ORIGINAL RESEARCH

Transplant for Pediatric Patients with Acute Leukemia Outcomes in Florida

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ABSTRACT

Background: Risk of relapse following allogeneic hematopoietic stem cell transplantation (alloSCT) remains high for children with acute leukemia. Graft versus host disease (GVHD) is the major complication affecting post-alloSCT quality of life. GVHD-free relapse-free survival (GRFS) is a composite end-point defined as survival post alloSCT free of grade III/IV acute GVHD (aGVHD), moderate/severe chronic GVHD (cGVHD), or relapse. We present data on different outcome measures [overall survival (OS), RFS, acute GVHD (grade III/IV)/RFS (aGRFS), and GRFS] and infectious complications stratified by donor type, in a recent population-based retrospective pediatric cohort of children with hematologic malignancy (HM).

Methods: We analyzed 152 pediatric patients with median age of 10 years who underwent their first alloSCT between 2015 to 2020 in five participating c enters of the Florida Pediatric BMT and Cell Therapy Consortium. The patients were grouped by donor types.

Results: Groups were similar by age, gender, Karnofsky/Lansky Score, number of comorbidities and disease status at time of transplant. Recipients of matched unrelated donor (MUD) had improved outcomes by all measures, with statistical significance reached for 2-year OS when compared with 7/8 MMUD, and 2-year RFS and aGRFS when compared to 7/8 MMUD and haploidentical hematopoietic stem cell transplant (haploHCT) recipients.

Conclusion: Our analysis of outcomes by donor suggests that more pediatric data are needed before asserting all alternative donors as equal.

INTRODUCTION

Acute leukemia accounts for at least thirty percent of all pediatric cancers. Acute lymphoblastic leukemia (ALL) in pediatric patients following alloSCT has a five year overall survival (OS) of 80%, while acute myeloid leukemia (AML) has not exceeded an OS of 70%.[1,2] Often high risk relapsed/refractory ALL and high risk AML require allogeneic stem cell transplantation (alloSCT). Despite significant efforts toward risk stratified treatment, the risk of relapse for AML remains high at 30 to 45%.[3]

GVHD is a major complication of alloSCT affecting 40 to 60% of matched alloSCT patients and contributing to 15% of deaths.[4] Approximately 50% of alloSCT recipients will develop cGVHD despite their donor source and GVHD prophylaxis. GVHD is associated with a decrease in quality of life and requires prolonged immunosuppression leading to an increased risk of acquiring infections.[5]

Approximately 70% of patients will not have a matched related donor (MRD) and will rely on alternative sources such as matched unrelated donor (MUD), mismatched unrelated donor (MMUD), cord blood unit, or related haploidentical donor.[6] Techniques using post-transplant cyclophosphamide (PtCy) and ex-vivo graft manipulation have been developed to alleviate the burden GVHD brings to alloSCT recipients. PtCy has been used to decrease the risk of GVHD, particularly in human leukocyte antigen (HLA)-mismatched transplants, or in recipients of peripheral blood stem cell transplantation. Similar overall disease-free survival when compared with MUD recipients with hematologic malignancy (HM) following first transplantation has been reported in adults utilizing this technique.[7] Limitations of this approach include the need for high dose cytotoxic chemotherapy and associated long term effects, the continued need for GVHD prophylaxis, and prolonged immune suppression.[8]

Many retrospective studies in adults showed similar outcomes of alloSCT for HM between different alternative donor sources including haploidentical (haploHCT), 8/8 HLA-MUD, and a MMUD (≤7/8 HLA matched) using PtCy for GVHD prophylaxis.[9] Similar data are scarce for children undergoing alloSCT for HM.

GVHD-free relapse-free survival (GRFS) is a composite end-point and is defined as survival free of grade III/IV aGVHD, moderate/severe cGVHD, relapse and or death post alloSCT. A recent publication demonstrated that GRFS at 1 year post alloSCT in pediatric patients with acute leukemia was 29% in 7/8 MMUD bone marrow transplants and 38% in umbilical cord transplants.[10] GRFS data for haploHCT recipients in pediatric patients are limited.

From 2009 to 2019 the Center for International Blood and Marrow Transplant Research (CIBMTR) reported 4,244 pediatric allogeneic transplants were performed for HM with approximately 17.3% of these transplants being haploidentical transplants.

Our analyses revealed that pediatric transplant centers in Florida use haploidentical transplants with PtCy in almost one third (32.9%) of patients receiving alloSCT for HM. Here we provide data on different outcome measures [overall survival (OS), relapse free survival (RFS), acute GVHD (grade III/IV)/RFS (aGRFS), and GRFS stratified by donor type. We also provide data on the rates of GVHD and infections in a recent retrospective pediatric cohort of children with HM who received alloSCT in one of the 5 centers participating in Florida Pediatric Bone Marrow Transplant and Cell Therapy Consortium (FPBCC).

Hypothesis

Understanding the rate and risk factors for GRFS and infections, in pediatric patients undergoing alloSCT for HM, will provide information required for development of best practices on how to improve GRFS and reduce infectious complications.

