dose escalation (see table). Given the variability of metabolism in children, first dose pharmacokintics are recommended. Additionally, the starting dose in infants is lower than the currently recommended dose.

Table.

Age/ Weight	Starting Dose (mg/kg)	AUC μmol · min: Median (range)	Final Dosing (mg/kg): Median (range)	Percent of Patients Requiring Dose Adjustment	Dose Increased/ Dose Decreased
3-10 kg (n = 12)	0.8	1167 (825-1869)	0.93 (0.67-1.25)	50%-6/12 pts	4 ↑ /2 ↓
10 kg-4 years (n = 11)	1	1142 (908-1518)	1 (0.76-1.25)	27%-3/11	2 ↑ /1 ↓
>4 years (n = 22)	0.8	1089 (620-1827)	0.82 (0.57-1.25)	65%-15/23	11 ↑ /4 ↓

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LARGE VOLUME LEUKAPHERESIS FOR AUTOLOGOUS PERIPHERAL BLOOD STEM CELL COLLECTION IN CHILDREN WEIGHTING LESS THAN 25 KG

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Peripheral blood stem cells (PBSC) are the most frequent source of hematopoietic stem cells used to rescue patients from high-dose chemotherapy. The theoretical advantages of PBSC collections are decreased tumor contamination and faster hematological engraftment after the transplant. Small children are usually not eligible for such protocols due to little experience of most Hematotherapy teams, poor venous access and concern with a large extracorporeal volume. In large volume leukapheresis (LVL) three or more blood volumes are processed in the same procedure. LVL is also warranted in pediatric patients to decrease the number of procedures and potentially decrease tumor contamination. Twenty-five patients underwent LVL using a Cobe Spectra® cell separator between 2000-2003. All had the circuit primed with irradiated, filtered and resuspended red blood cells. All patients needed a central venous catheter placed for the procedure. During the procedure, the patients received continuous IV infusion with 10% calcium gluconate 2cc/kg, 10% magnesium sulfate 1 cc/kg, 19.1% potassium chloride 0.3 mEq/kg/hr over four hours to decrease the adverse effects of ADC infusion. They had vital signs, EKG and O2 saturation continuously monitored. Patients were 13M:12F with a median age of 3.5 years-of-age (1-10). The median weight was 14 kg (8-24). Underlying diagnoses were neuroblastoma (21), germ cell tumors (2), non-Hodgkin's lymphoma (1) and alveolar soft tissue sarcoma (1). The median number of procedures was 2 (1-4). The median total nucleated cell count/kg was 16 (5-66) and CD34+/kg 6 (0.6-71). In conclusion, LVL can be safely performed in small children if vital signs are adequately monitored and electrolytes are replaced and promptly corrected.

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AUTOLOGOUS STEM CELL TRANSPLANTATION FOR THE TREATMENT OF PEDIATRIC SOLID TUMORS IN BRAZIL

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High-dose chemotherapy and autologous stem cell rescue can be used in the treatment of poor prognosis responsive pediatric solid tumors. Our objective is to describe the experience of four Brazilian hematopoietic stem cell transplantation (HSCT) centers in

treating such patients. Sixty-three autologous HSCT were performed from August, 1994 to September, 2003; 80% of them were after 1999. Thirty-four patients were male (54%). The median age was 7 years (1 to 23). The underlying diagnoses were neuroblastoma (24), Wilms' tumor (10), Ewing's Sarcoma (9), medulloblastoma/ central nervous system primitive neuroectodermal tumor (8), germ cell tumors (6), rhabdomyosarcoma (5) and desmoplasic small round cell tumor (1). Twenty-one patients with neuroblastoma, two with medulloblastoma (under 3 years of age) and one with metastatic rhabdomyosarcoma were in first remission. The others were in second or third remission or had refractory disease (39). Melphalan, etoposide and carboplatin was the conditioning regimen used in 68% of the patients. The peripheral blood was the source of stem cells in 72% of them. The overall and disease free survival at four years were 39 ± 8% and 33 ± 7%, respectively. The median survival was 22 ± 6 months. The overall survival, according to diagnosis, was 53 ± 11% for neuroblastoma, 58 ± 16% for Wilms' tumor, 33 ± 16% for Ewing's sarcoma, 58 ± 19% for medulloblastoma, 50 ± 29% for germ cell tumors and 20 ± 18% for rhabdomyosarcoma. Relapse was the main cause of death (21/63-32%). Nine patients (14%) died due to transplant-related toxicity or infections. In conclusion, HSCT is feasible but carries a high transplant-related mortality. A Brazilian HSCT registry is being organized. National trials are warranted for better indication and evaluation of the role of stem cell transplantation in the treatment of high-risk or relapsed pediatric solid tumors.

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AUTOLOGOUS STEM CELL TRANSPLANTATION (SCT) IN PEDIATRIC PATIENTS WITH ADVANCED HODGKIN'S LYMPHOMA (HL): THE ROLE OF INTERFERON-ALPHA POST-TRANSPLANT

