A G E N D A
CIBMTR WORKING COMMITTEE FOR GRAFT SOURCES & MANIPULATION
Orlando, FL
Friday, February 17, 2022, 12:00 p.m. – 2:00 p.m. (EST)

Co-Chair:	**Claudio Brunstein, MD, PhD, Cleveland Clinic Foundation, Cleveland, OH; Telephone: 216-444-9310; E-mail: brunst@ccf.org**
Co-Chair:	**Filippo Milano, MD, PhD, Fred Hutchinson Cancer Center, Seattle, WA; Email: fmilano@fredhutch.org; Phone: 206-667-5925**
Co-Chair	**Cara Benjamin, PhD, University of Miami, Miami, FL; Email: c.benjamin3@miami.edu; Phone: (305) 243-5534**
Scientific Director:	**Stephen Spellman, MBS, CIBMTR/NMDP, Minneapolis, MN; Telephone: 763-406-8334; E-mail: sspellma@nmdp.org**
Statistical Director:	**Mei-Jie Zhang, PhD, CIBMTR Statistical Center, Milwaukee, WI; Telephone: 414-456-8375; E-mail: meijie@mcw.edu**
Statistician:	**Molly Allbee-Johnson, MPH, CIBMTR Statistical Center, Milwaukee, WI; Telephone: 414-805-2258, E-mail: mallbeejohnson@mcw.edu**

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1. **Introduction**
   a. **Minutes from April 2022 meeting** (Attachment 1)
   b. **Biospecimen Accrual Tables** (Attachment 2)
   c. **Introduction of incoming Co-Chair:**
   Parinda Mehta, MD; Cincinnati Children's Hospital;
   E-mail: parinda.mehta@cchmc.org; Telephone: (513) 636-5917

2. **Presentations, Published or Submitted Papers**

   a. **GS19-02** Graft Failure in MDS and Acute Leukemia Patients After Allogeneic Stem Cell Transplantation Receiving Post Transplant Cyclophosphamide ***Oral presentation at the ASH 2022 Annual Meeting.***

3. **Studies in Progress** (Attachment 3)

   a. **GS19-02** Graft Failure in MDS and Acute Leukemia Patients After Allogeneic Stem Cell Transplantation Receiving Post Transplant Cyclophosphamide (C Hickey et al) **Manuscript Preparation.**
   b. **GS22-01** HLA matched sibling versus well-matched unrelated donor: Update including HLA-DPB1 match status in recipients of allogeneic hematopoietic cell transplantation (Nath et al) **Protocol Development.**

4. **Proposals**
   Future/proposed studies

   a. **PROP 2210-84/ PROP 2210-286** Outcomes of Non-First Degree Relative Haploidentical Blood or Marrow Transplantation Using Post-transplant Cyclophosphamide (P Munshi/ S McCurdy/ S Mirza/ L Gowda) (Attachment 4)

b. **PROP 2210-121** Impact of donor source in second allogeneic hematopoietic cell transplant (HCT) in patients with acute leukemia/MDS who relapsed after prior allograft during the current era (2014-2020)(A Lucas/ A Scaradavou) (Attachment 5)
c. **PROP 2210-228** Impact of Adherence to Cord Blood Guidelines (L Metheny/ F Milano) (Attachment 6)
d. **PROP 2210-272** Does use of ex vivo expanded cord blood lead to improved outcomes compared to unmanipulated umbilical cord blood or haploidentical graft in myeloablative hematopoietic cell transplant? (A Trunk/ C Brunstein) (Attachment 7)

Dropped proposed studies

a. **PROP 2208-02** A comparison of post transplant cyclophosphamide with post donor leukocyte infusion (but pre CD34 selected stem cell) cyclophosphamide with haplo-identical donors. *Small sample size.*
b. **PROP 2210-03** Outcomes of Haploidentical versus Mismatched Unrelated Donor Hematopoietic Stem Cell Transplantation in Patients with Acute Myeloid Leukemia (AML), and myelodysplastic syndrome (MDS). *Overlap with current study.*
c. **PROP 2210-39** Impact of Donor and Recipient ABO incompatibility on outcomes after post-transplant cyclophosphamide based haploidentical transplant in patients with hematological malignancies. *Overlap with recent publication.*
d. **PROP 2210-41** Compare haploidentical stem cell donor with HLA mismatched unrelated donor selection in relapsed-refractory HL. *Small sample size.*
e. **PROP 2210-50** MMUD vs Haplo Allogeneic hematopoietic stem cell transplant outcome using PTCY as GVHD prophylaxis. *Overlap with current study.*
f. **PROP 2210-67** Comparison of outcomes depending on graft source (Mobilized peripheral blood stem cells -PBSC- versus bone marrow graft-BM) for haploidentical transplants using post-transplant cyclophosphamide (PTCy) in patients with Acute Myeloid Leukemia (AML) or Myelodysplastic Syndrome (MDS). *Overlap with recent publication.*
g. **PROP 2210-90** Outcomes after HLA-mismatched unrelated donor versus haploidentical hematopoietic stem cell transplantation using posttransplant cyclophosphamide-based GVHD prophylaxis. *Overlap with current study.*
h. **PROP 2210-106** Clinical outcomes following Graft Failure in Pediatric Patients after post-transplant cyclophosphamide based haploidentical allogeneic stem cell Transplant? *Overlap with current study.*
i. **PROP 2210-123** Impact of anti-fungal prophylaxis regimen on invasive fungal infections in allogeneic transplantation with alternative donors. *Duplicate proposal.*
j. **PROP 2210-129** Use of DLI in relapse after Haploidentical Stem Cell Transplant. *Small sample size*
k. **PROP 2210-149** Comparison of outcomes of allogeneic stem cell transplantation using older female HLA-matched related donors and younger male alternative donors in patients with hematologic malignancies - a propensity score matched analysis. *Overlap with current study.*
l. **PROP 2210-152** Comparison of Outcomes of the Use of Post-stem Cell Transplantation Donor Lymphocyte Infusion and Stem Cell Boost in Patients with Hematologic Malignancies. *Small sample size.*
m. **PROP 2210-186** Outcomes after bone marrow versus peripheral blood haploidentical hematopoietic stem cell transplantation using posttransplant cyclophosphamide-based GVHD prophylaxis in acute myeloid leukemia and myelodysplastic syndromes. *Overlap with recent publication.*
n. **PROP 2210-190** The Outcomes of Allogeneic Stem Cell Transplantation Using Bone Marrow Grafts According to Total Nucleated Cell Dose. *Overlap with recent publication.*
o. **PROP 2210-234** The efficacy of the Two-Step Myeloablative Haploidentical Transplant, A CIBMTR Cohort Analysis. *Small sample size.*
p. **PROP 2210-277** Optimizing Haploidentical Donor Selection Based on HLA-B Leader and -DRB1 Matching Compared to 8/8 HLA-Matched Related or Unrelated Donor Hematopoietic Cell Transplantation Using

Posttransplant Cyclophosphamide-Based Prophylaxis for Acute Leukemia and Myelodysplastic Syndrome. *Overlap with recent publication.*

q. **PROP 2210-282** Best Donor Type for Allogeneic Hematopoietic Cell Transplantation in High-Risk Acute Leukemia and Myelodysplastic Syndrome: Optimally Selected Haploidentical Donor, Double Unrelated Cord Blood or Matched Unrelated Donor? *Overlap with recent publication.*

r. **PROP 2210-288** HLA-haploidentical versus Mismatched Unrelated Donor Transplants with Post-transplant Cyclophosphamide based GVHD prophylaxis for Acute Leukemia and MDS. *Overlap with current study.*

s. **PROP 2210-290** Outcomes of CD34-selected stem cell boost for the management of poor graft function in pediatric and adult allogeneic hematopoietic cell transplantation. *Small sample size.*

5. Other Business

MINUTES AND OVERVIEW PLAN
CIBMTR WORKING COMMITTEE FOR GRAFT SOURCES & MANIPULATION
Salt Lake City, UT
Monday, April 25, 2022, 12:15 pm – 1:45 pm MDT

Co-Chair:	**Ian McNiece, PhD, CellMED Consulting, Miami, FL;** **Telephone: 305-510-7057; E-mail: aussiflier@aol.com**
Co-Chair:	**Claudio Brunstein, MD, PhD, University of Minnesota, Minneapolis, MN;** **Telephone: 612-625-3918; E-mail: bruns072@umn.edu**
Co-Chair	**Filippo Milano, MD, PhD, Fred Hutchinson Cancer Research Center, Seattle, WA;** **Email: fmilano@fredhutch.org; Phone: 206-667-5925**
Scientific Director:	**Stephen Spellman, MBS, CIBMTR/NMDP, Minneapolis, MN;** **Telephone: 763-406-8334; E-mail: sspellma@nmdp.org**
Statistical Director:	**Mei-Jie Zhang, PhD, CIBMTR Statistical Center, Milwaukee, WI;** **Telephone: 414-456-8375; E-mail: meijie@mcw.edu**
Statistician:	**Molly Allbee-Johnson, MPH, CIBMTR Statistical Center, Milwaukee, WI;** **Telephone: 414-805-2258, E-mail: mallbeejohnson@mcw.edu**

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1. **Introduction**

   Dr. Brunstein opened the meeting at 12:15 by welcoming the work committee members to the Graft Sources and Manipulation Working Committee (GSWC) meeting. He disclosed the funding and conflict of interest information for the working committee leadership and for the CIBMTR. He introduced the GSWC's leadership and welcomed Dr. Benjamin to the committee. Dr. Brunstein thanked Dr. Eapen (past Scientific Director) and Dr. McNiece for their many contributions over the years. He then discussed the working committee membership, goals, proposal selection, voting and rules of authorship. Dr. Brunstein invited Mr. Spellman to review the current portfolio and presentations.

2. **Presentations, published or submitted papers**

   Mr. Spellman highlighted the committees' recent publications and presentations and invited Dr. Milano to introduce the proposal presenters.

3. **Future/proposed studies**

   a. **PROP 2110-79/PROP 2110-125/PROP 211-284/PROP 2110-300:** This combined proposal seeks to compare outcomes for haploidentical hematopoietic cell transplants (HCT) using post-transplant cyclophosphamide (ptCy) using a first-degree or non-first-degree related donor.

   The CIBMTR identified n=3,312 cases of adults with malignant disease who received their first allogeneic transplant with bone marrow or peripheral blood between 2008 and 2019. There were n=152 with non-first degree related donors and n=3,160 cases with first-degree related donors.

   The primary objective of this proposal is to compare the impact of relatedness on overall survival. The secondary outcomes of interest in this proposal are progression-free survival, relapse, non-relapse mortality and acute and chronic GVHD.

   There was discussion on the opportunity of a third donor group to explore half-siblings (n=323). The overall goal of the study is to assess the potential to expand the related donor pool beyond first degree relatives. Dr. Soiffer asked if there are sufficient numbers to adjust for the age discrepancy where the donor age is younger for first degree related donors. The GSWC Statistical Director, Dr. Zhang,

indicated that if there is little to no overlap we cannot adjust. There was also discussion on the collection of HLA data from donors that are tested for match degree but not used for transplant. Mr. Spellman addressed that this information is not collected at the CIBMTR.

b. **PROP 2110-113/ PROP 2110-248/ PROP 2110-340:** This combined proposal seeks to evaluate the optimal donor selection in second allo HCT in cases with relapsed malignant disease.

The CIBMTR identified n=1232 cases of adult second allo transplants after previous transplant with relapse between 2014 and 2019. Of these cases, n=970 had the same donor in the second transplant.