METHODS

Data Collection

Retrospective analysis was performed on pooled data from the five transplant programs participating in the FPBCC who received a first alloSCT for HM from 2015-2020. Institutional Review Board approval was obtained from all five centers for this retrospective analysis. Data were obtained from the Enhanced Data Back to Center platform of the Center for CIBMTR with additional collection from participating centers of data related to relapse, GVHD and infections. All participants signed an informed consent for CIBMTR data collection. All patients included in this report were ages 1 to 28 years of age and received an alloSCT between January 2015 to December 2020. This age range represents some centers treating adolescent and young adults on the pediatric service.

Patients who received umbilical cord blood transplantations, single antigen mismatched related donor transplantation, and those with myelodysplastic syndrome were excluded from the analysis.

HLA Typing and Donor Types

Donors and recipients underwent high resolution HLA-typing, which included HLA-A, B, C, and DRB1. A related donor was considered haploidentical if they were mismatched at two or more antigens.

Supportive care and GVHD Prophylaxis

Due to retrospective nature of the study, GVHD prophylaxis and other supportive care was provided by individual institutional

guidelines. Blood product replacement and antimicrobial prophylaxis was per institutional practice. Post-transplant cyclophosphamide was given to all haploHCT recipients in this cohort per institutional practice. All centers performed weekly monitoring via PCR and treated viral infections aggressively.

Statistical Analysis

Descriptive statistics was used when summarizing patient and transplant characteristics. Continuous variables were described using median and range. Chi square statistics and Fisher's exact (FE) tests were used to compare homogeneity of categorical values. The Kaplan-Meier method was used to estimate overall survival, RFS and aGRFS. Relapse free survival was defined as the length of time after transplantation without any signs of relapse of primary disease. Acute GVHD was staged and graded per MAGIC standardization criteria.[11] GRFS is a composite end-point defined as not having evidence of grade III/IV aGVHD or moderate to severe cGVHD with relapse free survival. Kaplan-Meier method was used for calculating GRFS with patients censored at the time of first event (e.g., diagnosis of acute or chronic GVHD or relapse, whichever came first). Other described variables included rates of GVHD and infections.

RESULTS

From January 2015 to October 2020, 200 pediatric patients underwent their first alloSCT for HM within FPBCC centers. We excluded umbilical cord recipients (n=34), one HLA- antigen mismatched related donors (n=3), and patients with diagnosis of myelodysplastic syndrome (n=11) from analysis (Figure 1).

Characteristics of Patients

We analyzed 152 pediatric patients with a median age of 10 years (0.6-28), 5.2% of patients were >18 years of age. Of these patients, 32 underwent MRD, 41 received MUD, 29 received 7/8 MMUD and 50 received haploHCT donors (Table 1). The groups were similar by age, gender, Karnofsky/Lansky Score, the number of comorbidities, conditioning intensity and disease status at the time of transplant. Compared to Whites (W), African-Americans (AA) were overrepresented in mismatched donor groups (17/21 AA vs 52/112 W, 2-tailed Fisher Exact (FE) $p<0.001$).

Survival

At a median follow-up of 41 months, 36% of patients were deceased, 17% due to relapse and 19% due to non-relapse causes (Table 1). Recipients of MUD grafts had statistically significant superior outcomes regarding 2-year OS, 2-year RFS and aGRFS when compared to 7/8 MMUD and haploHCT recipients (Fig. 2 A-D). Two-year OS was 82.6% in MUD recipients compared to 39.7% in 7/8 MMUD recipients and 69.5% haploHCT recipients, two- year RFS was 80.3% in MUD recipients compared to 41.5% of 7/8 MMUD and 49.3% of haploHCT recipients. Also, the 2-year acute GRFS was significantly higher in 72.9% of MUD recipients compared to 38.8% in 7/8 MMUD and 45.3% in haploHCT recipients. Recipients of MRD grafts did not demonstrate a statistically significant difference in outcomes when compared with haploHCT and 7/8 MMUDs, except for infectious rates. Relapse rates were higher in MRD (50%) and haploHCT recipients (41.7%) when compared to MUD donors (12.2%) (FE=0.0006, 0.0042, respectively). Recipients of 7/8 MMUD grafts had a relapse rate of 17.2%, which was not significantly different when compared to MUD recipients. Non-relapse mortality (NRM) was significantly higher in 7/8 MMUD (41%) when compared to other donor types (MRD 9.4%, MUD 14.6%, HaploHCT 16%).

Infections

Infections by day 100 were examined based on donor type and detailed rates of viral reactivations and other infections are presented in Table 2. CMV serostatus is presented in Table 1 and there were no differences amongst donor types, though there was a statistically significant higher incidence of CMV D-/R+ in MRD compared to haploHCT. Patients who underwent MRD alloSCT were less likely to experience viral reactivation when compared to other donor types [MRD (31.2%), MUD (63.4%), 7/8 MMUD (86.2%), haploHCT (52%), FE= 0.009, 0.0001, 0.07, respectively]. Patients with 7/8 MMUD were more likely than MRD recipients to have a CMV and BK viral reactivation (RR 4) (Table 2). There was no significant difference when compared to MUD recipients. Comparisons were made between donor types and other types of infections (i.e., bacterial and fungal infections), but none were clinically significant. Seven patients died prior to day 100 and these were secondary to infection: one due to HHV6 infection, one to adenovirus, one to toxoplasma, and four due to bacterial infections (Table 3). Two of the patients with bacterial infections had grade III/IV aGVHD present. All patients who died prior to day 100 were recipient of HLA-mismatched transplants. Five of the patients received 7/8 MMUD (17.2%) and two received haploHCT (4%).

