there is still a dichotomy in outcome for patients who present in Chronic Phase (CP) versus Accelerated Phase (AP) or with acute leukemic blast crisis (BC) CML. For patients with CP-CML prognosis is excellent when treated with TKIs alone while for patients with AP- or BC-CML, the goal of therapy is to get back into chronic phase CML and then proceed to an allogeneic bone marrow transplant (allo-BMT). Even with this intensified approach, patients with advanced CML historically have had a poor prognosis with an OS of ~65% one year after allo-BMT. In the pre-TKI era roughly 20% of patients with CML would progress to blast crisis. This has declined to ~1% in the TKI era, but the overall survival of these patients has not changed.

Methods: After obtaining IRB approval, we reviewed the medical records of all patients evaluated for allo-BMT for CML at our institution between January 1, 2010 and June 30, 2013. There were five children who presented with CML in accelerated phase or blast crisis.

Results: Five patients developed advanced stage CML during the observed period. Ages ranged from 12-18 years old at the time of transplant (median age 13). The male:female ratio was 4:1. 4/5 presented in lymphoid blast crisis and 1/5 in accelerated phase. All patients were started on imatinib though two required a second or third line TKI to achieve stable phase prior to transplant. Prior to transplant, all patients were in at least a morphologic and cytogenetic remission; 3/5 also were in a molecular remission. 4/5 patients received a matched unrelated donor transplant; the other underwent a matched sibling transplant. Conditioning was TBI (1440 cGy) and Cyclophosphamide. GVHD prophylaxis was Cyclosporine and Methotrexate with Prednisone added for unrelated donors per our institutional standard. Median day of engraftment was + 24. 1/5 patients developed stage 2-4 aGVHD and none developed grade 3-4 aGVHD. TKI's were restarted in all patients (median day 114) with a goal of continuing until 2 years post transplant. One patient developed joint pain and night sweats which resolved with dose reduction, another myelosuppression which resolved with TKI holiday and dose reduction. All patients are alive and remain in molecular remission with undetectable BCR-ABL transcript with an average duration of remission of 435 days [190-1347].

Discussion: The outcomes of children with CML presenting in blast crisis in the era of TKIs has not been previously documented. The use of TKI's pre- and post-transplant may lead to improved disease free survival for this group. Disease control prior to SCT and close monitoring remain essential for optimal outcome.

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Repeated Dosing of Autologous Cord Blood Is Safe and Feasible in Babies with Congenital Hydrocephalus

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Background: Congenital hydrocephalus affects 0.3 to 1.5 per 1000 live births, is typically diagnosed *in utero*, and may occur in isolation or as a result of a genetic or other underlying cause. Current standard therapy involves ventriculoperitoneal shunt placement shortly after birth to divert the flow of cerebrospinal fluid and decrease intracranial pressure. However, survivors face the sequelae of brain injury resulting from the prolonged hydrocephalic state *in utero*. Umbilical cord blood (CB) has been shown to lessen the clinical and radiographic impact of hypoxic brain injury and stroke in animal models. Based on this data, we began to treat infants with congenital hydrocephalus with multiple autologous CB infusions during the first 1-2 years of life to determine the safety and feasibility of the procedure.

Methods: Parents of children diagnosed with congenital hydrocephalus *in utero* elected to store their child's CB in a private or public bank as a directed donor. CB units were deemed eligible based on results of, cell count, sterility, potency and infectious disease screening. On the day of infusion, CB units were thawed and washed in dextran-albumin and infused via peripheral IV in the outpatient clinic after premedication with acetaminophen, diphenhydramine, and methylprednisolone. When possible, CB units were fractionated to allow for multiple doses over time.

Results: Since 2006, 70 patients with congenital hydrocephalus have been treated with 129 autologous CB infusions. Most babies received repeated doses, for a total of 2 (N=24), 3 (N=12), or 4 (N=4) infusions. Median age at the first infusion was 2 months (range 6 days – 4 years). Median cell doses per infusion were TNC $2.0x10^7$/kg (range 0.1-$13.3x10^7$/kg) and CD34 count 0.7 $x10^5$/kg (range 0.04-$6.4x10^5$/kg). The infusions were well tolerated, with no acute or chronic adverse events. Anecdotally, parents report that their children are making developmental gains after autologous CB infusion.

