median age of 16 (2-80) months at transplantation with a median follow-up of 8.9 (3-22.6) years after last HCT. Post-transplant leukocyte IDUA enzyme levels below the lower reference were seen in 25% of patients due to mixed-chimerism or the use of a carrier donor. Following successful HCT, the clinical course of HS patients is strikingly improved, evident in all organ systems. Residual disease burden is present in the majority of the patients with high variability between patients. A better cognitive status at HCT was a major predictor for superior cognitive development after HCT (figure 1). Significant predictors for superior long-term outcome in all organ systems were the presence of "normal IDUA enzyme levels obtained after HCT" and a "younger age at transplantation". See the association between the leukocyte IDUA enzyme level obtained after HCT and surgical intervention for cord compression and growth, in figure 2 and 3 respectively.

Conclusion: Although HCT significantly improved the clinical course in HS patients, residual disease burden was observed in the majority of transplanted HS patients. Using exclusively non-carrier donors and accepting only full donor-chimerism will improve the prognosis of HS patients. Reducing the age at HCT through newborn screening could further improve the outcomes of HS patients after HCT.

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Allogeneic Stem Cell Transplantation for Children with Sickle Cell Disease Achieves Quality of Life Similar to Normal Children and Is Cost Effective

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Allogeneic stem cell transplantation (alloSCT) remains the only curative option for sickle cell disease (SCD). However, no systematic analysis exists comparing cost and quality of life (QOL) among this population. We investigated the QOL outcomes and health care utilization associated with alloSCT in children with SCD.

Internal financial data from 2002-2011 was analyzed retrospectively across two groups – post-alloSCT patients (>day+365) and patients with SCD referred for alloSCT and/or HLA typed. Surviving alloSCT recipients (A) and SCD controls (B) were surveyed with age appropriate Pediatric Quality of Life Inventory (PedsQL**a**) and EuroQOL (EQ-5D**a**) questionnaires. Group A siblings without SCD (C) were also surveyed as unaffected controls. Mean QOL scores were calculated for each group with a max score of 100. Utility scores were determined based on EQ-5D responses. These scores and costs for groups A and B were used to calculate cost per quality adjusted life month (QALM) for the cohort of patients surveyed. Wilcoxon test was used to determine statistical significance.

	Post-AlloSCT (>D+365, group A)	Controls (group B)	p-value
Mean outpatient visits	0.93	1.81	<0.0001
Mean outpatient cost ($)	831.10	739.2	0.840
Mean outpatient cost per QOL ($/QALM)	723.67	442.16	0.3506
Mean inpatient visits	0.02	0.52	<0.0001
Length of stay	0.06	1.05	<0.0001
Mean inpatient cost ($)	293.80	2050.20	0.115
Mean inpatient cost per QOL ($/QALM)	345.69	769.08	0.0023

Group A, B, and C had 16 (mean age - 14yrs), 19 (mean age - 12yrs), and 14 children (mean age - 14yrs), respectively. SCD therapy included hydroxyurea (group A n=8, group B n=10) and chronic transfusions (group A n=7, group B n=2). Mean PedsQL scaled scores were 83, 81, and 88, respectively. Mean EQ-5D visual analogue scale scores were 92, 87, 96, respectively. Mean utility scores were 0.87, 0.91, and 0.89, respectively. All QOL scores were not statistically significant ($p = 0.2638$). Healthcare utilization among groups A and B was previously reported (see details in table below). The median inpatient cost per QALM for group A was $0 and $514 for group B ($p = 0.0023$). Outpatient cost per QALM for group A was $353 and $236 for group B ($p = 0.3506$).

SCD patients' post-alloSCT QOL scores are similar to unaffected siblings, indicating that QOL has normalized. Controls with SCD also had scores similar to unaffected controls. However, a statistically significant difference exists in the inpatient cost per QALM post-alloSCT compared to controls with SCD. Outpatient was not significant which may reflect the limitations of the study period as post-alloSCT QOL and cost can change over time (Felder-Puig 2006; Majhail 2010). Ultimately, this study provides the first combined analysis of QOL as an outcome and the economic impact of alloSCT for pediatric SCD patients. Further analysis is ongoing to affirm that alloSCT is a beneficial and cost effective management option for patients.