GVHD

There was no statistically significant difference in the rate of grade III/IV aGVHD or moderate and severe cGVHD in any donor category when compared to MRD (grade III/IV aGVHD in MRD (6.3%), MUD (17%), 7/8 MMUD (20.7%), HaploHCT (8%), FE= 0.28, 0.16, 1, respectively); and moderate to severe cGVHD (MRD (15.6%), MUD (12.2%), 7/8 MMUD (0%), HaploHCT (10%), FE= 0.74, 0.05, 0.5, respectively).

DISCUSSION

Multiple adult studies have demonstrated that PtCy for haploHCT recipients provides comparable outcomes to MUD donor types. One-year **NRM** is reported to be as low as 7% following haploHCT with a 1-year relapse rate of 45% and no reported clinically significant differences in OS between donor types.[12] With the adult studies demonstrating comparable outcomes, our consortium was hopeful this would be similar to our pediatric cohort due to the majority of our patients requiring alternative donors. However, our experience in a recent cohort of pediatric patients in Florida with HM shows MUD recipients to have superior overall outcomes when compared to 7/8 MMUD and haploHCT recipients. MUD recipients maintained a clinically significant improved RFS, aGRFS, and GRFS at 2 years following alloSCT when compared to haploHCT recipients and 7/8 MMUD recipients. The less favorable outcomes in haploHCT recipients can be due to a learning curve of small pediatric centers adapting haploHCT where it was not widely utilized years prior to this analysis.

The data demonstrate a clinically significant increase in relapse rates when using haploHCT donors with PtCy, though NRM was not different. Of note when comparing infection rates, MRD recipients were significantly less likely to develop viral infections when compared to other donor types. Recipients of 7/8 MMUD grafts were significantly higher to have CMV and BK infections.

Rates of grade III/IV acute GVHD were not clinically significant between the various donor sources, ranging from 6 to 20% of patients. This is consistent with literature utilizing PtCy in haploidentical donors. The results obtained from this review did demonstrate very low cGVHD in 7/8 MMUD recipients; however, it should be noted that 55.2% of these patients had died, which may have prevented review of cGVHD. This distribution of cGVHD does not match current literature and should be evaluated further, though there was no statistical difference between donor types.

When determining transplant outcomes based on donor types, we often focus on incidence and severity of GVHD, infections, NRM, relapse rates; however, do not summarize the overall picture and GRFS. By utilizing GRFS, in addition to leukemia-free survival we can better assess post-transplant quality of life.

Use of haploidentical donors have made transplant available to a number of patients who otherwise would not have an acceptable donor. While PtCy is technically simple and widely available procedure the graft manipulation field is moving towards further improving the graft component to reduce relapse rates and infections. Currently two most promising methods geared towards improving haploidentical grafts include ex-vivo graft manipulation with alpha/beta T cell and B cell depletion and Orca graft engineering (purified polyclonal donor regulatory T cells); however, these methods are still not available in many small transplant centers. Thus, it is important to continue studying graft manipulation techniques in hematologic malignancies to determine these overall outcomes.

Limitations of our study includes its retrospective nature with donor selection based on availability and center preferences; however, we have not observed significant differences in disease risks (CR1/CR2 vs CR3/primary induction failure), performance score, or comorbidity number among different donor types, which are considered the main risk factors for survival outcomes. The numbers are small in each donor category and some of the NRM could be attributed to the introduction of haploHCT in centers who historically did not provide them causing a learning curve in supportive care of these transplants. All centers do provide weekly viral surveillance via PCR testing and treat viral infections empirically to mitigate target organ involvement. Some approaches to MUD transplants in adult patients are to utilize PtCy in order to decrease GVHD and maintain similar OS. In children this may not be beneficial for OS and GRFS and should be utilized case by case rather than a standard approach, until further pediatric data are available.

CONCLUSION

Our analysis of a recent cohort of 152 pediatric patients undergoing their first alloSCT for HM indicated significant differences in RFS and aGRFS and GRFS based on donor type. Our data will inform donor selection in pediatric alloSCT practice and development of prospective trials evaluating different donor types, while focusing on individualized care. This retrospective study was supported by the Florida Department of Health, Live Like Bella Grant.

Data Availability Statement: Data are available from the authors upon reasonable request and with permission of University of Florida IRB.