The primary aim of the proposal is to evaluate impact of donor selection on leukemia-free survival in the pediatric and adult recipients for second allo transplant. Secondary aims include examining the cell dose for second transplant, same or different haplo donor, and GVHD development after first transplant impact on relapse in the second transplant.

There was brief discussion that focused on the lack of prospective data on the choice of an optimal donor for second allo HCT and the potential importance of measurable residual disease (MRD) data for evaluation. As much of the data is CRF level, MRD assessments should be available.

c. **PROP 2110-250:** This proposal seeks to examine the impact of CD34+ cell dose in peripheral blood transplants with matched sibling and unrelated donors.

The CIBMTR identified n=24,757 cases of adults with first allo peripheral blood HCT for malignant disease between 2008 and 2019.

The primary aim of this proposal is to examine CD34+ cell dose impact on overall survival. Secondary aims are to examine impact on engraftment, relapse, non-relapse mortality, and treatment related mortality.

There was a question about the type of cell dose (cryo vs infused dose). It was clarified that infusion dose would be used. Dr. Kanakry brought up the discussion around institutional practices and heterogeneity of doses. The study would examine center effect to adjust for any institutional practice differences. Dr. Brunstein discussed the impact of actual and ideal absolute infused dose.

d. **PROP 2110-301:** This proposal aims to identify the optimal cell dose for haplo peripheral blood HCT with ptCy for GVHD prophylaxis

The CIBMTR identified n= 1729 haploidentical cases transplanted for AML, ALL or MDS reported to the CIBMTR (2014-2019) who received post-transplant cyclophosphamide for GVHD prophylaxis.

The primary aim is to examine progression-free survival with CD34+, CD3+ and TNC to determine impact of the cell dose. Secondary aim is to examine cell dose on OS, relapse, non-relapse mortality, GVHD, engraftment and GVHD-free/relapse-free survival.

Dr. Brunstein asked if it would be important to examine days of collection for the patients and the age of the donor. Dr. Elmariah agreed if that information was available it would be valuable to include in the study. Study leadership does not believe the registry collects the length of product collection. There was also discussion on the inclusion of CRS, the data is available for more recent transplants. Dr. Strouse asked about the urgency of a transplant being a confounding factor. Dr. Elmariah stated this might be a minor issue in the analysis, might be a center related decision with lower cell doses. Dr. Brunstein added the goal is to evaluate certain cell thresholds to help guide practice.

4. Future/proposed studies to be presented at the CIBMTR Collaborative Working Committee Study Proposals Session

a. **PROP 2110-50/PROP 2110-317:** Optimizing HLA Matched Sibling versus Alternative (Well-Matched Unrelated and Haploidentical) Donor Selection: Update Including Donor Age and HLA-DPB1 Match Status in Recipients of Allogeneic Hematopoietic Cell Transplantation (K Nath/ B Shaffer/ H Choe)

5. Other Business

a. **Discussion on Future Research Priorities:** *Dr. Milano facilitated a discussion with the working membership regarding future areas of focus for the GSWC. The role of CD34 boosts was discussed and concerns raised about the completeness of the data reported to CIBMTR. Dr. Milano invited the committee membership to submit proposals for consideration in the next review cycle.*

Mr. Spellman thanked everyone for attending and then closed the session after reminding everyone to vote and attend the collaborative proposal session. The session closed at 1:15pm.

Working Committee Overview Plan for 2022-2023

Study Number and Title	Current Status	Chair Priority
GS19-02: Graft Failure in MDS and Acute Leukemia with PT-Cy	Manuscript preparation	1
GS22-01: HLA Matched Sibling versus Alternative Donor Selection: Allogeneic HCT	Protocol pending	1

Working Assignments for Working Committee Leadership (May 2022)

Claudio Brunstein	**GS19-02:** Graft Failure in MDS and Acute Leukemia with PT-Cy
Filippo Milano	**GS22-01:** HLA Matched Sibling versus Alternative Donor Selection: Allogeneic HCT

Unrelated Donor HCT Research Sample Inventory - Summary for First Allogeneic Transplants in CRF and TED with biospecimens available through the CIBMTR Repository stratified by availability of paired samples, recipient only samples and donor only samples, Biospecimens include: whole blood, serum/plasma and limited quantities of viable cells and cell lines (collected prior to 2006), Specific inventory queries available upon request through the CIBMTR Immunobiology Research Program

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Number of patients	47323	19111	12053
Source of data			
CRF	24443 (52)	7079 (37)	5666 (47)
TED	22880 (48)	12032 (63)	6387 (53)
Number of centers	264	241	378
Disease at transplant			
AML	16388 (35)	7160 (37)	3977 (33)
ALL	6871 (15)	2478 (13)	1928 (16)
Other leukemia	1469 (3)	423 (2)	310 (3)
CML	3528 (7)	1111 (6)	1028 (9)
MDS	6936 (15)	3307 (17)	1526 (13)
Other acute leukemia	501 (1)	230 (1)	142 (1)
NHL	4211 (9)	1361 (7)	904 (8)
Hodgkin Lymphoma	947 (2)	258 (1)	212 (2)
Plasma Cell Disorders, MM	940 (2)	292 (2)	206 (2)
Other malignancies	58 (<1)	14 (<1)	22 (<1)
Breast cancer	7 (<1)	3 (<1)	1 (<1)
SAA	1519 (3)	594 (3)	510 (4)
Inherited abnormalities erythrocyte diff fxn	728 (2)	255 (1)	231 (2)
Inherited bone marrow failure syndromes	26 (<1)	32 (<1)	20 (<1)
Hemoglobinopathies	22 (<1)	22 (<1)	15 (<1)
Paroxysmal nocturnal hemoglobinuria	4 (<1)	7 (<1)	2 (<1)
SCIDs	827 (2)	328 (2)	370 (3)
Inherited abnormalities of platelets	40 (<1)	16 (<1)	12 (<1)
Inherited disorders of metabolism	301 (1)	89 (<1)	143 (1)
Histiocytic disorders	387 (1)	125 (1)	129 (1)
Autoimmune disorders	27 (<1)	14 (<1)	11 (<1)
Other	53 (<1)	18 (<1)	25 (<1)
MPN	1507 (3)	947 (5)	297 (2)
Disease missing	26 (<1)	27 (<1)	32 (<1)
AML Disease status at transplant			
CR1	8855 (54)	4408 (62)	1974 (50)
CR2	3149 (19)	1237 (17)	782 (20)
CR3+	337 (2)	108 (2)	92 (2)
Advanced or active disease	3862 (24)	1364 (19)	984 (25)
Missing	185 (1)	43 (1)	145 (4)
ALL Disease status at transplant			
CR1	3403 (50)	1426 (58)	814 (42)
CR2	1956 (28)	631 (25)	557 (29)
CR3+	570 (8)	167 (7)	180 (9)

Refresh date: Dec 2022

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Advanced or active disease	860 (13)	230 (9)	257 (13)
Missing	82 (1)	24 (1)	120 (6)
MDS Disease status at transplant			
Early	1480 (21)	609 (18)	351 (23)
Advanced	4487 (65)	2464 (75)	836 (55)
Missing	969 (14)	234 (7)	339 (22)
NHL Disease status at transplant			
CR1	598 (14)	262 (19)	125 (14)
CR2	781 (19)	259 (19)	145 (16)
CR3+	365 (9)	114 (8)	80 (9)
PR	448 (11)	112 (8)	95 (11)
Advanced	1928 (46)	588 (43)	424 (47)
Missing	71 (2)	18 (1)	32 (4)
Recipient age at transplant			
0-9 years	3974 (8)	1246 (7)	1582 (13)
10-17 years	3152 (7)	969 (5)	1122 (9)
18-29 years	5720 (12)	1928 (10)	1607 (13)
30-39 years	5327 (11)	1851 (10)	1428 (12)
40-49 years	7110 (15)	2503 (13)	1748 (15)
50-59 years	9750 (21)	3711 (19)	2071 (17)
60-69 years	10023 (21)	5257 (28)	2052 (17)
70+ years	2267 (5)	1646 (9)	443 (4)
Median (Range)	48 (0-84)	53 (0-82)	42 (0-84)
Recipient race/ethnicity			
White	39105 (83)	15871 (83)	8419 (70)
Black or African American	2150 (5)	753 (4)	555 (5)
Asian	1167 (2)	602 (3)	520 (4)
Native Hawaiian or other Pacific Islander	59 (<1)	31 (<1)	32 (<1)
American Indian or Alaska Native	172 (<1)	73 (<1)	49 (<1)
Hispanic	2873 (6)	1076 (6)	718 (6)
Missing	1797 (4)	705 (4)	1760 (15)
Recipient sex			
Male	27519 (58)	11189 (59)	7161 (59)
Female	19804 (42)	7922 (41)	4892 (41)
Karnofsky score			
10-80	16419 (35)	7366 (39)	3802 (32)
90-100	29141 (62)	11142 (58)	7620 (63)
Missing	1763 (4)	603 (3)	631 (5)
HLA-A B DRB1 groups - low resolution			
<=3/6	31 (<1)	54 (<1)	5 (<1)
4/6	246 (1)	98 (1)	58 (1)
5/6	6320 (14)	1956 (12)	1680 (15)
6/6	39021 (86)	13671 (87)	9199 (84)
Unknown	1705 (N/A)	3332 (N/A)	1111 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	907 (2)	104 (1)	82 (1)
6/8	1783 (4)	159 (1)	224 (3)

Refresh date: Dec 2022

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
7/8	8777 (20)	2047 (16)	1797 (23)
8/8	33290 (74)	10596 (82)	5866 (74)
Unknown	2566 (N/A)	6205 (N/A)	4084 (N/A)
HLA-DPB1 Match			
Double allele mismatch	11284 (29)	1543 (23)	914 (26)
Single allele mismatch	20903 (54)	3374 (51)	1832 (52)
Full allele matched	6608 (17)	1716 (26)	787 (22)
Unknown	8528 (N/A)	12478 (N/A)	8520 (N/A)
High resolution release score			
No	11606 (25)	19036 (>99)	11519 (96)
Yes	35717 (75)	75 (<1)	534 (4)
KIR typing available			
No	33478 (71)	19085 (>99)	11980 (99)
Yes	13845 (29)	26 (<1)	73 (1)
Graft type			
Marrow	16451 (35)	5091 (27)	4800 (40)
PBSC	30790 (65)	13824 (72)	7191 (60)
BM+PBSC	10 (<1)	6 (<1)	1 (<1)
PBSC+UCB	38 (<1)	170 (1)	10 (<1)
Others	34 (<1)	20 (<1)	51 (<1)
Conditioning regimen			
Myeloablative	28854 (61)	10141 (53)	7518 (62)
RIC/Nonmyeloablative	18244 (39)	8909 (47)	4372 (36)
TBD	225 (<1)	61 (<1)	163 (1)
Donor age at donation			
To Be Determined/NA	396 (1)	563 (3)	147 (1)
0-9 years	5 (<1)	37 (<1)	4 (<1)
10-17 years	2 (<1)	13 (<1)	1 (<1)
18-29 years	23149 (49)	9900 (52)	5152 (43)
30-39 years	13299 (28)	4964 (26)	3623 (30)
40-49 years	7988 (17)	2533 (13)	2357 (20)
50+ years	2484 (5)	1101 (6)	769 (6)
Median (Range)	30 (0-123)	29 (0-121)	32 (0-123)
Donor/Recipient CMV serostatus			
+/+	11583 (24)	4767 (25)	3042 (25)
+/-	5466 (12)	2181 (11)	1479 (12)
-/+	15215 (32)	5254 (27)	3593 (30)
-/-	13359 (28)	4498 (24)	3132 (26)
CB - recipient +	34 (<1)	136 (1)	9 (<1)
CB - recipient -	4 (<1)	42 (<1)	2 (<1)
CB - recipient CMV unknown	0	1 (<1)	0
Missing	1662 (4)	2232 (12)	796 (7)
GvHD Prophylaxis			
No GVHD prophylaxis	200 (<1)	94 (<1)	67 (1)
Ex vivo T-cell depletion	1160 (2)	319 (2)	408 (3)
CD34 selection	720 (2)	339 (2)	194 (2)
Post-CY + other(s)	3020 (6)	2569 (13)	743 (6)

