Allogeneic hematopoietic stem cell transplantation is the only curative therapy. Many patients do not have a suitable donor. Between 1995 – 2006, 25 pediatric patients lacking matched living stem cell donors were transplanted with unrelated umbilical cord blood (UCB). M:F ratio of the study group was 1.8; Eight (32%) patients belonged to ethnic minorities; the median age was 9.77 years (range 1.11-19.73) and median weight was 32.8 kg (range 8.3-62.6). Five patients had therapy-related MDS (3 ALL, 1 NHL, 1 Neuroblastoma). MDS stage was RA/RC 10 pts, RAEB 7 pts, RAEB-T 3pts, and AML 5 pts. Monosomy 7 was present in 17 (68%) pts. Median time from diagnosis to transplant was 7.17 months (range 2-61). Preparative regimen was TBI based in 17 pts (68%). Cyclosporine was used for GVHD prophylaxis with Solu-medrol in 24 pts and CellCept in 1 pt. Grafts were matched at HLA Class I (A and B) at low resolution and HLA Class II (DRB1) at the allelic level. 6 pts were 5/6, 18 pts were 4/6, and 1 pt was 3/6 HLA matched. The grafts contained a median of 4.39 × 10e7 (range 1.68-29.16) nucleated cells/kg pre-cryopreservation and 3.58 × 10e7/kg (range 1.01-21.25) infused. The median CD 34+ cell dose infused was 1.5 × 10e5/kg (range 0.17-28.46). Cumulative incidence of neutrophil engraftment (ANC > 500/ μL) at day 100, platelet engraftment (>50K untransfused) at day 180, acute GVHD grades 2-4 at day 100, chronic GVHD, relapse and non relapse mortality at 1 yr were 72%, 56%, 20%, 32%, 8% and 36.5% respectively. 5 yr probabilities of OS and EFS were 46% and 41%. Thirteen patients died, 5 of infectious complications (1 toxoplasmosis, 1 aspergillosis, 2 EBV including 1 LPD, 1 adenovirus), 4 of relapse, 1 of graft failure, and 3 of multi system organ failure. EFS of pts < 10 yrs of age (p = 0.05) , weighing < 33kg (p = 0.03), and those with monosomy 7 (p = 0.05) was superior. These results, especially in younger patients with Monosomy 7 and early stage MDS are equivalent to matched allogeneic bone marrow transplant data. We conclude that unrelated UCB donors should be actively considered for pediatric patients with MDS who lack a living related or unrelated stem cell donor to enable transplantation when the disease is in early stage.

Event Free Survival by Covariates

	N	Events	1 yr estimate %(95% CI)	3 yr estimate (95% CI)	p-value
KARYOTYPE					**0.05**
Monosomy 7 present	**17**	**8**	**64.7 (42-87.4)**	**58.8 (35.4-82.2)**	
Monosomy 7 absent	**8**	**6**	**37.5 (4-71)**	**18.8 (0-49.7)**	
RECIPIENT AGE					**0.05**
> 10 years	**11**	**9**	**45.5 (16-74.9)**	**27.3 (1.0-53.6)**	
<= 10 years	**14**	**5**	**64.3 (39.2-89.4)**	**64.3 (39.2-89.4)**	
RECIPIENT WT.					**0.03**
> 33 kg	**12**	**10**	**41.7 (13.8-69.6)**	**25 (0.5-49.5)**	
<= 33 kg	**13**	**4**	**69.2 (44.1-94.3)**	**69.2 (44.1-94.3)**	

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MYELOABLATIVE HSCT FOR CHILDREN AND ADOLESCENTS WITH LYMPHOMA REFRACTORY TO PRIMARY THERAPY: A SINGLE INSTITUTION EXPERIENCE

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Primary therapy of high-risk lymphomas in children and adolescents is very successful, however refractory lymphoma presents major challenges and optimal therapy remains uncertain. Between 1994 and 2006, 22 pediatric patients with high-risk lymphoma underwent myeloablative therapy and HSCT; 16 autologous and 7 allogeneic (5 sibling; 2 unrelated HSCT). The overall EFS was 61% with a median follow up in survivors of 1243 days after HSCT. In 8 Hodgkin's patients the overall EFS was 54%; all patients had failed primary therapy, received autologous PBPC and engrafted and one had a planned non-myeloablative sibling allogeneic HSCT. Relapse occurred in 3 of 4 patients not in CR at 181, 248 and 812 days from HSCT. In contrast, the 4 of the 5 relapse-free survivors (median follow up of 833 days; range 305 to 2127) had attained a CR2. The 14 NHL patients' diagnoses included 6 anaplastic large cell lymphomas, 2 peripheral T lymphomas and 6 lymphoblastic lymphomas (4 T and 2 B precursor phenotype). Allogeneic HSCT were performed in 7 NHL patients (5 MS; 2 URD), while 8 patients received autologous PBPC (one autologous patient relapsed at day 60, then received an allograft). All relapses occurred before day 100 and 4/5 relapses were in patients who either had CNS relapses and/or had residual disease at the time of HSCT. The EFS for all NHL patients was 67% with a median follow up in survivors of 1756 days (range 224 to 3606 days). In autologous HSCT recipients, the EFS was 50% (median follow up in survivors was 1071 days; range 224 to 2527), while after allogeneic HSCT for NHL, the EFS was 83% (median follow up in survivors was 2283 days; range 496 to 3606). There were no toxic deaths in any patient group. GVHD occurred in 3/7 allogeneic HSCT patients and resolved with therapy in all patients. Opportunistic infections typical for allogeneic HSCT (specifically aspergillus, CMV and RSV) occurred more often in the lymphoma patients undergoing autologous PBPC HSCT compared to pediatric autologous HSCT in patients with solid tumors. We conclude that myeloablative HSCT offers significant salvage potential in patients with lymphoma who have disease refractory to primary therapy. Those patients who attain disease control prior to HSCT do very well. We prefer to use TBI-based myeloablation and perform allogeneic HSCT in pediatric NHL patients to overcome potential chemotherapy resistance, decrease the potential of re-infused tumor and to potentially elicit a GVL effect.