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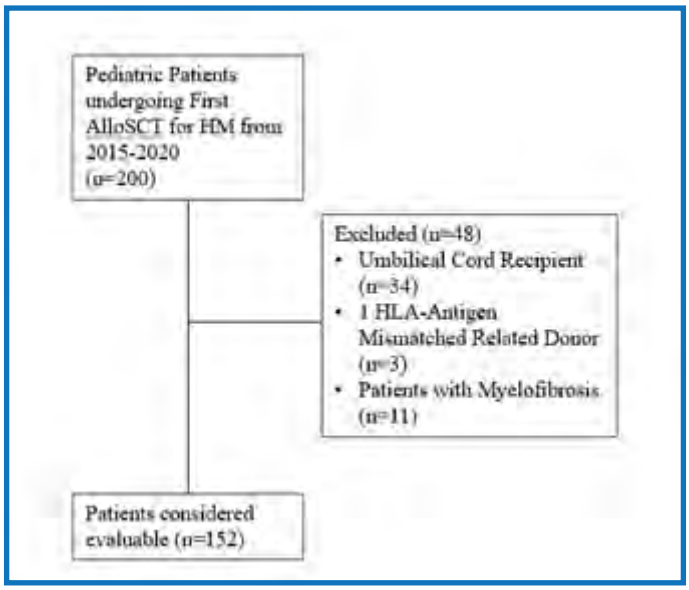

Figure 1: Exclusion Criteria Flow Chart

Figures 2A-D: Outcomes of Transplant Recipients Based on Donor-Type

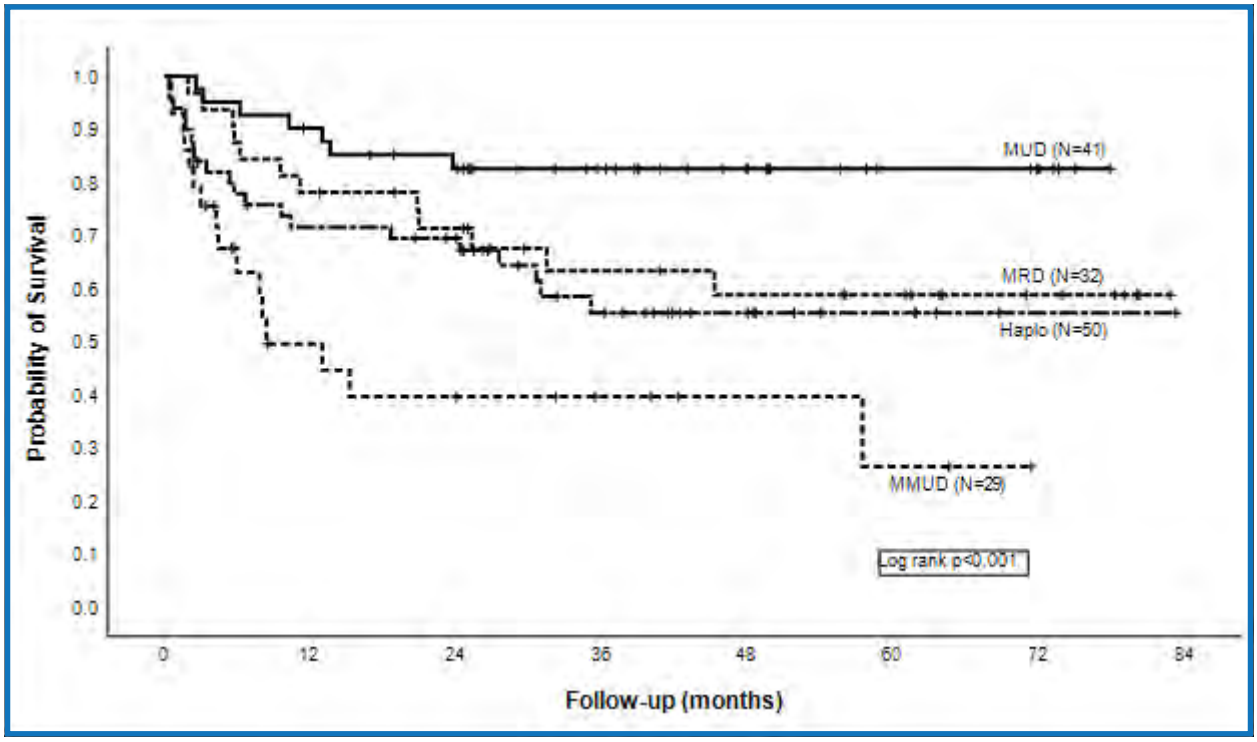

Figure 2A: Overall Survival Based on Donor Type (log rank p<0.001)