Refresh date: Dec 2022

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Post-CY alone	228 (<1)	109 (1)	58 (<1)
Tacrolimus + MMF +- others	5383 (11)	1947 (10)	920 (8)
Tacrolimus + MTX +- others (except MMF)	20389 (43)	8407 (44)	3390 (28)
Tacrolimus + others (except MTX, MMF)	2432 (5)	1220 (6)	469 (4)
Tacrolimus alone	1182 (2)	484 (3)	216 (2)
CSA + MMF +- others (except Tacrolimus)	3083 (7)	909 (5)	1017 (8)
CSA + MTX +- others (except Tacrolimus, MMF)	6993 (15)	1899 (10)	3358 (28)
CSA + others (except Tacrolimus, MTX, MMF)	1089 (2)	335 (2)	452 (4)
CSA alone	482 (1)	136 (1)	402 (3)
Other GVHD prophylaxis	752 (2)	270 (1)	208 (2)
Missing	210 (<1)	74 (<1)	151 (1)
Donor/Recipient sex match			
Male-Male	19283 (41)	7409 (39)	4699 (39)
Male-Female	11786 (25)	4525 (24)	2668 (22)
Female-Male	8013 (17)	3384 (18)	2383 (20)
Female-Female	7842 (17)	3072 (16)	2157 (18)
CB - recipient M	18 (<1)	96 (1)	3 (<1)
CB - recipient F	20 (<1)	83 (<1)	8 (<1)
Missing	361 (1)	542 (3)	135 (1)
Year of transplant			
1986-1990	350 (1)	46 (<1)	106 (1)
1991-1995	1839 (4)	439 (2)	748 (6)
1996-2000	3305 (7)	1185 (6)	1215 (10)
2001-2005	5345 (11)	1074 (6)	1880 (16)
2006-2010	9622 (20)	1923 (10)	1829 (15)
2011-2015	13414 (28)	3587 (19)	2563 (21)
2016-2020	10431 (22)	7184 (38)	2758 (23)
2021-2022	3017 (6)	3673 (19)	954 (8)
Follow-up among survivors, Months			
N Eval	20064	9350	5352
Median (Range)	60 (0-385)	24 (0-362)	40 (0-372)

Cord Blood HCT Research Sample Inventory - Summary for First Allogeneic Transplants in CRF and TED with biospecimens available through the CIBMTR Repository stratified by availability of paired samples, recipient only samples and donor only samples, Biospecimens include: whole blood, serum/plasma and limited quantities of viable cells and cell lines (collected prior to 2006), Specific inventory queries available upon request through the CIBMTR Immunobiology Research Program

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Number of patients	6214	1700	2170
Source of data			
CRF	4494 (72)	1137 (67)	1068 (49)
TED	1720 (28)	563 (33)	1102 (51)
Number of centers	154	142	223
Disease at transplant			
AML	2354 (38)	580 (34)	706 (33)
ALL	1279 (21)	373 (22)	468 (22)
Other leukemia	98 (2)	30 (2)	37 (2)
CML	132 (2)	36 (2)	57 (3)
MDS	559 (9)	168 (10)	172 (8)
Other acute leukemia	96 (2)	24 (1)	44 (2)
NHL	403 (6)	98 (6)	134 (6)
Hodgkin Lymphoma	103 (2)	27 (2)	36 (2)
Plasma Cell Disorders, MM	38 (1)	12 (1)	13 (1)
Other malignancies	11 (<1)	1 (<1)	3 (<1)
SAA	97 (2)	32 (2)	49 (2)
Inherited abnormalities erythrocyte diff fxn	171 (3)	51 (3)	45 (2)
Inherited bone marrow failure syndromes	4 (<1)	3 (<1)	3 (<1)
Hemoglobinopathies	2 (<1)	1 (<1)	0
SCIDs	278 (4)	91 (5)	165 (8)
Inherited abnormalities of platelets	20 (<1)	5 (<1)	10 (<1)
Inherited disorders of metabolism	387 (6)	118 (7)	142 (7)
Histiocytic disorders	107 (2)	29 (2)	51 (2)
Autoimmune disorders	9 (<1)	0	6 (<1)
Other	10 (<1)	2 (<1)	9 (<1)
Disease missing	4 (<1)	3 (<1)	0
MPN	52 (1)	16 (1)	20 (1)
AML Disease status at transplant			
CR1	1222 (52)	324 (56)	350 (50)
CR2	636 (27)	149 (26)	188 (27)
CR3+	66 (3)	9 (2)	26 (4)
Advanced or active disease	422 (18)	96 (17)	138 (20)
Missing	8 (<1)	2 (<1)	4 (1)
ALL Disease status at transplant			
CR1	574 (45)	159 (43)	202 (43)
CR2	480 (38)	137 (37)	166 (35)
CR3+	148 (12)	54 (14)	61 (13)
Advanced or active disease	76 (6)	22 (6)	38 (8)
Missing	1 (<1)	1 (<1)	1 (<1)

Refresh date: Dec 2022

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
MDS Disease status at transplant			
Early	173 (31)	41 (24)	72 (42)
Advanced	337 (60)	113 (67)	78 (45)
Missing	49 (9)	14 (8)	22 (13)
NHL Disease status at transplant			
CR1	63 (16)	9 (9)	25 (19)
CR2	75 (19)	22 (22)	35 (26)
CR3+	45 (11)	11 (11)	12 (9)
PR	68 (17)	12 (12)	16 (12)
Advanced	149 (37)	43 (44)	42 (32)
Missing	0	1 (1)	3 (2)
Recipient age at transplant			
0-9 years	1868 (30)	612 (36)	771 (36)
10-19 years	655 (11)	158 (9)	255 (12)
20-29 years	745 (12)	152 (9)	234 (11)
30-39 years	599 (10)	150 (9)	210 (10)
40-49 years	655 (11)	172 (10)	203 (9)
50-59 years	856 (14)	210 (12)	280 (13)
60-69 years	722 (12)	212 (12)	201 (9)
70+ years	114 (2)	34 (2)	16 (1)
Median (Range)	27 (0-83)	24 (0-78)	20 (0-78)
Recipient race/ethnicity			
White	3432 (55)	996 (59)	1090 (50)
Black or African American	893 (14)	221 (13)	263 (12)
Asian	366 (6)	120 (7)	163 (8)
Native Hawaiian or other Pacific Islander	32 (1)	3 (<1)	17 (1)
American Indian or Alaska Native	45 (1)	10 (1)	19 (1)
Hispanic	1108 (18)	253 (15)	297 (14)
Missing	338 (5)	97 (6)	321 (15)
Recipient sex			
Male	3439 (55)	968 (57)	1241 (57)
Female	2775 (45)	732 (43)	929 (43)
Karnofsky score			
10-80	1647 (27)	437 (26)	556 (26)
90-100	4361 (70)	1157 (68)	1433 (66)
Missing	206 (3)	106 (6)	181 (8)
HLA-A B DRB1 groups - low resolution			
<=3/6	101 (2)	57 (4)	32 (2)
4/6	2448 (41)	557 (40)	789 (40)
5/6	2664 (45)	596 (43)	854 (43)
6/6	750 (13)	184 (13)	294 (15)
Unknown	251 (N/A)	306 (N/A)	201 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	2891 (55)	569 (55)	881 (55)
6/8	1271 (24)	248 (24)	370 (23)
7/8	730 (14)	141 (14)	221 (14)
8/8	349 (7)	70 (7)	123 (8)

Refresh date: Dec 2022

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Unknown	973 (N/A)	672 (N/A)	575 (N/A)
HLA-DPB1 Match			
Double allele mismatch	859 (39)	99 (38)	164 (40)
Single allele mismatch	1117 (51)	136 (52)	209 (51)
Full allele matched	202 (9)	25 (10)	33 (8)
Unknown	4036 (N/A)	1440 (N/A)	1764 (N/A)
High resolution release score			
No	4674 (75)	1650 (97)	2145 (99)
Yes	1540 (25)	50 (3)	25 (1)
KIR typing available			
No	4941 (80)	1694 (>99)	2150 (99)
Yes	1273 (20)	6 (<1)	20 (1)
Graft type			
UCB	5836 (94)	1521 (89)	2034 (94)
BM+UCB	1 (<1)	0	0
PBSC+UCB	347 (6)	170 (10)	122 (6)
Others	30 (<1)	9 (1)	14 (1)
Number of cord units			
1	5200 (84)	0	1809 (83)
2	1012 (16)	0	360 (17)
3	1 (<1)	0	0
Unknown	1 (N/A)	1700 (N/A)	1 (N/A)
Conditioning regimen			
Myeloablative	4030 (65)	1076 (63)	1346 (62)
RIC/Nonmyeloablative	2168 (35)	619 (36)	807 (37)
TBD	16 (<1)	5 (<1)	17 (1)
Donor age at donation			
To Be Determined/NA	4858 (78)	646 (38)	1741 (80)
0-9 years	1081 (17)	844 (50)	348 (16)
10-19 years	58 (1)	88 (5)	17 (1)
20-29 years	65 (1)	37 (2)	15 (1)
30-39 years	57 (1)	38 (2)	21 (1)
40-49 years	46 (1)	21 (1)	11 (1)
50+ years	49 (1)	26 (2)	17 (1)
Median (Range)	4 (0-112)	5 (0-73)	4 (0-119)
Donor/Recipient CMV serostatus			
+/+	0	0	1 (<1)
-/-	0	0	1 (<1)
CB - recipient +	3888 (63)	1027 (60)	1306 (60)
CB - recipient -	2227 (36)	613 (36)	790 (36)
CB - recipient CMV unknown	99 (2)	60 (4)	72 (3)
GvHD Prophylaxis			
No GVHD prophylaxis (forms under review)	23 (<1)	8 (<1)	14 (1)
Ex vivo T-cell depletion	25 (<1)	9 (1)	8 (<1)
CD34 selection	213 (3)	100 (6)	61 (3)
Post-CY + other(s)	12 (<1)	9 (1)	13 (1)
Post-CY alone	0	0	1 (<1)