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REDUCED INTENSITY CONDITIONING (RIC) AND HEMATOPOIETIC STEM CELL TRANSPLANTATIATION (HSCT) USING PHOTOPHERESIS (ECP), FLUDARABINE, AND TARGETED SINGLE DOSE BUSULFAN AS AN OUTPATIENT PROCEDURE IN CHILDREN: PRELIMINARY RESULTS

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ECP is an immunomodulatory therapy for immune-mediated disorders, including GVHD. We hypothesize that combining ECP with RIC prior to and following HSCT will reduce incidence of GVHD and 100-day transplant related mortality (TRM) without affecting time to engraftment. Ten children have been enrolled with a mean age of 14 years (10 – 17), with CML (n=2), severe aplastic anemia (SAA) (n=4), ALL in CR2 (n=1), peripheral T-cell lymphoma (n=1), and relapsed Hodgkin's after autologous transplant (n=2). Stem cell sources included peripheral blood from matched related (n=6), mismatched related (n=1), and matched unrelated (n=3) donors. Conditioning included 2 weekly treatments of ECP (treatment=2 consecutive days) beginning two weeks prior to transplant, fludarabine 30mg/m2/d (days -6 to -2) and targeted dose busulfan to reach a daily AUC of 4000 μmol*min (days -5, -4); GVHD prophylaxis was: MMF, CSA, and weekly ECP once total chimerism reached 50% through day +100. Median follow-up is 100 days (33 – 446). Full engraftment (>95% total donor chimerism) was achieved by a median of 29 days (12 – 81) in 9/10 patients. Two required immune modulation for falling chimerism; 1 responded to removal of immune suppression, 1 required donor lymphocyte infusion. Major complications were infectious: central line infections (n=5, with 1 episode of hypotension), adenovirus antigenemia (n=1), and CMV reactivation (n=5/5 at risk); they underwent pre-emptive treatment without development of disease. There was 1 TRM: a patient with heavily treated SAA died of fungal infection after no engraftment. Acute GVHD only occurred in those undergoing immune modulation (2/10, grade 3). Of 8 evaluable, 2 developed extensive cGVHD; 1 limited. There were no episodes of veno-occlusive disease or mucositis; none required parenteral nutrition. Patients were admitted to the hospital for 2 days during the

preparative regimen (IV busulfan); from day 0 to 100 patients were admitted for a median of 11 days (0 – 25). We conclude that in children, using ECP as part of RIC and GVHD prevention is well tolerated and feasible, time to engraftment is acceptable, and complications are minimal as evidenced by short inpatient stays. However, immune suppression appears to be excessive given the rates of CMV reactivation and declining chimerism of two patients while on ECP. ECP appears to be effective in preventing aGVHD, as the only patients who developed aGVHD were those requiring immune modulation.

Table #1

	Daignosis	Donor	Chimerism > 50% (days)	Chimerism > 95% (days)	aGVHD	cGVHD	Disease Status
1	CML	Matched Sibling	13	29	None	None	NED following DLI & Imatinib for rising BCR/ABL, day +446
2	SAA	Matched Sibling	8	26	None	Extensive	NED, day +390
3	CML	Matched Sibling	26	63 (Following DLI)*	Grade 3	Extensive	NED, day +340
4	SAA	Mismatched Related	12	81 (Following removal of immune supression)*	Grade 3	Limited	NED, day +284
5	Relapsed ALL (CR2)	Matched Sibling	12	28	None	None	Relapse, day +100
6	Recurrent HD (CR3)	MUD	20	33	None	None	Relapse, day +100, died of PD
7	SAA	Matched Sibling	7	12	None	None	NED, day +187
8	Recurrent HD (CR2)	Matched Sibling	28	47	None	None	NED, day +124
9	SAA	MUD	No engraftment	No engraftment	None	N/A	Died day +37, fungal infection
10	Peripheral T-cell Lymphoma	MUD	12	12	None	N/A	NED, day +33

*Interventions due to falling chimerism

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COMBINED TACROLIMUS (FK-506) AND MYCOPHENOLATE MOFETIL (MMF) FOR GRAFT-VERSUS-HOST DISEASE (GVHD) PROPHYLAXIS IN CHILDREN UNDERGOING CORD BLOOD TRANSPLANTATION (CBT)

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Background: Effectiveness of FK-506 and MMF combination as prophylaxis for GVHD is still under investigation. We studied the feasibility and effectiveness of this regimen in preventing GVHD in children undergoing matched unrelated donor (MUD) CBT to avoid methotrexate and methylprednisone toxicity.