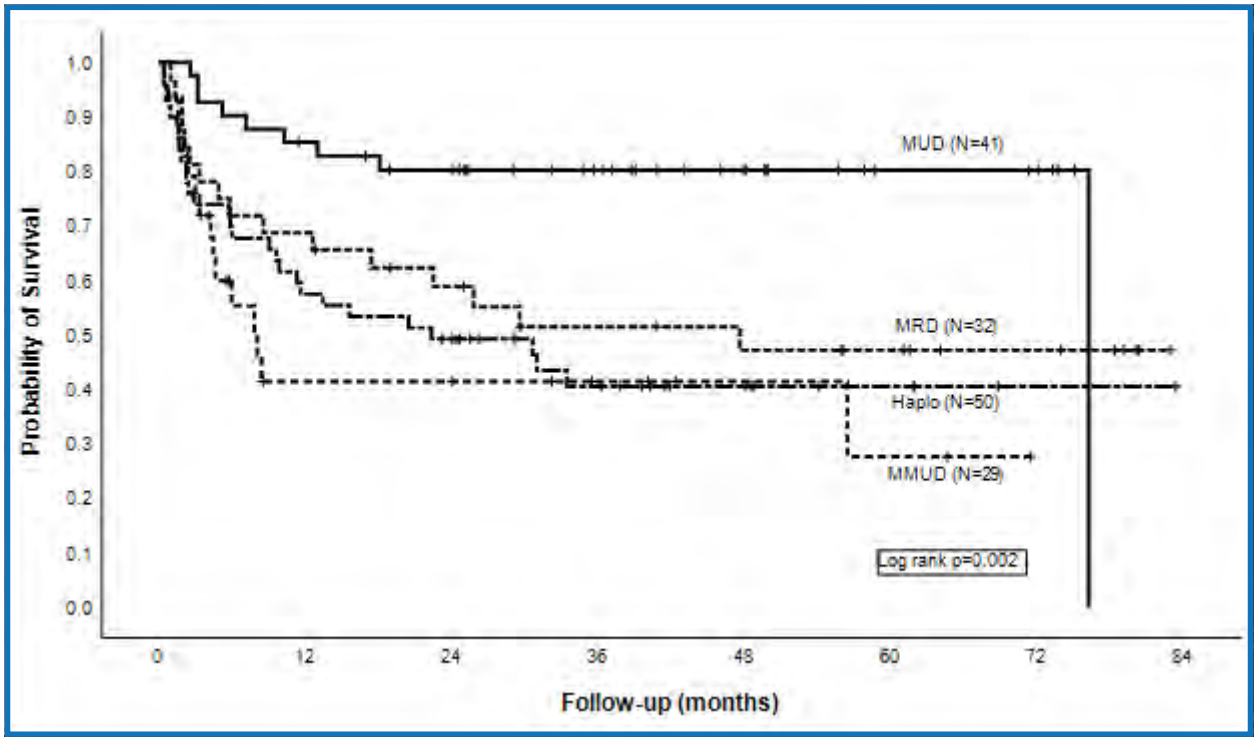

Figure 2B: Relapse-Free Survival Based on Donor Type (log rank p=0.002)

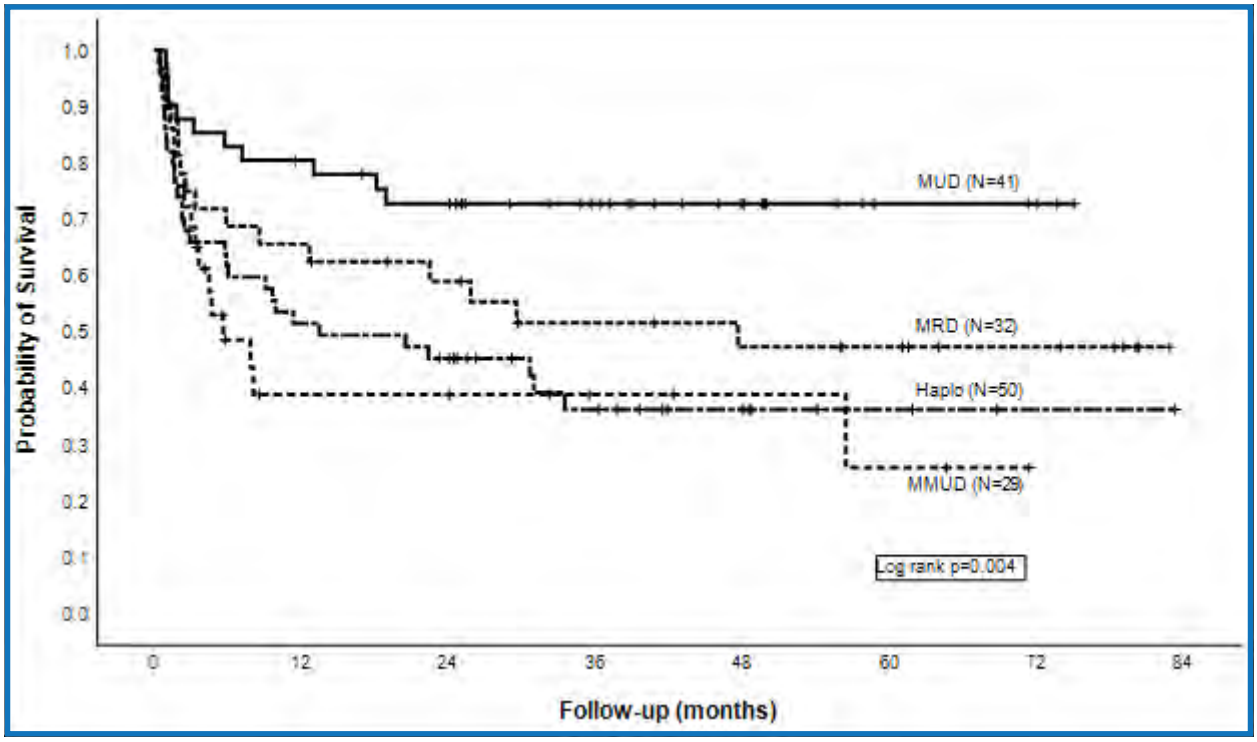

Figure 2C: Acute GVHD-Free, Relapse-Free Survival Based on Donor Type (log rank p=0.004)

