Table 1: Relapse rates in patients with MC and FD chimerism in whole BM, PB, and subsets

Chimerism	N*	Mixed chimerism (MC)		Full donor chimerism (FDC)		EFS
		N with MC	**Relapse rate in pts with MC**	**N with FDC**	Relapse rate in pts **with FDC**	Log Rank **P value**
Whole BM	39	26	35%	13	15%	0.1
BM - CD3 subset	29	24	25%	5	0%	0.09
BM - Leukemia specific subset	**33**	**17**	**35%**	**16**	**6%**	**0.002**
BM- CD34 subset	31	21	33%	10	10%	0.04
All BM subsets	**37**	**30**	**33%**	**7**	**0%**	**0.03**
Whole PB	42	22	32%	20	25%	0.8
PB -CD3 subset	42	31	32%	11	18%	0.6
PB - Leukemia specific subset	42	19	26%	23	30%	0.8
All PB subsets	43	35	34%	8	12%	0.14

* Number of patients who had early post-HCT chimerism test done on a specific subset.

immunosuppression (FWI) and donor lymphocyte infusions (DLI) in children receiving HCT for leukemia. We enrolled 43 patients. Donors and stem cell sources included matched related (49%), matched unrelated (30%) and mismatched unrelated donors (21%) of BM (53%) and peripheral blood (PB) (47%). Chimerism analyses on whole PB and BM and subsets were done using a semi-quantitative PCR-based method (1% sensitivity), on day 32.5±SD8 (PB) and day38±10 (BM). If mixed chimerism (MC) was found in any PB or BM subset on 2 tests, FWI over 2-4 weeks was initiated, followed by DLI if MC persisted. The end point for IT was full donor (FD) chimerism in all PB subsets or development of GVHD. Patients with GVHD or FD chimerism in all subsets were assigned to the observation group (N=12); patients with MC in any subset were assigned to the IT group (N=26). 15 patients received FWI and DLI and 11 received FWI only. Five patients could not be assigned to either group due to early toxic death (N=1) or relapse (N=4). Follow-up of living patients is 28.8±9.7 months. Events included relapse (N=13) and toxic death (N=2), one of which was intervention related, resulting in 4% treatment-related mortality. Estimated 36-mos EFS is 83±10% for the observation group, 54±14% for the IT group and 56±10% for the entire cohort, including unassigned patients. Acute and/or chronic GVHD developed in 5/26 (19%) patients following IT. Residual disease (RD) prior to HCT remained a predictor of EFS. Despite IT 7/11 patients with RD and 6/26 without, developed relapse (Log Rank $p<0.001$). Early post-HCT BM chimerism was better predictor of EFS than PB chimerism (Table 1). We recommend that post-HCT IT continues until 100% chimerism in all BM subsets is achieved.

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Durable Engraftment, Correction of Genetic Defects and Prevention of Veno-Occlussive Disease, Following Blood and Marrow Transplantation with an HLA-Matched Sibling DONOR, Using a Reduced Toxicity Conditioning Regimen with Busulfan, Reduced Dose Cyclophos

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Background: Genetic lymphohematopoietic diseases have been effectively cured by performing allogeneic blood and marrow transplant (BMT) from a histocompatible sibling, following a standard conditioning regimen with busulfan (BU), cyclophosphamide (CY), and antithymocyte globulin (ATG). However, the high levels of transplant related mortality (TRM) and morbidity with this regimen limits its more widespread use as curative therapy.

Objective: To determine the safety, donor chimerism and complications associated with de-escalation of CY, in a reduced toxicity conditioning regimen with fludarabine and alemtuzumab, prior to HLA-matched sibling donor transplantation among pediatric recipients with genetic lymphohematopoietic diseases.

Methods: Eligible patients were consented at Children's Hospital Los Angeles, Stanford Hospital and Lucile Packard Children's Hospital between 2008 and 2013. The conditioning regimen consisted of Busulfan 16 mg/kg, Cyclophosphamide 105 mg/m2 Fludarabine 105 mg/m2, and Alemtuzumab 52 mg/m2. Graft versus host disease prophylaxis consisted of steroids and a calcineurin inhibitor.

Results: The study population was 68% female with a median age of 5.25 (± 5.9 years). Patients pre-transplant diagnoses included Sickle Cell Disease (n=7), Thalassemia (n=4); Kostmann's Syndrome (n=2), Chronic Granulomatous Disease (n=1), Chediak Higashi syndrome (n=1), hemophagocytic lymphohistiocytosis (n=2), Cartilage Hair Hypoplasia (n=1), Diamond Blackfan Anemia (n=2), and Hurler's syndrome (n=2). The median total nucleated cell count (TNC) and CD34 dose was 4.6x108 (± 2.26x108) cells/kg and 8.5x106 (± 5.2x106) cells/kg respectively. All patients had an initial donor chimerism >90% (median 99%). The median time to neutrophil engraftment (>500 cells/μL) and platelet engraftment (>20K cells/microliter) were 19 (±9.7) and 23.5 (± 26.2) days respectively. One patient required a stem cell boost on day +83 (poor count recovery due to CMV). There were no cases of veno-occlussive disease or Grade III/IV acute or extensive chronic GVHD. Infectious complications (Figure 2) included CMV viremia (n=5), EBV viremia (n=1), mucoromycosis (n=1) and adenoviremia (n=1); two patients expired, one from pneumonitis (EBV viremia) and the other from mucormycosis. Overall survival (OS) at 100 days was 95%; with a median follow up of 1 (± 2.05) years, the OS is 90%, with all patients sustaining high-level donor chimerism and a median Lansky/Karnofsky score of 100. Conclusion: A reduced toxicity conditioning regimen with reduced doses of CY achieves durable engraftment of stem cells from related donors among patients with genetic lymphohematopoietic diseases and low rates of transplant related mortality and morbidity. Longer follow-up is required to assess for a potential reduction in late effects associated with this regimen.