remains a serious problem. New strategies for CMV prophylaxis & therapy, and studies of the determinants of CMV-specific immune recovery, are a priority for this patient population.

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Long Term Outcomes of Pediatric Patients with Sickle Cell Disease Who Underwent a Reduced Intensity T Cell Depleted Haploidentical Transplantation

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Allogeneic hematopoietic stem cell transplant (HCT) is a curative therapy for sickle cell disease (SCD). However, majority of patients lack a matched sibling or unrelated donor. The use of a partially matched related donor would provide donors for majority of the patients. We report the results of 8 consecutive pediatric patients with SCD who had a prior stroke, who underwent a T cell depleted HLA-haploidentical HCT using a reduced intensity conditioning regimen without total body irradiaiton. The median age was 7±5 yrs (4-17) with the median follow up of 7±3 yrs (3-9). The first 3 patients received fludarabine (150-200 mg/m^2), thiotepa (10mg/kg), targeted busulfan (900 ng/ml for 4 d), rabbit antithymocyte globulin (rATG) (10mg/kg x 3 d), and OKT3 (0.1mg/kg maximum over d +1 to +20). The subsequent 5 patients received busulfan (900ng/ml x 4 d), thiotepa (10mg/kg), cyclophosphamide (200 mg/kg) and OKT3 (0.1mg/kg max on d-10 to +17) as well as mycophenolate mofetil for graft versus host (GVHD) prophylaxis. The product consisted of a CD34$^+$ selected product infused on d0 and a CD3$^+$ depleted product infused on d+1. The infused products had a mean total nucleated cell (TNC) of 450±680 x 10^6 kg (10-1890), CD34$^+$ cells of 25.4±16.3 x 10^6/kg (6-57) and CD3$^+$ cells of 0.07±0.07 x 10^6/kg (0.006-0.168). All 8 patients achieved donor engraftment with a median of 12 d (10-14). Donor engraftment was maintained in 5 patients, with one patient requiring a second stem cell infusion. The median time to rejection for the 4 patients was 30 d (22-44) after HSCT. Of the 5 engrafted patients, 4 patients developed acute GVHD (3 with grade I-II and 1 with Grade III). Of the 5 engrafted patients, 3 developed chronic GVHD (1 with limited and 2 with extensive). The 2 patients with extensive GVHD died of complication of GVHD. The 3 surviving patients have been transfusion independent with no evidence of SCD related complications. Indices of hemolysis decreased after HCT with decreased reticulocyte count, bilirubin and LDH. The median hemoglobin increased from 9.6 ± 0.6 to 13.6 ± 2. Renal and cardiac were stable after HCT. MRI showed no new infarct or vessel occlusion. In summary, 3 patients survived free of SCD, 2 engrafted but died of complications from GVHD and 3 had recurrent SCD after graft rejection. Despite good outcomes in 3 of the 8 patients, rejection, chronic GVHD and transplant related mortality were significant problems. Recently, Bolaños-Meade et al. published the result of haploidentical HCT for SCD using post-transplant cyclophosphamide. Both regimens encountered graft failure, however GVHD and mortality was not as prevalent as our report. Though limited, our data suggest that for patients with SCD, graft-versus-host disease prophylaxis after haploidentical HCT with high dose cyclophosphamide may be a safer regimen and further studies are warranted.

Table 1
Patients and donors characteristics

Patient number	Age (years)	Sex	Donor Age (years)	Donor Sex	Source of Progenitor	Age Difference (years)	Disease	Acute GVHD	Chronic GVHD	Patient Status
1	6	Male	62	Male	PB	56	ALL	Yes	No	Full chimerism/Alive
2	5	Male	60	Female	PB	55	TM II	Yes	No	Full chimerism/Alive
3	2.5	Female	45	Female	BM	42.5	LAD I	Yes	Yes	Full chimerism/Alive
4	5.5	Female	63	Male	PB	57.5	FA	Yes	No	Full chimerism/Alive
5	7	Male	75	Female	PB	68	TM II	Yes	No	Rejected/Dead
6	2	Female	60	Female	PB	58	AML	No	No	Rejected/Alive
7	11	Male	69	Male	PB	58	FA	No	No	Full chimerism/Alive
8	8.5	Female	68	Male	PB	59.5	CD_4 dif.	Yes	Yes	Full chimerism/Alive
9	9.5	Female	46	Female	BM	36.5	AML	Yes	No	Rejected/Dead
10	2	Male	48	Female	BM	46	MPS I	Yes	No	Full chimerism/Alive
11	1	Male	74	Male	PB	73	LAD I	Yes	Yes	Full chimerism/Alive
12	9	Male	62	Male	PB	53	TM III	No	No	Rejected/Alive
13	0.25	Female	71	Male	PB	70.75	SCID	Yes	No	Full chimerism/Alive

PB: Peripheral Blood, BM: Bone Marrow, ALL: Acute Lymphoblastic Leukemia, TM: Thalassemia Major, LAD: Leukocyte Adhesion Deficiency, FA: Fanconi Anemia, CD_4 dif: CD_4 deficiency, AML: Acute Myeloid Leukemia, MPS: Mucopolysaccharidoses, SCID: Severe Combined Immunodeficiency.