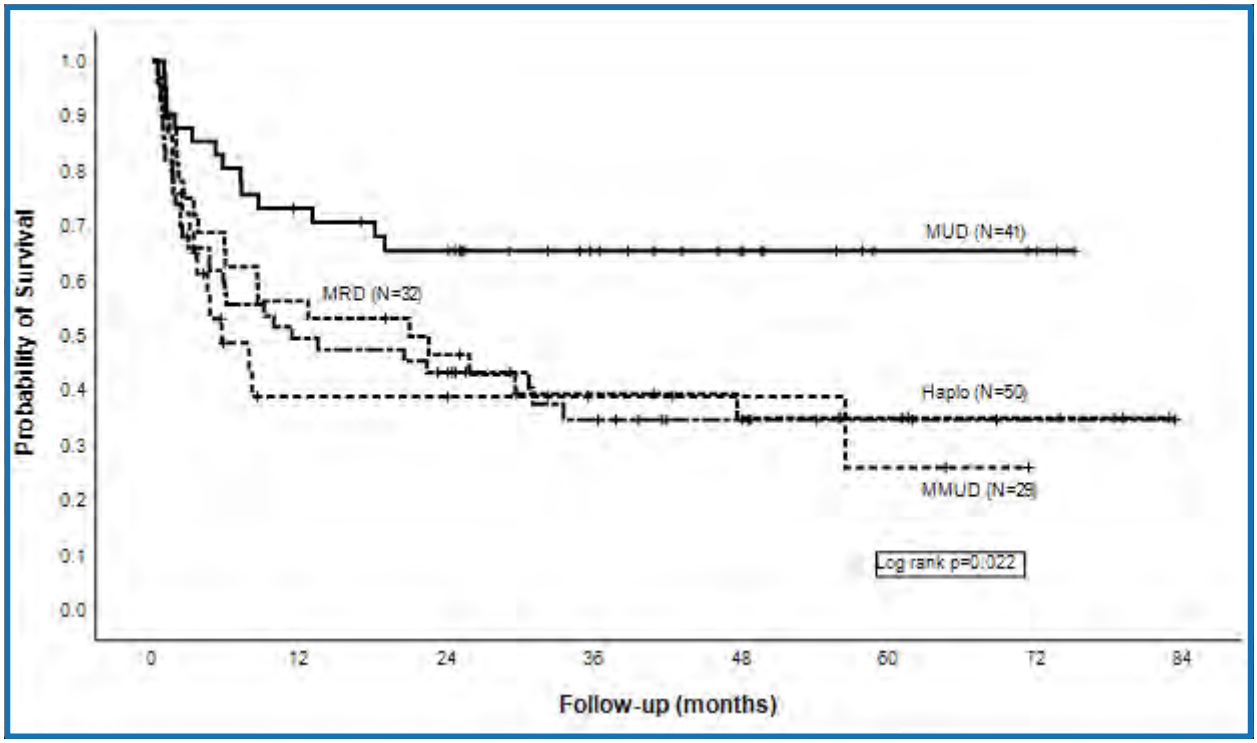

Figure 2D: Cumulative GVHD-Free, Relapse-Free Survival Based on Donor Type (log rank p=0.022)

	8/8 Related Donor N=32 N [%]	8/8 MUD N=41 N [%]	7/8 MUD N=29 N [%]	Haploidentical Related Donor N=50 N [%]	Total N=152 N [%]
Patient and treatment characteristics					
Gender					
Male	19 [59.4%]	23 [56.1%]	20 [69.0%]	24 [48.0%]	86 [56.6%]
Female	13 [40.6%]	18 [43.9%]	9 [31.0%]	26 [52.0%]	66 [43.4%]
Median Age (range)	12 (2-21)	10 (0.6-20)	10 (1-21)	1 (1.2-28)	10 (0.6-28)
White NOS	25 [78.1%]	35 [85.4%]	19 [65.5%]	33 [66.0%]	112 [73.7%]
AA	1 [3.1%]	3 [7.3%]	5 [17.2%]	12 [24.0%]	21 [13.8%]
Asian	2 [6.3%]	1 [2.4%]	0 [0%]	2 [4.0%]	5 [3.3%]
Other	0 [0%]	0 [0%]	0 [0%]	0 [0%]	0 [0%]
Unknown	4 [12.5%]	2 [4.9%]	5 [17.2%]	3 [6.0%]	14 [9.2%]
Bone Marrow	19 [59.4%]	31 [75.6%]	21 [72.4%]	44 [88.0%]	115 [75.7%]
PBSC	13 [40.6%]	10 [24.4%]	8 [27.6%]	6 [12.0%]	37 [24.3%]
Karnofsky/Lansky					
≥80%	28 [87.5%]	39 [95.1%]	27 [93.1%]	47 [94.0%]	141 [92.8%]
Comorbidity number					
≤1	24 [75.1%]	32 [78.0%]	25 [86.2%]	38 [76.0%]	119 [78.3%]
number >1	8 [24.9%]	9 [22.0%]	4 [13.8%]	12 [24.0%]	33 [21.7%]
AML	15 [46.9%]	21 [51.2%]	7 [24.1%]	25 [50.0%]	68 [44.7%]
APL	2 [6.3%]	2 [4.9%]	1 [3.4%]	0 [0%]	5 [3.3%]
ALL	15 [46.9%]	18 [43.9%]	21 [72.4%]	25 [50.0%]	79 [52.0%]
CR1/CR2	29 [90.6%]	34 [82.9%]	22 [75.9%]	43 [86.0 %]	128 [84.2%]
≥CR3 or IF	3 [9.4%]	7 [17.1%]	7 [24.1%]	7 [14.0%]	24 [15.8%]
CNI+MTX	24 [75.0%]	36 [87.8%]	26 [89.7%]	1 [2.0%]	87 [57.2%]
Post-Cy	1 [3.1%]	0 [0%]	2 [6.9%]	49 [98.0%]	52 [34.2%]
Other	7 [21.9%]	5 [12.2%]	1 [3.4%]	0 [0%]	13 [8.6%]
ATG-used	4 [12.5%]	18 [43.9%]	27 [93.1%]	1 [2.0%]	50 [32.9%]
Conditioning					
Bu-based	15 [46.9%]	16 [39.0%]	8 [27.5%]	16 [32.0%]	55 [36.2%]
Thio/Mel/Flu	3 [9.4%]	6 [14.6%]	1 [3.3%]	8 [16.0%]	18 [11.8%]
TBI-based	14 [43.8%]	18 [43.9%]	20 [69.0%]	26 [52.0%]	78 [51.3%]
Other	0 [0%]	1 [2.4%]	0 [0%]	0 [0%]	1 [0.7%]
Donor-Recipient CMV Match					
Pos-pos	10 [31.3%]	16 [39.0%]	14 [48.3%]	27 [54.0%]	67 [44.1%]
Pos-neg	1 [3.1%]	6 [14.6%]	3 [10.3%]	9 [18.0%]	19 [12.5%]
Neg-pos	14 [43.8%]	13 [31.7%]	10 [34.5%]	10 [20.0%]	47 [30.9%]
Neg-neg	7 [21.9%]	6 [14.6%]	2 [6.9%]	4 [8.0%]	19 [12.5%]
Intensity Prep Regimen					
Myeloablative	29 [90.6%]	40 [97.6%]	28 [96.6%]	47 [94.0%]	144 [94.7%]
Non-myeloablative	0 [0%]	0 [0%]	0 [0%]	1 [2.0%]	1 [0.7%]
Reduced intensity	3 [9.4%]	1 [2.4%]	1 [3.4%]	2 [4.0%]	7 [4.6%]