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Interferon alpha (IFNα) has known anti-proliferative and immunomodulating effects and might enhance immunity for better control of any residual HL after SCT. Between May 1994 and August 2003 a total of 12 pediatric (8 males) patients with HL (8 NS, 2 LP, 1MC, 1 NS+ALCL) underwent autologous SCT in our center. Their median age was 16 (range 11-20) years. The median interval between diagnosis and transplant was 16 months (range 6mos-9 y). All patients had received a median of 3 prior treatments (range 2-4) and all but two additional involved-field radiotherapy. Disease status at the time of SCT was: PD (4 patients), SD (2), PR (4), and CR(2). The conditioning regimens were BEAM (n = 6), CBV (n = 3), or other(n = 3) The source of SC was autoBM in 2 cases and autoPBSC in 10. All patients achieved ANC and PLT engraftment after a median time of 10 (9-16) and 12 (11-31) days respectively. Nine patients received IFNa immunotherapy when the ANC and the platelet count exceeded 1,500 and 50,000 respectively. Three did not, two due to rapidly progressive disease. Interferon-α administration was initiated at a dose of 0.5 million Units/m^2 tiw (Klingerman et al, Blood 1991,78: 3306) at a median of 49 days post-transplant (range 33-127). Patients received IFNα for 1 to 24 months (median 12 months post-transplant). Observed toxicity was hematologic and constitutional, with escalation of dose and/or frequency as permitted by toxicity. The median tolerated weekly dose was 3.5(range 1.5-6.5) mU/m^2. With a median follow-up of 41(range 2-113) months, nine patients are alive and well (two less than a year post SCT). Of the 10 patients who received IFNα, nine are alive with no evidence of disease. Three patients died: two from rapidly progressive HL (did not receive IFNα) and one from relapse following allogeneic BMT. One patient, who relapsed after transplant, was treated with IFNα and chemotherapy and remains in remission 5 years later. In conclusion, IFN-α administration to pediatric patients following SCT for advanced HL is safe and may confer survival advantage.

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STEM CELL TRANSPLANTATION (SCT) FOR PATIENTS(PTS) WITH GENETIC DISEASES: A CALL FOR PHYSICIANS FROM DEVELOPING COUNTRIES TO DISCUSS ABOUT STRATEGIES TO IMPROVE DIAGNOSIS AND EARLY REFERRAL TO BMT CENTERS

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Background: Brazil is a huge Latin-American country with many social and economic disparities and more than 3 million live births every year. SCT for pts with genetic diseases (GD) has a specific timing because engraftment of donor cells does not always correlate with improved quality of life or survival. **Material and Methods:** Between 10/79 and 09/03 more than 1400 SCT were performed in our BMT Unit but only 51 pts had GD. Median age: 3yr (range: 0,1 to 22). Gender: F11/M40; Diagnoses: Dyskeratosis Congenita (DC): 5pts;Diamond-Blackfan Anemia (DBA): 5pts; Congenital Dyserythropoietic Anemia (DBA): 1pt; Amegakaryocytic Purpura (AmegaP): 1pt; Hemoglobinopathies: 4pts; Kostmann Syndrome: 1pt; Wiskott-Aldrich syndrome (WAS): 7pts; Severe Combined Immunodeficiency (SCID): 7pts; Histiocytoses: 1pt; Gaucher disease: 1pt; Mucopolysaccharidosis: 6pts (MPS-I: 3pts, MPS-III: 1pt, MPS-VI: 2pts); Adrenoleukodystrophy (COCALD): 3pts; Globoid Cell Leukodystrophy (GLD-Krabbe): 1pt; Osteopetrosis (OP): 8pts. Bone marrow (BM) was the stem cell source for 30 HLA-identical siblings, 3 other related and 1 haploidentical (mother). 17pts received an unrelated transplant (11CB, 6BM). Conditioning regimen: Chemotherapy only: 41pts, Chemotherapy +TBI: 7pts. No conditioning regimen: 3pts. GVHD prophylaxis: Csa was given to 47pts. **Results:** 48pts were evaluable for engraftment and 10pts had primary graft failure (osteopetrosis: 6pts). Thirty-three pts (DBA: 3pts; Gaucher: 1pt; MPS: 3pts; OP: 2pts, DC: 5pts, Hemoglobinopathies: 4pts, SCID: 6pts, WAS: 5pts; COCALD: 2pts; AmegaP: 1pt Histiocytoses: 1pt) are alive 6 to 5688 days post-BMT (Median: 1377days). Four pts are alive with an autologous recovery (OP: 2pts, Hemoglobinopathies: 2pts). All pts with storage disease that are alive improved or stabilized their neurological function, except for 1pt with MPS-III. Eighteen pts died (14pts before day +100). GVHD or graft-failure associated with infections was responsible for most deaths. **Conclusion:** Medical education to improve early diagnosis and referral to specialized centers is the key to success in GD. This has to be done together with the commitment from the health system in each country to guarantee that all pts will be able to receive adequate treatment despite their economic or social background. It is urgent that developing countries work together with international centers to improve diagnosis, data collection and specific treatments in these rare diseases.

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UNRELATED UMBILICAL CORD BLOOD TRANSPLANTATION FOR FAMILIAL ERYTHROPHAGOCYTIC LYMPHOHISTIOCYTOSIS

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Background: Patients with Familial Erythrophagocytic Lymphohistiocytosis (FEL) or Hemophagocytic Lymphohistiocytosis (HLH) die of progressive disease early in life. Allogeneic stem cell transplantation may be curative. However, many children lack a suitably matched living related or unrelated donor. This study investigated the feasibility of substituting partially HLA-mismatched, banked unrelated-donor umbilical cord blood (UCB) as an alternative source of hematopoietic stem cells for transplantation in children with FEL lacking traditional HLA matched stem cell donors. **Methods:** Five infants with FEL, with a median age of 0.58 years, (range 0.33-0.98) received myeloablative doses of busulfan, cyclophosphamide and ATG followed by unrelated UCB transplantation between 11/98 and 2/02. Patients were evaluated for donor cell engraftment, toxicity and effects of this therapy on the natural history of the disease. Patients did not receive any post transplant intrathecal therapy. No radiation therapy was administered at any time during therapy. **Results:** UCB donors mismatched at 1-2 HLA markers delivering a median cell dose of