Refresh date: Dec 2022

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Tacrolimus + MMF +- others	1857 (30)	539 (32)	446 (21)
Tacrolimus + MTX +- others (except MMF)	216 (3)	56 (3)	78 (4)
Tacrolimus + others (except MTX, MMF)	225 (4)	64 (4)	84 (4)
Tacrolimus alone	153 (2)	45 (3)	30 (1)
CSA + MMF +- others (except Tacrolimus)	2847 (46)	683 (40)	1039 (48)
CSA + MTX +- others (except Tacrolimus, MMF)	101 (2)	29 (2)	50 (2)
CSA + others (except Tacrolimus, MTX, MMF)	341 (5)	117 (7)	223 (10)
CSA alone	52 (1)	18 (1)	70 (3)
Other GVHD prophylaxis	137 (2)	20 (1)	42 (2)
Missing	12 (<1)	3 (<1)	11 (1)
Donor/Recipient sex match			
Male-Female	0	0	1 (<1)
Female-Male	0	0	1 (<1)
CB - recipient M	3439 (55)	968 (57)	1239 (57)
CB - recipient F	2775 (45)	732 (43)	928 (43)
CB - recipient sex unknown	0	0	1 (<1)
Year of transplant			
1996-2000	1 (<1)	2 (<1)	5 (<1)
2001-2005	112 (2)	86 (5)	34 (2)
2006-2010	1850 (30)	426 (25)	601 (28)
2011-2015	2682 (43)	510 (30)	839 (39)
2016-2020	1341 (22)	528 (31)	547 (25)
2021-2022	228 (4)	148 (9)	144 (7)
Follow-up among survivors, Months			
N Eval	2964	887	1105
Median (Range)	64 (0-196)	49 (0-213)	43 (0-240)

Related Donor HCT Research Sample Inventory - Summary for First Allogeneic Transplants in CRF and TED with biospecimens available through the CIBMTR Repository stratified by availability of paired samples, recipient only samples and donor only samples, Biospecimens include: whole blood, serum/plasma and limited quantities of viable cells and cell lines (collected prior to 2006), Specific inventory queries available upon request through the CIBMTR Immunobiology Research Program

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Number of patients	11071	1859	851
Source of data			
CRF	3500 (32)	454 (24)	281 (33)
TED	7571 (68)	1405 (76)	570 (67)
Number of centers	93	78	63
Disease at transplant			
AML	3667 (33)	605 (33)	285 (33)
ALL	1843 (17)	362 (19)	163 (19)
Other leukemia	205 (2)	41 (2)	19 (2)
CML	337 (3)	45 (2)	24 (3)
MDS	1483 (13)	226 (12)	111 (13)
Other acute leukemia	164 (1)	33 (2)	11 (1)
NHL	936 (8)	168 (9)	76 (9)
Hodgkin Lymphoma	204 (2)	40 (2)	23 (3)
Plasma Cell Disorders, MM	257 (2)	39 (2)	23 (3)
Other malignancies	24 (<1)	0	1 (<1)
Breast cancer	1 (<1)	0	0
SAA	516 (5)	81 (4)	29 (3)
Inherited abnormalities erythrocyte diff fxn	494 (4)	72 (4)	20 (2)
Inherited bone marrow failure syndromes	16 (<1)	2 (<1)	4 (<1)
Hemoglobinopathies	111 (1)	22 (1)	8 (1)
Paroxysmal nocturnal hemoglobinuria	2 (<1)	0	0
SCIDs	228 (2)	36 (2)	16 (2)
Inherited abnormalities of platelets	10 (<1)	0	0
Inherited disorders of metabolism	16 (<1)	5 (<1)	2 (<1)
Histiocytic disorders	63 (1)	9 (<1)	5 (1)
Autoimmune disorders	11 (<1)	0	1 (<1)
Other	16 (<1)	0	0
Disease missing	10 (<1)	4 (<1)	1 (<1)
MPN	457 (4)	69 (4)	29 (3)
AML Disease status at transplant			
CR1	2403 (66)	411 (68)	186 (65)
CR2	562 (15)	86 (14)	36 (13)
CR3+	44 (1)	14 (2)	1 (<1)
Advanced or active disease	651 (18)	90 (15)	62 (22)
Missing	7 (<1)	4 (1)	0
ALL Disease status at transplant			
CR1	1119 (61)	226 (62)	103 (63)
CR2	522 (28)	91 (25)	40 (25)
CR3+	114 (6)	19 (5)	11 (7)
Advanced or active disease	86 (5)	26 (7)	9 (6)

Refresh date: Dec 2022

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Missing	2 (<1)	0	0
MDS Disease status at transplant			
Early	253 (17)	31 (14)	20 (18)
Advanced	1177 (79)	183 (81)	85 (77)
Missing	53 (4)	12 (5)	6 (5)
NHL Disease status at transplant			
CR1	174 (19)	39 (23)	16 (21)
CR2	176 (19)	34 (20)	10 (13)
CR3+	100 (11)	18 (11)	4 (5)
PR	68 (7)	13 (8)	7 (9)
Advanced	409 (44)	63 (38)	39 (51)
Missing	5 (1)	0	0
Recipient age at transplant			
0-9 years	1123 (10)	180 (10)	68 (8)
10-19 years	1071 (10)	139 (7)	63 (7)
20-29 years	1257 (11)	250 (13)	90 (11)
30-39 years	865 (8)	166 (9)	88 (10)
40-49 years	1356 (12)	218 (12)	99 (12)
50-59 years	2336 (21)	401 (22)	185 (22)
60-69 years	2583 (23)	431 (23)	226 (27)
70+ years	480 (4)	74 (4)	32 (4)
Median (Range)	49 (0-82)	49 (0-76)	51 (0-83)
Recipient race/ethnicity			
White	6869 (62)	977 (53)	514 (60)
Black or African American	1373 (12)	240 (13)	81 (10)
Asian	518 (5)	138 (7)	43 (5)
Native Hawaiian or other Pacific Islander	34 (<1)	5 (<1)	2 (<1)
American Indian or Alaska Native	47 (<1)	4 (<1)	4 (<1)
Hispanic	1677 (15)	357 (19)	151 (18)
Missing	553 (5)	138 (7)	56 (7)
Recipient sex			
Male	6513 (59)	1084 (58)	496 (58)
Female	4558 (41)	775 (42)	355 (42)
Karnofsky score			
10-80	3971 (36)	745 (40)	349 (41)
90-100	6760 (61)	1052 (57)	454 (53)
Missing	340 (3)	62 (3)	48 (6)
HLA-A B DRB1 groups - low resolution			
<=3/6	2161 (23)	346 (26)	166 (28)
4/6	636 (7)	112 (8)	65 (11)
5/6	204 (2)	37 (3)	21 (4)
6/6	6481 (68)	861 (63)	333 (57)
Unknown	1589 (N/A)	503 (N/A)	266 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	2647 (29)	416 (33)	200 (38)
6/8	118 (1)	26 (2)	14 (3)
7/8	143 (2)	26 (2)	15 (3)
8/8	6262 (68)	798 (63)	296 (56)

Refresh date: Dec 2022

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Unknown	1901 (N/A)	593 (N/A)	326 (N/A)
HLA-DPB1 Match			
Double allele mismatch	9 (<1)	0	0
Single allele mismatch	725 (26)	8 (18)	6 (25)
Full allele matched	2072 (74)	37 (82)	18 (75)
Unknown	8265 (N/A)	1814 (N/A)	827 (N/A)
High resolution release score			
No	4655 (42)	1830 (98)	835 (98)
Yes	6416 (58)	29 (2)	16 (2)
Graft type			
Marrow	3187 (29)	431 (23)	238 (28)
PBSC	7789 (70)	1395 (75)	599 (70)
UCB	2 (<1)	14 (1)	0
BM+PBSC	8 (<1)	4 (<1)	1 (<1)
BM+UCB	30 (<1)	9 (<1)	2 (<1)
PBSC+UCB	0	0	11 (1)
Others	55 (<1)	6 (<1)	0
Conditioning regimen			
Myeloablative	6168 (56)	1021 (55)	439 (52)
RIC/Nonmyeloablative	4849 (44)	825 (44)	395 (46)
TBD	54 (<1)	13 (1)	17 (2)
Donor age at donation			
To Be Determined/NA	15 (<1)	3 (<1)	8 (1)
0-9 years	761 (7)	119 (6)	32 (4)
10-19 years	843 (8)	139 (7)	52 (6)
20-29 years	1915 (17)	319 (17)	167 (20)
30-39 years	1633 (15)	323 (17)	161 (19)
40-49 years	1796 (16)	300 (16)	115 (14)
50+ years	4108 (37)	656 (35)	316 (37)
Median (Range)	42 (0-122)	41 (0-118)	41 (0-121)
Donor/Recipient CMV serostatus			
+/+	4485 (41)	812 (44)	288 (34)
+/-	1187 (11)	151 (8)	72 (8)
-/+	2766 (25)	443 (24)	198 (23)
-/-	2371 (21)	381 (20)	162 (19)
CB - recipient +	24 (<1)	14 (1)	7 (1)
CB - recipient -	8 (<1)	9 (<1)	6 (1)
Missing	230 (2)	49 (3)	118 (14)
GvHD Prophylaxis			
No GVHD prophylaxis (forms under review)	156 (1)	35 (2)	16 (2)
Ex vivo T-cell depletion	114 (1)	31 (2)	11 (1)
CD34 selection	119 (1)	33 (2)	13 (2)
Post-CY + other(s)	3488 (32)	547 (29)	309 (36)
Post-CY alone	76 (1)	11 (1)	8 (1)
Tacrolimus + MMF +- others	794 (7)	93 (5)	26 (3)
Tacrolimus + MTX +- others (except MMF)	4050 (37)	606 (33)	309 (36)
Tacrolimus + others (except MTX, MMF)	815 (7)	292 (16)	67 (8)
Tacrolimus alone	108 (1)	22 (1)	7 (1)

Refresh date: Dec 2022

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
CSA + MMF +- others (except Tacrolimus)	243 (2)	38 (2)	15 (2)
CSA + MTX +- others (except Tacrolimus, MMF)	719 (6)	95 (5)	43 (5)
CSA + others (except Tacrolimus, MTX, MMF)	81 (1)	11 (1)	3 (<1)
CSA alone	85 (1)	12 (1)	4 (<1)
Other GVHD prophylaxis	148 (1)	19 (1)	15 (2)
Missing	75 (1)	14 (1)	5 (1)
Donor/Recipient sex match			
Male-Male	3666 (33)	646 (35)	285 (33)
Male-Female	2322 (21)	388 (21)	182 (21)
Female-Male	2791 (25)	415 (22)	196 (23)
Female-Female	2200 (20)	374 (20)	164 (19)
CB - recipient M	21 (<1)	16 (1)	8 (1)
CB - recipient F	11 (<1)	7 (<1)	5 (1)
Missing	60 (1)	13 (1)	11 (1)
Year of transplant			
2006-2010	601 (5)	71 (4)	61 (7)
2011-2015	3701 (33)	503 (27)	203 (24)
2016-2020	5028 (45)	894 (48)	399 (47)
2021-2022	1741 (16)	391 (21)	188 (22)
Follow-up among survivors, Months			
N Eval	6629	1113	510
Median (Range)	35 (0-150)	24 (0-124)	24 (0-148)

Haplo Donor with PtCy HCT Research Sample Inventory - Summary for First Allogeneic Transplants in CRF and TED with biospecimens available through the CIBMTR Repository stratified by availability of paired samples, recipient only samples and donor only samples, Biospecimens include: whole blood, serum/plasma and limited quantities of viable cells and cell lines (collected prior to 2006), Specific inventory queries available upon request through the CIBMTR Immunobiology Research Program