Table 1: Summary of Patient Characteristics and Outcomes

Outcomes (median follow-up of living patients = 41 months)					
Death Total	12 [37.5%]	7 [17.1%]	16 [55.2%]	20 [40.0%]	55 [36.2%]
Death relapse	9 [28.1%]	1 [2.4%]	4 [13.8%]	12 [24.0%]	26 [17.1%]
Non-relapse mortality	3 [9.4%]	6 [14.6%]	12 [41.4%]	8 [16.0%]	29 [19.1%]
Relapse Rate	16 [50.0%]	5 [12.2%]	5 [17.2%]	20 [41.7%]	46 [30.7%]
GVHD					
Any grade					
aGVHD	12 [37.5%]	24 [58.5%]	14 [48.3%]	22 [44.0%]	72 [47.4%]
cGVHD	9 [28.1%]	12 [29.2%]	0 [0%]	7 [14.0%]	28 [18.4%]
aGVHD					
grade 0-2	30 [93.8%]	34 [82.9%]	23 [79.3%]	46 [92.0%]	133 [87.5%]
grade 3-4	2 [6.2%]	7 [17.1%]	6 [20.7%]	4 [8.0%]	19 [12.5%]
cGVHD					
none or mild	27 [84.4%]	36 [87.8%]	29 [100%]	45 [90.0%]	137 [90.1%]
moderate/severe	5 [15.6%]	5 [12.2%]	0 [0%]	5 [10.0%]	15 [9.9%]
KM 2-year OS	71.3% [55.4-87.2]	82.6% [70.8-94.4]*	39.7% [19.7-59.7]*	69.5% [56.6-82.4]	68.5% [60.9-76.1]
KM 2-year Relapse-free survival	59.0% [41.8-76.2]	80.3% [68.0-92.6]*	41.5% [21.7-61.3]*	49.3% [35.4-63.2]*	58.5% [50.5-66.5]*
KM 2-year aGRFS (acute grade 3/4)	59% [41.8-76.2]	72.9% [59.2-86.6]*	38.8% [19.4-58.2]*	45.3% [31.4-59.2]*	54.7% [46.7-62.7]
KM 2-year GRFS (acute 3/4 and chronic moderate/severe)	46.5% [29.1-63.9]	65.6% [50.9-80.3]	38.8% [19.4-58.2]	43.3% [29.4-57.2]	49.2% [41.2-57.2]

CNI= calcineurin inhibitor MTX= methotrexate, CR= complete remission, IF=induction failure AML= acute myelogenous leukemia, MPL= mixed phenotype leukemia, ALL=acute lymphoblastic leukemia, Bu- busulfan, Thio/Mel/Flu=thiotepa, melphalan, fludarabine