Conclusions: Autologous CB infusion is safe and feasible in babies with congenital hydrocephalus. Since the diagnosis is typically made *in utero*, there is sufficient time to plan for CB collection prior to delivery. As the patients are so young and small at the time of treatment, a single CB unit can often be fractionated to permit a multiple dosing strategy. While infants make developmental progress after the infusions, additional studies are necessary to determine if these gains are related to the CB treatment.

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A Single Center Experience of Haploidentical Stem Cell Transplants in Pediatric Diseases

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In Asia, where the chance of finding a HLA 10/10 allele matched adult donor in a short time is low; stem cell donors including mismatched unrelated cord blood and family haploidentical stem cell donors are feasible alternatives. Between Jan 2007 and Sep 2013, a total of 14 haploidentical stem cell transplants (SCT) in 13 patients were performed in our Pediatric SCT Program. Of the 9 boys and 4 girls, SCT was performed in 2 for non-malignant diseases (1 Hurler's, 1 Hepatitis Associated Severe Aplastic Anemia) and 11 for very high risks malignancies (4 ALL, 3 AML, 3 Lymphoma, 1 MDS/RAEB). Preparative regimen was tailored to pre-morbid status and was reduced intensity (N=6) which included single TBI 2 Gy ± Fludarabine/ Cyclophosphamide or full preparation (N=8) with Fludarabine, Thiotepa, Melphalan, ATG (Thymoglobulin), Rituximab and TLI 6-8Gy or TBI 6Gy.

Table

SCT	Diagnosis	Status at SCT	Preparative regimen	TBI/ TLI dose	Outcome	Survival at last follow-up (Oct 13)
1	Hurler's	Advanced disease	Full prep/CD34 selected PBSCT	-	Engrafted D+10; secondary graft failure; auto-reconstituted	Alive at 2 years/ lost to follow-up
2	Hepatitis Associated Aplastic Anemia	Post liver transplant/ prolonged aplasia	Reduced intensity/ T- deplete BMT	-	Engrafted D+14, secondary graft failure; auto-reconstituted	Alive at 4 years/ lost to follow-up
3	Hodgkin Lymphoma	3rd relapse	Reduced intensity/ *T replete* BMT	TBI 2Gy	Engrafted D+13; remission D+60; relapsed D+98	Died of disease D+192
4	Therapy- Related AML	1st remission	Reduced intensity/ *T- replete* BMT	TBI 2Gy	Engrafted D+14; remission D**+**21; relapsed D+61	Died of disease 0+164
5	Therapy- Related AML	Progressive disease/ NK cell therapy/ 2nd SCT	NK conditioning/ T-deplete PBSCT	TBI 2Gy	Engrafted D+9, remission D+2l, MRD relapsed D+176/ DLI & NK cell therapy	Alive, D+379
6	B Lineage ALL	2nd remission	Full prep/T- deplete PBSCT	TLI 8Gy	Engrafted D+10; remission since 0+21	Alive, D+365
7	B Lineage ALL	2nd remission	Full prep/T- deplete PBSCT	TLI 8Gy	Engrafted D+10; remission since D+21	Alive, D+365
8	Anaplastic Large Cell Lymphoma	Progressive disease	Reduced intensity/ T- deplete PBSCT	-	Engrafted D+1; remission since D+7, severe GVHD	Alive, D+200
9	Second AML	Progressive disease/ NK cell therapy/ 3rd SCT	Full prep/T- deplete (TCRαβ) PBSCT	TLI 6Gy	Engrafted D+10; remission 0+21: relapsed 0+60	Died of regimen-related tonicity (encephalopathy)/ disease D+90
10	Burkitt's lymphoma	Progressive disease/ NK cell therapy	Full prep/T- deplete (TCRαβ) PBSCT	TBI 6Gy	Engrafted D+8; remission D**+**21; relapsed D+31/ DLI therapy	Alive, D+97
11	Early T Cell All	1st remission	Full prep/T deplete (TCRαβ) PESCT	TBI 6Gy	Engrafted D+8; remission	Died of regimen- related tonicity (hepatic failure) D+21
12	MDS/RAEB	Evolving disease	Full prep/T- deplete (TCRαβ) PBSCT	TLI 6Gy	Engrafted transiently; graft failure	Alive, D+41, in 2nd SCT
13	**t lineage** AH	2nd remission	Full prep/T deplete (TTCRαβ) PBSCT	TLI 6Gy	Engrafted D**+**10, remission D+21	Alive, D+34
14	MDS/RAEB	Graft failure/ 2nd SCT	Redund intensity/ *T- replete* BMT	TBI 2Gy	Awaiting engraftment	Alive, D+13 of 2nd SCT