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Number of patients	2904	462	247
Source of data			
CRF	1082 (37)	136 (29)	98 (40)
TED	1822 (63)	326 (71)	149 (60)
Number of centers	71	53	42
Disease at transplant			
AML	1066 (37)	169 (37)	97 (39)
ALL	530 (18)	91 (20)	51 (21)
Other leukemia	42 (1)	7 (2)	5 (2)
CML	105 (4)	14 (3)	7 (3)
MDS	430 (15)	54 (12)	39 (16)
Other acute leukemia	45 (2)	9 (2)	3 (1)
NHL	214 (7)	49 (11)	16 (6)
Hodgkins Lymphoma	67 (2)	18 (4)	7 (3)
Plasma Cell Disorders, MM	42 (1)	3 (1)	3 (1)
Other malignancies	9 (<1)	0	0
SAA	101 (3)	15 (3)	4 (2)
Inherited abnormalities erythrocyte diff fxn	64 (2)	9 (2)	3 (1)
Inherited bone marrow failure syndromes	0	1 (<1)	1 (<1)
Hemoglobinopathies	24 (1)	3 (1)	1 (<1)
SCIDs	18 (1)	2 (<1)	1 (<1)
Inherited abnormalities of platelets	1 (<1)	0	0
Inherited disorders of metabolism	2 (<1)	0	0
Histiocytic disorders	14 (<1)	2 (<1)	1 (<1)
Autoimmune disorders	3 (<1)	0	0
Other	1 (<1)	0	0
Disease missing	2 (<1)	1 (<1)	0
MPN	124 (4)	15 (3)	8 (3)
AML Disease status at transplant			
CR1	670 (63)	110 (65)	59 (61)
CR2	187 (18)	28 (17)	12 (12)
CR3+	17 (2)	5 (3)	1 (1)
Advanced or active disease	191 (18)	25 (15)	25 (26)
Missing	1 (<1)	1 (1)	0
ALL Disease status at transplant			
CR1	303 (57)	57 (63)	31 (61)
CR2	160 (30)	25 (27)	15 (29)
CR3+	45 (8)	4 (4)	2 (4)

Refresh date: Dec 2022

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Advanced or active disease	22 (4)	5 (5)	3 (6)
MDS Disease status at transplant			
Early	66 (15)	8 (15)	5 (13)
Advanced	346 (80)	44 (81)	32 (82)
Missing	18 (4)	2 (4)	2 (5)
NHL Disease status at transplant			
CR1	53 (25)	12 (25)	4 (25)
CR2	52 (24)	11 (23)	2 (13)
CR3+	17 (8)	8 (17)	2 (13)
PR	4 (2)	0	0
Advanced	85 (40)	17 (35)	8 (50)
Missing	2 (1)	0	0
Recipient age at transplant			
0-9 years	184 (6)	21 (5)	12 (5)
10-17 years	230 (8)	19 (4)	9 (4)
18-29 years	405 (14)	71 (15)	27 (11)
30-39 years	248 (9)	42 (9)	33 (13)
40-49 years	355 (12)	63 (14)	21 (9)
50-59 years	541 (19)	95 (21)	50 (20)
60-69 years	720 (25)	125 (27)	79 (32)
70+ years	221 (8)	26 (6)	16 (6)
Median (Range)	51 (0-82)	52 (0-76)	55 (2-83)
Recipient race/ethnicity			
White, Non-Hispanic	1499 (52)	201 (44)	133 (54)
Black or African American, Non-Hispanic	550 (19)	97 (21)	35 (14)
Asian, Non-Hispanic	144 (5)	37 (8)	13 (5)
Native Hawaiian or Pacific Islander, Non-Hispanic	5 (<1)	1 (<1)	1 (<1)
American Indian or Alaska Native, Non-Hispanic	12 (<1)	0	2 (1)
Hispanic	506 (17)	94 (20)	45 (18)
Missing	188 (6)	32 (7)	18 (7)
Recipient sex			
Male	1719 (59)	288 (62)	147 (60)
Female	1185 (41)	174 (38)	100 (40)
Karnofsky score			
10-80	1255 (43)	216 (47)	124 (50)
90-100	1567 (54)	227 (49)	108 (44)
Missing	82 (3)	19 (4)	15 (6)
HLA-A B DRB1 groups - low resolution			
<=3/6	1884 (76)	290 (77)	156 (74)
4/6	558 (22)	85 (22)	51 (24)
5/6	41 (2)	4 (1)	4 (2)
Unknown	421 (N/A)	83 (N/A)	36 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	2312 (96)	344 (95)	179 (96)
6/8	85 (4)	17 (5)	8 (4)

Refresh date: Dec 2022

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Unknown	507 (N/A)	101 (N/A)	60 (N/A)
HLA-DPB1 Match			
Double allele mismatch	5 (1)	0	0
Single allele mismatch	570 (81)	8 (89)	3 (75)
Full allele matched	132 (19)	1 (11)	1 (25)
Unknown	2197 (N/A)	453 (N/A)	243 (N/A)
High resolution release score			
No	1488 (51)	460 (>99)	242 (98)
Yes	1416 (49)	2 (<1)	5 (2)
Graft type			
Marrow	1154 (40)	148 (32)	97 (39)
PBSC	1742 (60)	312 (68)	150 (61)
BM+PBSC	4 (<1)	1 (<1)	0
Others	4 (<1)	1 (<1)	0
Conditioning regimen			
Myeloablative	1299 (45)	201 (44)	96 (39)
RIC/Nonmyeloablative	1604 (55)	261 (56)	150 (61)
TBD	1 (<1)	0	1 (<1)
Donor age at donation			
To Be Determined/NA	1 (<1)	0	0
0-9 years	31 (1)	2 (<1)	2 (1)
10-17 years	144 (5)	30 (6)	10 (4)
18-29 years	859 (30)	147 (32)	73 (30)
30-39 years	812 (28)	136 (29)	77 (31)
40-49 years	619 (21)	92 (20)	46 (19)
50+ years	438 (15)	55 (12)	39 (16)
Median (Range)	35 (2-77)	34 (1-70)	34 (7-74)
Donor/Recipient CMV serostatus			
+/+	1239 (43)	214 (46)	84 (34)
+/-	305 (11)	33 (7)	23 (9)
-/+	794 (27)	126 (27)	63 (26)
-/-	542 (19)	81 (18)	48 (19)
Missing	24 (1)	8 (2)	29 (12)
GvHD Prophylaxis			
Post-CY + other(s)	2889 (99)	459 (99)	246 (>99)
Post-CY alone	15 (1)	3 (1)	1 (<1)
Donor/Recipient sex match			
Male-Male	1105 (38)	203 (44)	90 (36)
Male-Female	635 (22)	103 (22)	48 (19)
Female-Male	614 (21)	85 (18)	57 (23)
Female-Female	550 (19)	71 (15)	52 (21)
Year of transplant			
2006-2010	15 (1)	1 (<1)	5 (2)
2011-2015	449 (15)	59 (13)	30 (12)
2016-2020	1742 (60)	258 (56)	150 (61)

Refresh date: Dec 2022

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
2021-2022	698 (24)	144 (31)	62 (25)
Follow-up among survivors, Months			
N Eval	1740	265	154
Median (Range)	22 (0-133)	13 (2-82)	13 (0-114)

CIBMTR®
CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH

TO: Graft Sources and Manipulation Working Committee Members

FROM: Steve Spellman; Scientific Director for the Graft Sources Working Committee

RE: Studies in Progress Summary

GS19-02: Graft Failure in MDS and Acute Leukemia Patients After Allogeneic Stem Cell Transplantation Receiving Post Transplant Cyclophosphamide (C Hickey et al). The aim of this study is to examine graft failure and overall survival of haploidentical with PTCy, matched donor with PTCy in the reduced intensity conditioning setting. The study is in manuscript preparation.

GS22-01: HLA matched sibling versus well-matched unrelated donor: Update including HLA-DPB1 match status in recipients of allogeneic hematopoietic cell transplantation (Nath et al). The aim of this study is to examine the impact of donor selection for allo HCT recipients aged 50 and over. The primary outcome is overall survival after HCT with younger matched unrelated and alternative donors compared to older matched sibling donor (aged 50 years and older). The study is in protocol development.

CIBMTR Study Proposal

Study Title:
Outcomes of Non-First Degree Relative Haploidentical Blood or Marrow Transplantation Using Post-transplant Cyclophosphamide

Key Words: haploidentical, non-first degree, post-transplant cyclophosphamide

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Institution Name: Hospital of the University of Pennsylvania, Perelman School of Medicine

Proposed Working Committee:
Graft Sources and Manipulation

Research Question: Are survival and graft-versus-host disease (GVHD) outcomes after non-first-degree relative (non-FDR) donor haploidentical transplantation using post-transplant cyclophosphamide comparable to those after haploidentical transplantation using 1st degree related haploidentical donors?

Research Hypotheses:
Outcomes of haploidentical hematopoietic cell transplantation (haplo-HCT) from non-first-degree relative (non-FDR) donors do not significantly differ when compared to first-degree relative (FDR) donors when utilizing post-transplant cyclophosphamide (PTCy).

Specific Objectives:

1) To determine the overall survival of patients who receive haplo-HCT from non-FDR donors compared to FDR donors.
2) To determine the disease-free survival and cumulative incidence of acute and chronic graft-versus-host disease (GVHD) after 2 and 3rd degree haploidentical donors with PTCy.

Secondary outcomes including the following parameters between non-FDR vs. FDRs:

- Disease-free survival (DFS)
- Causes of death
- Cumulative incidence (CuI) of relapse, non-relapse mortality (NRM) and transplant related mortality (TRM)
- CuI of grade II-IV acute graft-versus-host disease (GVHD) and moderate-severe chronic GVHD
- GVHD-free, relapse-free survival (GRFS) and chronic GVHD-free, relapse-free survival (CRFS)
- Predictive factors (age, ABO, CMV) of relapse, NRM, GVHD

Scientific Impact:

The data for haploidentical transplantation (haplo-HCT) outcomes using non-first-degree related (non-FDR) donors are currently limited to single institution experiences or case series and many centers are still reluctant to perform non-FDR haplo-HCT. We propose a study in collaboration with the CIBMTR to compare outcomes after first-degree related haplo-HCT and non-FDR haplo-HCT with PTCy. If outcomes are comparable, this could expand the potential donor pool to non-FDRs. If non-FDR donors are found to be safe and effective, this has the potential to benefit patients who lack a first-degree haplo related suitable donor, but also allow the prioritization of other factors when selecting a donor. The current donor selection algorithm for FDR haplo donors focuses on donor age,[1] sex, blood groups, CMV serostatus[2,3] and recently, the discovery that HLA-B leader matching and HLA-DRB1 and HLA-DPB1 mismatching impact survival after PTCy[4] (Disease-Free Survival Calculator (b12x.org)). Therefore, if non-FDR haplo-HCT with PTCy is associated with comparable survival to FDR haplo with PTCy, then it will allow other potentially more impactful variables to be prioritized in donor selection.

Scientific Justification:

Only 30% of patients have HLA-identical sibling donors.[5,6] The development of post-transplant cyclophosphamide (PTCy) has overcome the HLA barrier preventing severe graft-versus-host disease (GVHD) after HLA-mismatched transplantation and led to the widespread adoption of haploidentical hematopoietic cell transplantation (haplo HCT). When using PTCy, outcomes for haplo donors are comparable to those after HLA-matched sibling donor [7,8], and HLA-matched unrelated donor HCT. [9]

Given the advent of PTCy as GVHD prophylaxis, second- or third-degree relative donors (i.e. nephew, niece, uncle, aunts, cousins, grandchildren) may be considered as viable graft sources. A few single institution prospective studies by Elmariah et al.[10] and Ye et al.[11] evaluated 33 and 99 non-first degree haplo-identical related donors respectively and showed an acceptable toxicity profile. However, neither study compared outcomes to those after haplo-HCT from 1st degree relative donors and use of non-FDR haplo donor use is not standard.