Patients and Methods: Between 5/1/04-9/1/06, 11 children undergoing MUD CBT have received FK-506 and MMF combination as prophylaxis for GVHD. Thymoglobulin (Rabbit ATG, 2.5-5mg/kg total) was used as part of the conditioning regimen. Both myeloablative (n=9) and non-myeloablative (n=2) preparative regimens were used and majority of the children (n=7) have received one antigen mismatch (Class I/II-antigen disparate) CBT. FK-506, 0.015mg/kg IV every 12 hours (infused over 6 hours) was started on day-2 (trough level maintained 5-15 ng/ml),rather than as a continuous infusion. MMF was started on day +1 at 15mg/kg /dose IV q 8-12 hours and stopped on day +30, if there were no signs of GVHD. Both were converted to PO formulation at the time of discharge. MMF levels (active MPA) were monitored weekly.

Results: The regimen was well tolerated. Only major side-effect noted was hypertension in the first 2 patients, which was controlled with prophylactic anti-hypertensive use in subsequent patients. Tremors occurred in 2 patients and responded to MMF taper. No major neuro- or nephrotoxicity was noted. All children have engrafted (median=16 days). No patient has developed >Grade II GVHD (Glucksberg staging criteria). 6/11 patients (54.5%) had developed Grade I/II GVHD, limited only to skin and gut (1 pt.) that was steroid-responsive. Only 1/6 patients continued to have limited chronic GVHD of the skin (median follow-up: 255days ; range: 62-725 days). Immune-reconstitution was not delayed. MMF levels ranged from <0.5-5.7 mcg/ml. No correlation was seen between the MMF levels and the incidence of GVHD in this study.

Conclusion: FK-506/MMF combination is well tolerated, does not affect engraftment kinetics or immune-reconstitution and is efficacious in preventing GVHD in CBT.

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HHV-6 INFECTION FOLLOWING CAMPATH1H BASED REDUCED INTENSITY CONDITIONING (RIC) REGIMEN IN PEDIATRIC PATIENTS UNDERGOING SCT FOR NON-MALIGNANT DISORDERS

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Background: Human Herpes Virus 6 (HHV-6) infections have been recently recognized as complications of SCT in young patients. Limited information is available on patterns and impact of HHV-6 infection following RIC transplants using increased immunosuppression. We describe our multi-institutional experience with HHV-6 infections during SCT following a Campath IH based RIC regimen.

Patients and Methods: 12 patients underwent SCT for non-malignant disorders and received Campath 1H (33mg/48mg, day -21 and day-19); Fludarabine (150mg/m^2,day -8 to -4) and Melphalan (70 or 140mg/m^2, day-3) prior to stem cell infusion (BM/PBSC/CB) from related or unrelated donors. Two patients had also received Thiotepa (10mg/kg on day-2). Acyclovir was used for viral prophylaxis. Patients were tested for HHV-6 pre-transplantation by a PCR based assay. Patients were monitored by HHV-6 PCR if they had fever, delayed engraftment/myelo-suppression, rash or malaise. Serial quantitative real-time PCRs (viral load) data was collected in some of these patients (Viracor Laboratories, Missouri) to gauge response to treatment.

Results: All 12 patients undergoing SCT were negative for HHV-6 by PCR pre-transplant. 7 patients (58.3%) had HHV-6 detected during the course of their SCT. Infections occurred during the first month (n=4), second month (n=1), at 4 months (n=1) and at 6months (n=1) post-SCT. Common symptoms encountered were fever, rash and pancytopenia/delayed engraftment. No case of pneumonitis or encephalitis was seen. HHV-6 infection responded rapidly to Foscarnet or Gangcyclovir with decrease in viral load and was associated with no deaths. No HHV-6 infections were seen after immune-reconstitution (6 months).

Conclusions: Infection with HHV-6 infection is more frequent following Campath based regimen. Most of the infections occur within the first 4 weeks and may delay engraftment; but late infections are also common due to intense immunosuppression. Therefore, close monitoring and early treatment is advocated in pediatric patients receiving Campath 1H.

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UNRELATED DONOR UMBILICAL CORD BLOOD TRANSPLANT FOLLOWING INTRAUTERINE TRANSFUSIONS FOR TREATMENT OF ALPHA THALASSEMIA MAJOR

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Homozygous α^0-thalassemia (deletion of all 4 α-globin genes) results in Hb Bart's (γ_4 tetramers). Almost universally fetal death from hydrops occurs prior to diagnosis, therefore not allowing the opportunity for treatment. Advancement of maternal-fetal medi-