Ex-vivo T cell depletion using either CD3 (N=6) or TCRab (N=4) depletion was performed in 10 SCT and CD34 positive selection in 1. The other 3 patients received T-replete SCT with post-transplant cyclophosphamide as per Hopkins protocol. For the 11 T-deplete SCT, the median CD34 ($x10^6$/kg) was 8.8 (range, 3.4-24.2) and CD3 ($x10^4$/kg) was 5 (range, 0-11). For the 3 T-replete SCT, the median TNC ($x10^8$/kg) was 2.9 (range, 2.9-4.2); CD34 ($x10^6$/kg) was 3.9 (range, 1.4-5.5) and CD3 ($x10^8$/kg) was 0.4 (range, 0.2-2.9). For the 2 patients with non-malignant diseases, both suffered secondary graft failure, auto-reconstituted and survived. For the 11 patients with high risk cancers; 6 had progressive disease at time of SCT; 4 are surviving (1 in remission, 3 with disease) and 2 died of disease. Of the 5 patients entering SCT in remission; 3 are alive and in remission; 1 died of disease and another of regimen-related toxicity. In 11 T-deplete SCT, viral reactivations of CMV, Adenovirus, EBV, BK virus occurred in 8, 3, 3, and 2 patients, respectively. The preliminary experience of haploidentical SCT in our small cohort of patients is encouraging with no infective mortality and good engraftment rates even for patients entering SCT with bulky disease. 'Graft versus leukemia/ lymphoma' effects are evident and may be exploited further through adoptive cell therapy in post-transplant settings to achieve more durable remissions.

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Fludarabine, Busulfan and Melphalan Conditioning in Pediatric Myeloid Malignancies Undergoing Hematopoietic Stem Cell Transplantation

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Standard conditioning regimes for myeloid malignancies are TBI or Busulfan-based with Cyclophosphamide. The reported event-free survival (EFS) is 40-60% and transplant-related mortality (TRM) of 4-30%. We designed a regime of Fludarabine, Busulfan and Melphalan (FluBuMel) in an attempt to increase the survival rate without increased TRM.

Methods: Retrospective review of pediatric patients with myeloid malignancies who underwent HSCT at our institution from September 2005 to September 2010.

Results: There were 19 patients who underwent HSCT in the time period. Median age is 5 (*range*, 1-20) years. There were 15 patients in CR1, 2 patients in CR2 and 2 patients not in CR. Patients received Fludarabine (120mg/m2) + Busulfan, weight-based dosing + Melphalan 140mg/m2 (15 patients) decreased to 70 mg/m2 (3 patients), and 1 infant with weight adjusted dose with Cyclosporine + ATG + MTX as GVHD prophylaxis. Average length of stay from Day 0 to discharge is 28 (*range,* 17-51) days. All patients achieved neutrophil recovery at median 14 (range, 10-46) days. All patients achieved > 95% chimerism (D+21) and 100% (D+100). Regimen-related toxicities were CTC grade 2-3 mucositis (89%), seizures (10%) and sinusoidal obstruction syndrome (SOS) (15%). Decreasing the Melphalan dose did not decrease the occurrence of mucositis and SOS in the 3 patients. Busulfan pharmacokinetics was not measured; all patients received phenytoin prophylaxis at therapeutic levels. The 100-day TRM is 0%. Overall, 47% had grade 1-2 aGVHD, 21 % grade 3-4 aGVHD and 76% had cGVHD. The 2-year overall survival (OS)