It has now been demonstrated that degree of HLA-mismatch does not negatively influence outcomes after haplo HCT with PTCy.[12,13] Therefore, recent studies have explored the impact of other donor

characteristics in order to improve donor selection. For instance, in a CIBMTR study, patient and disease characteristics were more influential than either the age of the donor or donor-recipient relationship with regards to survival and GVHD.[14] Graft failure rates were highest when transplanted from a parent donor without any difference in maternal or paternal donor source. In contrast, a single-center study from Johns Hopkins demonstrated less non-relapse mortality when utilizing younger haploidentical donors.[1] Then, just this year, class II HLA mismatching was shown to reduce relapse and improve survival in a large CIBMTR study, while HLA B-leader matching was demonstrated to improve NRM.[4] Thus, prioritizing younger donors or class II mismatched donors over first degree related donors may improve outcomes of haplo-HCT with PTCy. For instance, using a grandchild rather than a 50-year-old child as a donor could be associated with improve NRM. Or using a cousin with an HLA-DRB1 mismatch over an HLA-DRB1 matched sibling may lessen relapse. Thus, if outcomes are similar using a non-FDR donor when compared with a FDR haplo donor, the donor pool would grow and allow the prioritization of other factors identified as important in HCT outcomes.

Despite advances in haplo-HCTs there is still much to learn about graft sources, HLA disparity, and donor selection. The CIBMTR database can effectively answer these important practice-guiding questions that could allow the use of non-FDR when faced with limited first-degree or unrelated donor options. Furthermore, it could pave the way for new donor selection algorithms prioritizing younger or class II mismatched donors over first-degree related donor HCT with PTCy.

Patient Selection Criteria:

- Inclusion:
  - Patient's age ≥18 undergoing first haplo-SCT followed by post-transplant cyclophosphamide for hematologic malignancies between the years 2010-2021.
  - Non-FDR may include second- or third-degree relatives who shared 1 inherited haplotype with the patient.
- Exclusion:
  - Unrelated donors
  - Ex vivo graft manipulation or T-cell depletion (e.g. ATG, alemtuzumab, CD34 selection)

Data Requirements:

Forms:
2000: Recipient baseline data
2005: Confirmation of HLA typing (for both donor and recipient)
2450: Post-transplant essential data (for engraftment, chimerism, GVHD, relapse, non-relapse mortality, survival)
We believe the data available through the CIBMTR forms will be adequate to answer our question. We proposed this study last year which was well received by the working committee but eventually did not rank high at presentation. Many factors may account for that and we therefore would like to re-submit as scientific merit remains.

Patient-Reported Outcome (PRO) Requirements:

If available, we request to use the 8 Promise domains – Physical function, Fatigue, Sleep disturbance, Anxiety, Depression, Cognitive function, Ability to participate in social roles and activities, and Sexual function.

Sample Requirements:
No requirements for samples.

Study Design:
The primary endpoint is overall survival after non-FDR haplo with PTCy compared with that after FDR haplo with PTCy. Power calculations will be based on this primary endpoint.

Additional objectives are to compare the incidences of acute and chronic graft-versus-host disease, relapse, non-relapse mortality, composite endpoints (CRFS and GRFS), and the Kaplan-Meier disease-free survival between the groups.

Outcomes shall be analyzed for the entire population and/or according to the following planned subgroups: 1) Donor Age ≥40 vs. <40; 2) stem cell source (peripheral blood vs. bone marrow); 3) Disease risk index; 4) Recipient Age and 5) HCT-CI

Variables to be analyzed for inclusion in the multivariable analysis:

Patient related:

- Age at HCT - as a continuous variable and in increments of 10 years and by age <40, 40-60, 60+ years
- Performance status - KPS at HCT
- HCT-CI at HCT
- Sex
- Ethnicity
- Diagnosis
- Time from diagnosis to HCT: 0-6 versus 6-12 versus >12 months and continuous
- Prior lines of therapy
- Remission status at the time of transplant
- CMV status
- ABO blood type
- Donor chimerism at days +30, +100, +180
- Disease Risk Index

Donor:

- HLA matching level (5/10, 6/10, 7/10, 8/10, 9/10)
- Donor age
- Donor-recipient gender match: M-M vs. M-F vs. F-M vs. F-F
- Donor-recipient CMV status: +/+ or -/+ vs. +/- vs. -/-
- Donor type (1st degree – parents/full siblings/children, 2nd degree - grandparents, grandchildren, aunts, uncles, nephews, nieces, 3rd degree - first-cousins, great-grandparents or great grandchildren)
- HLA-DRB1 mismatching, HLA-DPB1 non-permissive mismatching

- HLA B-Leader match (if available)
- Donor-recipient ABO matching
- HLA typing: KIR typing if available

Disease related:

- Myeloid vs lymphoid
- Time from last treatment to haplo-HCT
- CR1 vs. CR2 vs. >CR2

Transplant related:

- Consolidation prior to transplant
- Conditioning regimen (MAC or RIC vs NMA)
- Viable CD34+ cells/kg of recipient infused (if available)
- TNC/kg of recipient before thawing
- CD3+/kg of recipient before thawing
- DSA present (yes/no)
- Prior allogeneic HCT (yes/no)
- Graft source: peripheral blood stem cells vs bone marrow
-

Outcomes:

- Overall survival
- Disease-free survival, GRFS, CRFS
- NRM, relapse, grade II-IV acute GVHD, grade III-IV acute GVHD, chronic GVHD, moderate or severe chronic GVHD,
- Causes of death
- Graft failure, immune reconstitution, and CMV reactivation

Characteristics of patients who underwent haploidentical HCT with PT-Cy for any malignant disease reported to the CIBMTR 2008-2019

	First Degree Relative	
Characteristic	**No**	**Yes**
No. of patients	437	2873
No. of centers	93	125
Age at HCT - no. (%)		
18-29	218 (50)	228 (8)
30-39	102 (23)	241 (8)
40-49	50 (11)	417 (15)
50-59	19 (4)	736 (26)
60-69	35 (8)	986 (34)

	First Degree Relative	
Characteristic	**No**	**Yes**
>=70	13 (3)	265 (9)
Relationship of donor - no. (%)		
Sibling, not identical twin	0 (0)	1001 (35)
Child	0 (0)	1862 (65)
Parent	0 (0)	10 (0)
Half-sibling	63 (14)	0 (0)
Other relative	374 (86)	0 (0)
Donor age - no. (%)		
<18	2 (0)	111 (4)
18-29	45 (10)	900 (31)
30-39	54 (12)	882 (31)
40-49	117 (27)	589 (21)
50-59	131 (30)	260 (9)
60-69	75 (17)	111 (4)
>=70	13 (3)	10 (0)
Not Reported	0 (0)	10 (0)
Primary disease for HCT - no. (%)		
AML	182 (42)	1204 (42)
ALL	111 (25)	426 (15)
Other leukemia	5 (1)	75 (3)
CML	15 (3)	101 (4)
MDS/MF	35 (8)	594 (21)
Other acute leukemia	8 (2)	42 (1)
NHL	31 (7)	306 (11)
HD	48 (11)	68 (2)
PCD	2 (0)	57 (2)
Graft Source - no. (%)		
Bone marrow	152 (35)	971 (34)
Peripheral blood	285 (65)	1902 (66)
Year of Transplant - no. (%)		
2008 – 2013	47 (11)	232 (8)
2014 – 2019	390 (89)	2641 (92)
Follow-up - median (range)	36 (3-144)	36 (3-151)

Non-CIBMTR Data Source:

We would be open to potential for collaboration with the EBMT if it is determined that additional patient numbers are needed for statistical power, but this is not a requirement for the study.

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Characteristics of patients who underwent haploidentical HCT for any malignant disease reported to the CIBMTR 2008-2019

Characteristic	No First Degree	First degree	Half-Sibling
No. of patients	154	4603	830
No. of centers	58	212	159
Age group (years) - no. (%)			
18-29	34 (22)	523 (11)	676 (81)
30-39	15 (10)	435 (9)	117 (14)
40-49	21 (14)	647 (14)	32 (4)
50-59	19 (12)	1104 (24)	3 (0)
60-69	43 (28)	1474 (32)	2 (0)
70+	22 (14)	420 (9)	0 (0)
Relationship of donor - no. (%)			
Sibling, not identical twin	0 (0)	1663 (36)	0 (0)
Child	0 (0)	104 (2)	0 (0)
Parent	0 (0)	2836 (62)	0 (0)
Half-sibling	0 (0)	0 (0)	830 (100)
Uncle/Aunt	12 (8)	0 (0)	0 (0)
Cousin	45 (29)	0 (0)	0 (0)
Grandchild	11 (7)	0 (0)	0 (0)
Niece/Nephew	30 (19)	0 (0)	0 (0)
TBD	56 (36)	0 (0)	0 (0)
Donor age group (years) - no. (%)			
<18	3 (2)	291 (6)	4 (0)
18-29	48 (31)	1497 (33)	55 (7)
30-39	48 (31)	1408 (31)	182 (22)
40-49	31 (20)	877 (19)	257 (31)
50-59	19 (12)	364 (8)	222 (27)
60-69	4 (3)	153 (3)	99 (12)
70+	1 (1)	11 (0)	11 (1)
Not Reported	0 (0)	2 (0)	0 (0)
Primary disease - no. (%)			
AML	60 (39)	1862 (40)	310 (37)
ALL	23 (15)	700 (15)	295 (36)
Other leukemia	1 (1)	91 (2)	3 (0)
CML	1 (1)	161 (3)	25 (3)
MDS	28 (18)	868 (19)	57 (7)
Other acute leukemia	2 (1)	62 (1)	16 (2)
NHL	17 (11)	422 (9)	39 (5)
HL	6 (4)	138 (3)	65 (8)

Characteristic	No First Degree	First degree	Half-Sibling
PCD/MM	0 (0)	72 (2)	2 (0)
Other Malignancies	1 (1)	1 (0)	14 (2)
MPN	15 (10)	226 (5)	4 (0)
Graft Source - no. (%)			
Bone marrow	55 (36)	1337 (29)	400 (48)
Peripheral blood	99 (64)	3266 (71)	430 (52)
TED or RES track - no. (%)			
Ted (registration) patient	79 (51)	1833 (40)	325 (39)
Research patient	69 (45)	2592 (56)	477 (57)
CRF change to Ted patient	1 (1)	17 (0)	1 (0)
Ted change to CRF patient for FN2	5 (3)	153 (3)	27 (3)
Auto no consent change to TED patient for FN2	0 (0)	3 (0)	0 (0)
Auto no consent change to CRF patient for FN2	0 (0)	5 (0)	0 (0)
Year of current transplant - no. (%)			
2010	3 (2)	25 (1)	4 (0)
2011	4 (3)	24 (1)	1 (0)
2012	6 (4)	41 (1)	8 (1)
2013	5 (3)	136 (3)	19 (2)
2014	1 (1)	232 (5)	52 (6)
2015	6 (4)	375 (8)	65 (8)
2016	10 (6)	533 (12)	89 (11)
2017	11 (7)	608 (13)	145 (17)
2018	28 (18)	719 (16)	122 (15)
2019	30 (19)	829 (18)	133 (16)
2020*	48 (31)	942 (20)	178 (21)
2021*	2 (1)	139 (3)	14 (2)

*Incomplete report

Response Summary:

This form is intended to be completed by a physician/researcher for the purpose of proposing a study. Content should not include Personal Identifiable Information (PII) or Protected Health Information (PHI). If you are a patient, do not complete this form. Patients: Contact your healthcare provider immediately for reports of problems with your treatment or problems with products received for your treatment. The CIBMTR uses de-identified data and is unable to associate reported treatment problems, adverse events, or corrections of information with a center, clinical trial, or healthcare provider.