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Low Day 100 Transplant-Related Mortality and Relapse Rate Following Clofarabine in Combination with Cytarabine, Total Body Irradiation and Allogenic Stem Cell Transplantaiton in Children, Adolescents and Young Adults with Poor-Risk Acute Leukemia

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Background: Children, adolescents, and young adults (CAYA) with Acute Leukemia in third complete remission

(CR3), induction failure (IF) or refractory relapse (RR) have a poor prognosis. (Gaynon, BJH 2005, Wells, JCO 2003, Hochster/Cairo, BJH 2013) Clofarabine (CLO), a purine antimetabolite, has been shown to have synergy with cytarabine (Faderl, Blood 2005) and induce lasting remissions following CLO and busulfan-based conditioning and allogeneic hematopoietic cell transplantation (AlloHCT) in poor-risk AML. (Magneau, Blood 2011).

Objectives: This study seeks to determine the safety, day-100 treatment-related mortality (TRM), and relapse rate associated with a conditioning regimen of CLO, cytarabine, and Total Body Irradiation (TBI) followed by AlloHCT in CAYA with poor-risk ALL or AML.

Methods: This is a multi-center Phase I/II trial of a novel conditioning regiment of CLO (maximal dose 52mg/m^2/d achieved without dose limiting toxicity) x5d, cytarabine 1000 mg/m^2 x6d 4 hours post-CLO, and TBI (1200cGy) followed by AlloHCT from matched related or unrelated donors in CAYA with ALL or AML in CR3, RR or IF. GVHD prophylaxis consisted of tacrolimus and MMF. (Oswunko/Cairo, BBMT 2004, Bhatia/Cairo, BBMT 2010) Supportive care consisted of growth factor support, and CMV and fungal prophylaxis as previously described. (Waxman/Cairo, Ped. Transplantation 2009, Shereck/Cairo, Ped. Blood Cancer 2007, Roman/Cairo, Ped. Blood Cancer 2008) Donor chimerism was assessed by semi-quantitative PCR-based methods as previously described. (Geyer/Cairo, BJH 2011) The Kaplan-Meier method was used to determine the probabilities of engraftment, GVHD, TRM, and overall survival (OS).

Results: 30 patients, median age: 11.9 yrs (range 1.5 – 21.8); M:F 21:9, ALL:AML 27:3 (10 CR3, 3RR, 17 IF), 11 related donors, 19 unrelated donors (11 BM/PBSCs, 8 UCB). Median TNC and CD34 dose was 4.49x10^8/kg and 4.2x10^6/kg for BM/PBSCs and 4.8x10^7/kg and 3.4x10^5/kg for UCB. Probabilities of neutrophil, platelet engraftment, grade II-IV aGVHD and chronic GVHD were 100%, 93%, 47%, and 35% respectively. Median Day 100, 180, and 365 whole blood chimerisms were all 100%. Day 100 TRM was only 6.7%. The probabilities of relapse, 1-yr progression-free survival and OS were 27% (CI_{95}: 13-52%), 40% (CI_{95}: 23-57%), and 47% (CI_{95}: 28-63%) respectively in this poor-risk population.

Conclusions: These preliminary results suggest that this novel conditioning regimen including CLO dose 52 mg/m^2 with Ara-C and TBI followed by AlloHCT is safe and tolerated in CAYA with poor-risk ALL or AML. Our results are promising with respect to a low risk of day 100 TRM and relapse rate in this poor risk population. This approach should be considered in better risk CAYA patients with ALL/AML who require AlloHCT.