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Grandparents Are Invaluable People as HLA-Matched Donors in Hematopoietic Stem Cell Transplantation

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Background: HLA matching is one of the most important factors affecting patients' prognosis after hematopoietic stem cell transplantation (HSCT). Currently when there are no HLA-match siblings, transplantation centers try to find unrelated HLA-matched donor through bone marrow and cord blood registries. However, few studies showed that searching extended families such as parents, grandparents, aunts and uncles for an appropriate donor is useful.
Methods: This is a retrospective study from our center in which the patients who underwent HSCT of any diseases and their grandparents were as donors included in the study. The principal data including graft-versus-host-disease

(GVHD) occurrence, overall survival (OS) and disease free survival (DFS) were used as main outcomes in these transplantations.

Results: Thirteen patients including 7 boys and 6 girls with mean age 5.33 years (range: 0.25-11) were detected through the data registry bank. The mean donors' age was 61.77 years (range: 45-75) and mean age difference was 56.44 years (range: 36.5-73) [Table 1]. Regarding GVHD occurrence, 10 patients did experience acute GVHD [Table 1]. With median follow-up of 16 months OS and DFS were 83% and 69% respectively.

Conclusion: Although searching the extended family for HLA-matched donors especially among grandparents seems very uncommon, this can increase the chance of well-tolerated and success transplantation especially in regions where consanguinity is common.

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Contrasting Patterns of Alloreactivity Amongst Malignant and Nonmalignant Diseases Receiving Haploidentical PBSC GRAFT and Post-Transplant Cyclophosphamide

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Haploidentical donor is often the only source of graft for most patients in developing countries due to lack of suitably matched donors from international registries and the prohibitive cost involved in the procurement process. We conducted a pilot study with posttransplant cyclophosphamide and haploidentical PBSC graft. The donors selected were either mother or NIMA mismatched siblings irrespective of NK cell alloreactivity. The conditioning protocol was developed based on Johns Hopkins regimen of Fludarabine and low-dose Cyclophosphamide pre-transplant with escalating dose Melphalan 70-140 mg/m2 replacing 2 Gy TBI. Post-transplant Cyclophosphamide was administered 72hrs after infusion of the graft at 50 mg/kg twice at 24 hrs interval followed by Cyclosporine and MMF.

8 patients (median age-16, 5-43) underwent Haplo-HCT; 5 patients with refractory AML had a median BM blast count of 50% (20-80%) having failed at least two lines of treatment. Two patients had severe aplastic anemia and one had thalassemia. The ones with AML received high dose AraC and mitoxantrone from day-14 to -12. The conditioning was tolerated without any major non-hematological toxicity. The median CD34 was 7.06 x 10^6/kg (range 5.05-11.06) and CD3 was 36 x 10^7/kg (range 8-79).

All patients engrafted with neutrophils $>$ 500/μl on day +14 (range12-17) and platelet count $>$ 20,000/μl on day +15 (range 9-38) with $>$ 95% donor chimerism on day +30 with morphological CR. None of the patients with leukemia developed de-novo GVHD. Three relapsed between days 100-150 and two of them achieved a CR following a second transplant from the same donor. Two patients in CR died of multi-drug resistant gram-negative bacterial sepsis. All three patients with non-malignant disease developed unexpected alloreactivity. One patient with SAA developed severe refractory HLH on day +21 and the other a periengraftment idiopathic pneumonitis. Both succumbed to their complications. Another patient with thalassemia developed severe HLH on day 60 related to EBV, whilst on treatment for grade 3 acute GVHD. In multiply treated advanced leukemia, the introduction of the PBSC graft without any immunosuppression for 72 hours probably allowed a strong GVL effect and post-transplant cyclophosphamide was successful in abrogating clinically significant GVHD. In sharp contrast, all the three patients with non-malignant disease experienced early and unexpected alloreactivity with the same protocol. We speculate that the lack of previous cytotoxic therapy might have left them vulnerable to such alloreactivity mediated by residual host APCs.

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Second Haploidentical PBSC Transplantation From the Same Donor After Early Relapse without GVHD in Patients with Acute Leukemia

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Early relapse (within 120 days) of high risk acute leukemia after any form of allogeneic HCT, augers a poor outcome. We report our experience with 4 such patients who relapsed within 120 days of undergoing a haploidentical PBSCT with or without posttransplant cyclophosphamide. None developed GVHD even with prophylactic DLI. Three had relapsed refractory AML at the time of the first haploidentical HCT and one was transplanted for high risk ALL. The marrow blast count at the time of second transplant was 20-80%. The patients were conditioned with Fludarabine or Cladribine with melphalan (70 mg/m^2) or oral busulfan (4mg/kg) and did not receive any GVHD prophylaxis. Cryopreserved PBSC graft was infused with CD34+ cells varying between 2-3 x 10^6/kg. All the patients engrafted within 14 days and all developed grade 2-3 acute GVHD by day 10. GVHD was treated with steroids and etanercept along with tacrolimus and MMF. One patient succumbed early to multidrug resistant Klebsiella sepsis on day 15. The BM on day 30 in the other 3 patients showed 100 % donor chimerism with MRD levels of less than 0.1% on flow cytometry. At a short follow up of 90 days from the second haploidentical HCT, two out of three patients are alive in CR with tapering immunosuppresion and the other was lost to follow up after 50 days. Our data shows that a haploidentical graft can induce a potent enough GVL effect to induce remission even in refractory leukemia. These findings highlight the fact that even if a patient with refractory leukemia relapses early after an allogeneic HCT without developing GVHD, they deserve a second graft from the same donor with minimally toxic conditioning with the purpose of inducing a GVHD/GVL effect.

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Decision Analysis of Donor Selection in Allogeneic Stem Cell Transplantation for Patients with Acute Leukemia in First Remission-Related Donor with HLA-1 Antigen Mismatch in the GVH Direction vs. HLA-8/8 Allele-Matched Unrelated Donor

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