Q1. Study Title

Impact of donor source in second allogeneic hematopoietic cell transplant (HCT) in patients with acute leukemia/MDS who relapsed after prior allograft during the current era (2014-2020)

Q2. Key Words

HCT, relapse, donor, second transplant, haplo-identical donor, cord blood, GvHD, GvL

Q3. PRINCIPAL INVESTIGATOR

Provide the following information for each investigator:

Principal Investigator #1:

First and last name, degree(s):	Alexandre Troullioud Lucas, MD, MSc
Email address:	troullia@mskcc.org
Institution name:	Memorial Sloan Kettering Cancer Center, NY
Academic rank:	Assistant Attending

Q4. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- Yes

Q5. Do you identify as an underrepresented/minority?

- No

Q6. Principal Investigator #2 (If applicable):

First and last name, degree(s):	Andromachi Scaradavou, MD
Email address:	scaradaa@mskcc.org
Institution name:	Memorial Sloan Kettering Cancer Center, NY
Academic rank:	Assocaite Attending

Q7. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- No

Q8. Do you identify as an underrepresented/minority?

- No

Q9. We encourage a maximum of two Principal Investigators per study. If more than one author is listed, please indicate who will be identified as the corresponding PI below:

Corresponding PI will be Alexandre Troullioud Lucas

Q10. If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:

N/A

LETTER OF COMMITMENT:

Please note: *A letter of commitment will be signed by Lead and Last authors as it describes the expectations for filling that role. By signing the letter of commitment, the authors accept their responsibilities and will be held accountable for timely completion of all steps in the project. More details regarding author responsibilities can be found here:* *https://www.cibmtr.org/Studies/Observational/StudyManagement/p*

Q12. CURRENT ONGOING WORK WITH CIBMTR: Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.

Machi Scaradavou: CIBMTR Executive Committee, GSWC and Pediatric Cancer WC

Q13. PROPOSED WORKING COMMITTEE:

- Graft Sources and Manipulation

Q14. Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.

- Yes

Q14a. If you have already spoken with a scientific director or working committee chair regarding this study, then please specify who:

Stephen Spellman

Q15. RESEARCH QUESTION:

Is there an impact of donor source (related, unrelated, haplo-identical or unrelated CB graft) on outcomes of second allogeneic HCT for treatment of relapse in pediatric and adult patients with acute leukemia/MDS who were transplanted during the current era (2014-2020)?

Q16. RESEARCH HYPOTHESIS:

The optimal donor for second allogeneic HCT (HCT-2) for patients who relapsed after their first transplant has not been established. Older retrospective studies have identified prognostic variables, but these may not be directly applicable to current practice. With recent treatment advances and expanded donor and graft choices, we expect improved Leukemia-free Survival (LFS) after HCT-2 performed during the period 2014-2020 compared to previously reported outcomes (1,2). We hypothesize that there is an impact of donor source on LFS, and this may be different for pediatric and adult recipients.

Q17. SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.) *Suggested word limit of 200 words:*

Primary Aim:
Evaluate the impact of HCT-2 donor (related, unrelated, haplo-identical or CB) on Leukemia-free Survival (LFS) at 1 year in patients transplanted during the period 2014-2020.
Secondary Aims:
1. Evaluate transplant outcomes after HCT-2 (LFS, overall survival [OS], relapse, transplant-related mortality [TRM], graft failure and acute/chronic GVHD) in the subgroup of patients who received unrelated CB grafts stratified by TNC/CD34 cell dose; analyze separately pediatric and adult patients.
2. Evaluate transplant outcomes after HCT-2 (LFS, OS, relapse, TRM, graft failure and acute/chronic GVHD) in the subgroup of patients who had haplo-donors stratified for same or different donor – with different shared haplotype.
3. Evaluate whether development of GvHD (acute or chronic) after HCT-1 impacts the incidence of relapse after HCT-2 stratified by the donor for HCT-2: same vs. different donor.

Q18. SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.

Relapse after allogeneic HCT remains the leading cause of mortality for patients with acute leukemia. The only potentially curative approach is a second transplant (1,2,3). As these patients have very high-risk disease the anti-leukemic potential of the donor graft of HCT-2 is of critical importance. This proposal evaluates donor-related variables that may enhance LFS after HCT-2.
There is an unmet need, in our opinion, to define optimal donor selection and identify modifiable variables that can further improve outcomes in children and adults after HCT-2. The strength of our study is to use data of a "contemporary" patient cohort, i.e., transplants performed during the period 2014-2020, so that results can be easily applicable to current practice and facilitate patient counseling and treatment decisions.

Q19. SCIENTIFIC JUSTIFICATION: Provide a background summary of previous related research and their strengths and weaknesses, justification of your research and why your research is still necessary.

Patients who relapse after allo-HCT have limited treatment options and poor survival. A second transplant represents the only curative treatment (1,2). The optimal donor for second allogeneic HCT (HCT-2) has not been established. Donor selection is based on prompt availability and potent antileukemic effect. This proposal evaluates donor-related variables that may improve outcomes after HCT-2.
Unrelated CB grafts exert a strong Graft-versus-Leukemia (GVL) effect after first allo-HCT (HCT-1), particularly in patients with Minimal Residual Disease (MRD) (4,5,6). Based on clinical experience and preclinical data, there is growing evidence of the unique immunological properties of CB T cells (7,8), making these grafts 'intrinsically' more effective as anti-leukemia treatment, and therefore preferable for HCT-2.
Changing the donor for HCT-2 to enhance the GVL effect has shown limited or no benefit in several prior analyses (9,10,11). Recently, however, promising data on improved leukemia control after HCT-2 using a different donor, HLA-haploidentical, have been reported (12). An advantage was also seen by switching the haplo donor of HCT-1 to another

haplo donor sharing a different haplotype for HCT-2, in a single institution study (13). A more extensive analysis is needed to help define the optimal haploidentical donor for HCT-2.
Importantly, both alternative donor sources (haplo-donors and CB grafts) can be readily available so that transplant logistics are simplified and treatment can be expedited.
Finally, it is understood that GvHD and GVL may have shared immunobiology, and thus GvHD can influence relapse (14). While several factors including disease status, time of relapse after HCT-1, and interval between the two transplants have an effect on outcomes (1-3, 9-13), the impact of GvHD following HCT-1 and/or HCT-2, as an indication of a possible GVL effect, has not been evaluated in association with the outcomes of HCT-2. This question becomes particularly relevant in the context of selecting the donor source for HCT-2, i.e., same vs. different donor, and donor types including CB grafts or haplo.
Historically, HCT-2 has been hampered with a high incidence of TRM. A CIBMTR analysis of second transplants in pediatric patients performed primarily before 2010 showed similar disappointing outcomes (2). However, these results do not reflect current treatment modalities and standards of care. In recent years, improved survival and lower TRM have been achieved with the use of new, less toxic cytoreduction regimens and better GvHD prophylaxis. For CB grafts, in particular, optimization of cytoreduction with omission of ATG treatment (15,16) and better graft selection (17,18) have led to improved survival after CB HCT-1 (7,19). Recent analyses indicate improved results after HCT-2 also: Our institutional analysis of 26 pediatric patients (MSKCC and Princess Maxima combined cohort) showed lower TRM after CB HCT-2 in the recent period, with an encouraging 3-year EFS of 63.2% +/- 9.9% (abstract in ref. 20; manuscript in preparation). Along the same lines, a Japanese registry analysis of 1109 adult patients with AML who relapsed after first allograft and received CB grafts for HCT-2 also showed significantly improved outcomes in more recent transplants (21). Finally, a French multicenter study of adult patients undergoing HCT-2 with haploidentical donors or CB grafts showed significantly improved outcomes for transplants performed anfter 2012 (22). Given these encouraging results, we believe that it is important to evaluate the outcomes of HCT-2 in a larger patient cohort.
In summary, we propose to evaluate the impact of donor source, and donor change, on outcomes of HCT-2 by analyzing a contemporary cohort of patients and identifying donor characteristics that may enhance the GVL effect and the efficacy of the transplant. The results will be directly applicable to current practice.
This proposal combines three previously submitted proposals from the following PIs:
Evandro Bezerra, MD
E-mail address: bezerra.evandro@mayo.edu
Institution name: Mayo Clinic, MN
Academic rank: Hematology/Oncology fellow (PGY-5)
Mark R. Litzow, MD
E-mail address: litzow.mark@mayo.edu
Institution name: Mayo Clinic, MN
Academic rank: Professor
Idoroenyi Amanam, MD
E-mail address: iamanam@coh.org
Institution name: City of Hope Medical Center, CA
Academic Rank: Assistant Professor
Ryotaro Nakamura, MD
E-mail address: rnakamura@coh.org
Institution name: City of Hope Medical Center, CA
Academic Rank: Professor
Alexandre G. Troullioud Lucas, MD, MSc
E-mail address: troullia@mskcc.org
Institution name: Memorial Sloan Kettering Cancer Center, NY
Academic Rank: Assistant Attending
Caroline A. Lindemans, MD, PhD
E-mail address: C.A.lindemans@prinsesmaximacentrum.nl
Institution name: Princess Maxima Center for Pediatric Oncology, Utrecht, Netherlands
Academic Rank: Associate Professor
Andromachi Scaradavou, MD (presenter at TCT 2022 if the proposal is selected by the GSWC)
E-mail address: scaradaa@mskcc.org
Institution name: Memorial Sloan Kettering Cancer Center, NY
Academic Rank: Associate Attending

Q19a. SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF)

N/A

Q20. PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.

Inclusion criteria:
Patient characteristics at HCT-2
• Age: all ages; age groups: 10 years;
For specific analyses: pediatric patients: 0-19 years
• Performance score: <80, 80 and above
• Comorbidity Index: 0, 1-2, ≥3
• CMV status: positive, negative
Transplant characteristics at HCT-1
• Donor: any (related, unrelated, haplo)
• Graft: any (BM, PB or CB)
• Cytoreduction: myeloablative or reduced-intensity
• GvHD prophylaxis: T cell depletion, CNI, PTCy, other
• Acute GvHD or not (if yes, grade); chronic GvHD or not
• Time to relapse after HCT-1: < 6 months, 6-12 months, >12 months
Disease characteristics at HCT-2
• Diagnosis: AML, ALL, other acute leukemia, MDS
• Status: CR or not, if CR, MRD present or not
• Disease Risk Index (DRI)
• Reason for HCT-2: relapse
Transplant characteristics at HCT-2
• Donor: any (related, unrelated, haplo)
Same or different donor
For CB: TNC and CD34 cell dose; HLA match; single/double CB graft
• Graft: any (BM, PB or CB)
• Cytoreduction: myeloablative or reduced-intensity; ATG or not
• GvHD prophylaxis: T cell depletion, CNI, PTCy, other
• Time from relapse to HCT-2: < 6 months, 6-12 months, >12 months
• Interval between HCT-1 and HCT-2: < 6 months, 6-12 months, >12 months
• Follow-up after HCT-2: >1 year
• Acute GvHD or not (if yes, grade); chronic GvHD or not
• Cause of death (if applicable)
• TC experience with haplo or CB transplants (reported >5 vs. less than 5)
Note 1: Patients could have received DLI of CAR T cell therapy before HCT-2.
Note 2: CB grafts will not be considered in the analysis of “different donor” for HCT-2.
Exclusion criteria:
For HCT-2 CB analysis: patients who received ATG; patients who received ex vivo expanded CB grafts; patients who received haplo+CB graft

Q21. Does this study include pediatric patients?