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Trend, Risk Factors and Outcome of Thrombotic Microangiopathy in Pediatric Hematopoietic Stem Cell Transplant Recipients: A Multi-Institutional Review

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Introduction: Thrombotic microangiopathy (TMA) is a rare but serious complication of hematopoietic stem cell transplantation (HSCT). Review of literature shows variable incidence of TMA following HSCT with high mortality but its true incidence and outcome in the pediatric population is not known. The purpose of our study is to estimate the incidence, prevalence and analyze the risk factors and outcome of TMA in children receiving HSCT.

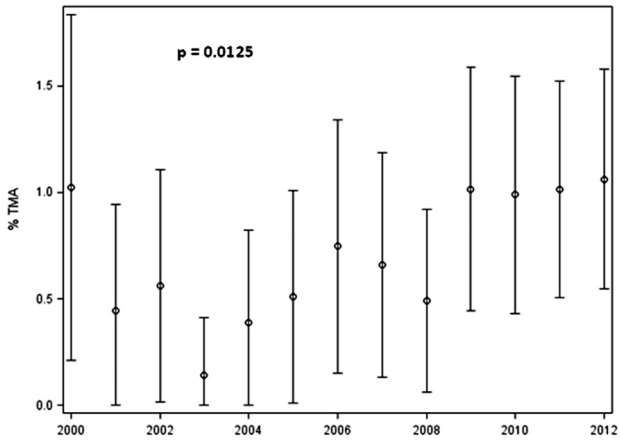

Figure 1. TMA trend in pediatric HSCT recipients

Figure 2
Demographics, risk factors and outcome of patients with TMA

Variable		Overall	No TMA	TMA	p
		12369	12276	93	
Age	0 – 1 years	1948 (15.7)	1939 (99.5)	9 (0.5)	0.109
	2 – 4 years	2819 (22.8)	2793 (99.1)	26 (0.9)	
	5 – 9 years	2775 (22.4)	2758 (99.4)	17 (0.6)	
	10 – 14 years	2339 (18.9)	2314 (98.9)	25 (l.1)	
	≥ 15 years	2488 (20.1)	2472 (99.4)	16 (0.6)	
Sex	Male	7239 (58.5)	7187 (99.3)	52 (0.7)	0.608
	Female	5130 (41.5)	5089 (99.2)	41 (0.8)	
Race	Non-Hispanic White	6974 (56.4)	6914 (99.1)	60 (0.9)	0.265
	Non-Hispanic Black	1450 (11.7)	1445 (99.7)	5 (0.3)	
	Hispanic	2304 (18.6)	2290 (99.4)	14 (0.6)	
	Asian	432 (3.5)	428 (99.1)	4 (0.9)	
	Other	1209 (9.8)	1199 (99.2)	10 (0.8)	
	Other	7560 (61.1)	7494 (99.1)	66 (0.9)	
HSCT Type	Autologous	4043 (32.7)	4031 (32.8)	12 (12.9)	<.001
	Allogeneic	8177 (66.1)	8099 (66)	78 (83.9)	
	Not specified	149 (1.2)	146 (1.2)	3 (3.2)	
Allo Source	Bone Marrow	3517 (43)	3492 (43.1)	25 (32.1)	0.045
	Peripheral blood	3195 (39)	3154 (38.9)	41 (52.6)	
	Cord blood	1475 (18)	1463 (18)	12 (15.4)	
CMV		958 (7.7)	940 (7.7)	18 (19.4)	<.001
HHV6		138 (1.1)	130 (1.1)	8 (8.6)	<.001
Fungal infection		835 (6.8)	814 (6.6)	21 (22.6)	<.001
GVHD		1471 (11.9)	1443 (11.8)	28 (30.1)	<.001
VOD		227 (1.8)	222 (1.8)	5 (5.4)	0.011
Hypertension		3288 (26.6)	3226 (26.3)	62 (66.7)	<.001
Renal failure		1280 (10.3)	1232 (10)	48 (51.6)	<.001
Plasmapheresis		119 (1)	91 (0.7)	28 (30.1)	<.001
Hemodialysis		385 (3.1)	363 (3)	22 (23.7)	<.001
Died		1531 (12.4)	1503 (12.2)	28 (30.1)	<.001