	8/8 Related Donor N=32 N [%]	8/8 MUD N=41 N [%]	7/8 MMUD N=29 N [%]	Haploidentical Related Donor N=50 N [%]	Total N=152 N [%]
Patient Characteristics of Infections					
Number of viral infections					
0	22 [68.8%]	15 [36.6%]	4 [13.8%]	24 [48.0%]	65 [42.8%]
1	9 [28.1%]	13 [31.7%]	8 [27.6%]	15 [30.0%]	45 [29.6%]
2	1 [3.1%]	12 [29.3%]	9 [31.0%]	9 [18.0%]	31 [20.4%]
3 or more	0 [0%]	1 [2.4%]	8 [27.6%]	2 [4.0%]	11 [7.2%]
Type of viral infections					
CMV (blood)	4 [12.5%]	10 [24.4%]	15 [51.7%]	12 [24.0%]	41 [27.0%]
Adeno (blood)	0 [0%]	2 [4.9%]	4 [13.8%]	2 [4.0%]	8 [5.3%]
COVID (nasal)	0 [0%]	0 [0%]	0 [0%]	2 [4.0%]	2 [1.3%]
EBV (blood)	1 [3.1%]	7 [17.1%]	2 [6.9%]	2 [4.0%]	12 [7.9%]
HHV6 (blood)	1 [3.1%]	6 [14.6%]	10 [34.5%]	7 [14.0%]	24 [15.8%]
BK (blood or urine)	5 [15.6%]	12 [29.3%]	19 [65.5%]	10 [20.0%]	46 [30.3%]
Parvovirus (blood)	0 [0%]	1 [2.4%]	0 [0%]	2 [4.0%]	3 [2.0%]
Norovirus (no site)	0 [0%]	0 [0%]	0 [0%]	1 [2.0%]	1 [0.7%]
HSV(mouth)	0 [0%]	0 [0%]	0 [0%]	1 [2.0%]	1 [0.7%]
Other	0 [0%]	2 [4.9%]	0 [0%]	0 [0%]	2 [1.3%]
Number of bacterial infections					
None	16 [50.0%]	29 [70.7%]	16 [55.2%]	33 [66.0%]	94 [61.8%]
1	10 [31.3%]	7 [17.1%]	11 [37.9%]	13 [26.0%]	41 [27.0%]
2	6 [18.8%]	5 [12.2%]	2 [6.9%]	3 [6.0%]	16 [10.5%]
3 or more	0 [0%]	0 [0%]	0 [0%]	1 [2.0%]	1 [0.7%]
Type of bacterial infections					
C. diff enteritis	8 [25.0%]	5 [12.2%]	6 [20.7%]	10 [20.0%]	29 [19.1%]
Gram Neg bacilli	5 [15.6%]	6 [14.6%]	6 [20.7%]	7 [14.0%]	24 [15.8%]
Staph epi	1 [3.1%]	0 [0%]	1 [3.4%]	3 [6.0%]	5 [3.3%]
Gram Pos other than Staph epi	8 [25.0%]	6 [14.6%]	2 [6.9%]	2 [4.0%]	18 [11.8%]
Fungal infections					
None	32 [100%]	40 [97.6%]	28 [96.6%]	49 [98.0%]	148 [98.0%]
Candida	0 [0%]	1 [2.4%]	1 [3.4%]	0 [0%]	2 [1.3%]
Scopulanopsis	0 [0%]	0 [0%]	0 [0%]	1 [2.0%]	1 [0.7%]
Relative Risk of Infections Compared to 8/8 Related Donor RR [95% CI]					
	8/8 Related Donor N=32 N [%]	8/8 MUD N=41 N [%]	7/8 MMUD N=29 N [%]	Haploidentical Related Donor N=50 N [%]	
CMV	1.95 [0.67-5.65]	4.14 [1.55-11.05]*	1.92 [0.68-5.44]	2.16 [0.83-5.60]	
BK	1.87 [0.74-4.77]	4.19 [1.80-9.78]*	1.28 [0.48-3.40]	1.94 [0.84-4.49]	
C. diff enteritis	0.49 [0.18-1.35]	0.83 [0.33-2.10]	0.80 [0.35-1.81]	0.76 [0.39-1.51]	
Gram Neg bacilli	0.94 [0.31-2.79]	1.32 [0.45-3.88]	0.90 [0.31-2.58]	1.01 [0.42-2.45]	
Gram Pos other than Staph epi	0.59 [0.23-1.52]	0.28 [0.06-1.19]	0.16 [0.04-0.71]*	0.47 [0.23-0.99]*	

Table 2: Summary of Infections

Sex and Age at trans	Donor	D-R CMV match	Graft type	PS	GVHD	Survival length	Primary cause of death
F 14	7/8 MMUD	Neg-pos	BM	100	none	1.58 months	HHV6 sepsis
M 5	7/8 MMUD	Neg-pos	BM	100	none	2.40 months	Adenovirus
M 11	7/8 MMUD	Pos-pos	BM	100	none	1.64 months	Toxoplasma
M 6	7/8 MMUD	Pos-neg	BM	100	none	0.56 months	E. coli sepsis
F 17	Haplo	Pos-pos	BM	90	aGVHD grade 2	2.40 months	Bacterial infection
M 14	7/8 MMUD	Pos-pos	PB	100	aGVHD grade 4	2.60 months	Sepsis
M 16	Haplo	Pos-pos	PB	80	none	0.39 months	Bacterial infection (Staph epi)

Table 3: Characteristics of Patients who Died with Infections within <100 Days of Transplant