- Yes

Q22. DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Data collection forms available at: http://www.cibmtr.org/DataManagement/DataCollectior Outline any supplementary data required. Additional data collection is extremely difficult and will make your proposal less feasible.

Age, diagnosis, disease status at HCT-1 (CR or not, MRD positive or negative), DRI, HCT-1 cytoreduction (myeloablative or not), HCT-1 donor (related, unrelated, haplo, CB), HCT-1 GvHD prophylaxis (T cell depletion, CNI, PTCy, other), acute GvHD (and stage), chronic GvHD, time to relapse after HCT-1, disease status at HCT-2, (MRD status if in remission, DRI), time interval between HCT-1 and HCT-2, cytoreduction for HCT-2 (myeloablative or not), ATG or not, HCT-2 donor (related, unrelated, haplo, CB), same or different donor, HCT-2 GvHD prophylaxis (T cell depletion, CNI, PTCy, other), time to ANC>500, time to plts>50K, donor chimerism, acute GVHD (and stage), chronic GVHD, CMV status, TC experience with haplo or CB transplants (reported >5 vs less than 5).
For haplo: same or different haplo donor
For CB grafts: TNC/CD34 cell dose, single or double, HLA match to patient (preferably allele level).
Statistical analysis: Cox proportional hazard and Fine-Gray competing risk analyses will be used. Statistical analyses will be done under the guidance of the CIBMTR Working Committee Statistician and Medical Director.

Q23. PATIENT REPORTED OUTCOME (PRO) REQUIREMENTS: If the study requires PRO data collected by CIBMTR, the proposal should include: 1) A detailed description of the PRO domains, timepoints, and proposed analysis of PROs; 2) A description of the hypothesis specific to PROS.

For additional information on what PRO measures have been collected and timepoints of collection, please reach out to the Late Effects and Quality of Life or Health Services Working Committee leadership: https://www.cibmtr.org/About/WhoWeAre/Com

No

Q24. **SAMPLE REQUIREMENTS: If the study requires biologic samples from the CIBMTR Repository, the proposal should also include: 1) A detailed description of the proposed testing methodology and sample requirements; 2) A summary of the investigator's previous experience with the proposed assay systems. PIs should be encouraged to review the inventory details, sample types collected and reach out to research_repos@nmdp.org with any questions.**

More information can be found at: https://www.cibmtr.org/Samples/Inventory/Pages/index

No biologic sample requirements from the NMDP repository.

Q25. **NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required, i.e., neither database contains all the data required to answer the study question.**

N/A

Q26. REFERENCES:

1. Ruutu T, de Wreede LC, van Biezen A, et al. Second allogeneic transplantation for relapse of malignant disease: retrospective analysis of outcome and predictive factors by the EBMT. Biol Blood Marrow Transplant. 2015;50:1542-1550.
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3. Gyurkocza B, Storb R, Chauncey T, et al. Second allogeneic hematopoietic stem cell transplantation for relapse after first allografts. Leukemia and Lymphoma. 2019;60 (7)1758-1766.
4. Milano F, Gooley T, Wood B, et al. Cord-Blood Transplantation in Patients with Minimal Residual Disease. N Engl J Med. 2016;375(10):944-953.
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7. Hiwarkar P, Hubank M, Qasim W, et al. Cord blood transplantation recapitulates fetal ontogeny with a distinct molecular signature that supports CD4+ T-cell reconstitution. Blood Adv. 2017;1:2206-2216.
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13. Imus PH, Blackford AL, Bettinotti M, et al. Major Histocompatibility Mismatch and Donor Choice for Second Allogeneic Bone Marrow Transplantation. Biol Blood Marrow Transplant. 2017; 23:1887-1894.
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17. Barker JN, Kurtzberg J, Ballen K, et al. Optimal Practices in Unrelated Donor Cord Blood Transplantation for Hematologic Malignancies. Biol Blood Marrow Transplant. 2017;23: 882-896.
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Q27. **CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning:**

1. Employment (such as an independent contractor, consultant or providing expert testimony)?
2. Relationships (such as executive and advisory committee positions, medical consultant, speaker's bureau)?
3. Ownership (such as equity, ownership or financial interests)?
4. Transactions (such as honoraria, patents, royalties and licenses)?
5. Legal (such as pending or current arbitration or legal proceedings)?

- No, I do not have any conflicts of interest pertinent to this proposal

Q27a. **If yes, provide detail on the nature of employment, name of organization, role, entity, ownership, type of financial transaction or legal proceeding and whether renumeration is >$5000 annually.**

N/A

BEFORE FINAL SUBMISSION, please review the PI checklist to ensure that you have completed all necessary steps. This will increase the likelihood of submitting a feasible and successful proposal.

Embedded Data:

N/A

Characteristics of patients who underwent second allo HCT for relapsed malignant disease reported to the CIBMTR 2008-2021

Characteristic	Different Donor	Same Donor
No. of patients	1374	405
No. of centers	197	131
Age (years) - no. (%)		
<1-<18	299 (22)	56 (14)
18-29	215 (16)	62 (15)
30-39	174 (13)	47 (12)
40-49	198 (14)	58 (14)
50-59	224 (16)	95 (24)
60-69	229 (17)	77 (19)
70+	35 (3)	10 (3)
Interval between first and second allo transplant - no. (%)		
<6 months	36 (3)	39 (10)
6-12 months	243 (17)	96 (24)
12-24 months	492 (36)	119 (29)
24+ months	603 (44)	151 (37)
Primary disease - no. (%)		
AML	853 (62)	270 (67)
ALL	330 (24)	72 (18)
Other leukemia	15 (1)	4 (1)
CML	31 (2)	6 (2)
MDS	114 (8)	42 (10)
MPN	31 (2)	11 (3)
Donor type - no. (%)		
HLA-identical sibling	94 (7)	227 (56)
Matched Related Donor (8/8)	2 (<1)	2 (1)
Mis-Matched Related Donor (7/8)	9 (1)	5 (1)
Haploidentical Donor (<=6/8)	399 (29)	32 (8)
Other Related Donor Match TBD	19 (1)	6 (2)
Well-matched unrelated (8/8)	522 (38)	94 (23)
Partially-matched unrelated (7/8)	116 (8)	18 (4)
Mis-matched unrelated (<= 6/8)	14 (1)	3 (1)
Multi-donor	9 (1)	2 (1)
Unrelated (matching TBD)	60 (4)	16 (4)
Cord blood	130 (10)	0 (<1)
Donor age group - no. (%)		

Characteristic	Different Donor	Same Donor
<18 years	68 (5)	43 (11)
18-29 years	550 (40)	70 (17)
30-39 years	327 (24)	59 (15)
40-49 years	164 (12)	47 (12)
50-59 years	103 (8)	53 (13)
60-69 years	38 (3)	41 (10)
70+ years	7 (1)	4 (1)
Not reported	117 (9)	88 (22)
Graft source - no. (%)		
Bone marrow	189 (14)	44 (11)
Peripheral blood	1055 (77)	361 (89)
Umbilical cord blood	130 (10)	0 (<1)
TED or RES track - no. (%)		
Ted (registration) patient	865 (63)	289 (71)
Research patient	394 (29)	99 (24)
CRF change to Ted patient	27 (2)	7 (2)
Ted change to CRF patient for FN2	88 (6)	10 (3)
Year of current transplant - no. (%)		
2008	2 (<1)	3 (1)
2009	1 (<1)	3 (1)
2010	3 (<1)	0 (<1)
2011	2 (<1)	1 (<1)
2012	7 (1)	6 (2)
2013	52 (4)	26 (6)
2014	147 (11)	65 (16)
2015	159 (12)	64 (16)
2016	165 (12)	50 (12)
2017	199 (15)	48 (12)
2018	242 (18)	47 (12)
2019	239 (17)	54 (13)
2020*	124 (9)	29 (7)
2021*	32 (2)	9 (2)
Follow-up - median (range)	35 (<1-144)	45 (<1-96)

*Incomplete reporting for these years

Response Summary:

This form is intended to be completed by a physician/researcher for the purpose of proposing a study. Content should not include Personal Identifiable Information (PII) or Protected Health Information (PHI). If you are a patient, do not complete this form. Patients: Contact your healthcare provider immediately for reports of problems with your treatment or problems with products received for your treatment. The CIBMTR uses de-identified data and is unable to associate reported treatment problems, adverse events, or corrections of information with a center, clinical trial, or healthcare provider.

Q1. Study Title

Impact of Adherence to Cord Blood Guidelines

Q2. Key Words

Cord Blood Transplant, Acute Myeloid Leukemia, Myelodysplasia, Acute Lymphocytic Leukemia

Q3. PRINCIPAL INVESTIGATOR

Provide the following information for each investigator:

Principal Investigator #1:

First and last name, degree(s):	Leland Metheny, MD
Email address:	leland.metheny.uhhospitals.org
Institution name:	University Hospitals Cleveland Medical Center
Academic rank:	N/A

Q4. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- No

Q5. Do you identify as an underrepresented/minority?

- No

Q6. Principal Investigator #2 (If applicable):

First and last name, degree(s):	Filippo Milano, MD, PhD
Email address:	fmilano@fredhutch.org
Institution name:	Fred Hutchinson Cancer Center
Academic rank:	N/A

Q7. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- No

Q8. Do you identify as an underrepresented/minority?

- No

Q9. We encourage a maximum of two Principal Investigators per study. If more than one author is listed, please indicate who will be identified as the corresponding PI below:

Leland Metheny

Q10. If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:

N/A

LETTER OF COMMITMENT:

Please note: *A letter of commitment will be signed by Lead and Last authors as it describes the expectations for filling that role. By signing the letter of commitment, the authors accept their responsibilities and will be held accountable for timely completion of all steps in the project. More details regarding author responsibilities can be found here:* *https://www.cibmtr.org/Studies/Observational/StudyManagement/p*

Q12. CURRENT ONGOING WORK WITH CIBMTR: Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.

N/A

Q13. PROPOSED WORKING COMMITTEE:

- Graft Sources and Manipulation

Q14. Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.

- Yes

Q14a. If you have already spoken with a scientific director or working committee chair regarding this study, then please specify who:

Steve Spellman

Q15. RESEARCH QUESTION:

1. How does adherence to published cord blood guidelines affect clinical outcomes in cord blood transplant for AML, ALL, and MDS?

Q16. RESEARCH HYPOTHESIS:

Adherence to published cord blood guidelines in cord blood transplant (TNC dose, CD34 dose, HLA matching, criteria for conditioning intensities, and GVHD prophylaxis) improves clinical outcomes, including treatment related mortality, relapse free survival, and overall survival when compared to non-adherence to cord blood guidelines.

Q17. SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.)

Suggested word limit of 200 words:

Primary Aim

1. Compare the overall survival, treatment related mortality, relapse rate and disease free survival between double cord blood transplants that adhered to cord blood guidelines (TNC dose, CD34 dose, HLA matching, criteria for conditioning intensities, and GVHD prophylaxis) with cord blood transplants that did not adhere to cord blood guidelines.

Secondary aims

1. Compared engraftment rates between double cord blood transplants that adhered to cord blood guidelines (TNC dose, CD34 dose, HLA matching, criteria for conditioning intensities, and GVHD prophylaxis) with cord blood transplants that did not adhere to cord blood guidelines.
2. Compare cumulative aGVHD rates and grades, cGVHD rates and grades, and GVHD-free relapse-free survival (GRFS) of double cord blood transplants that adhered to cord blood guidelines (TNC dose, CD34 dose, HLA matching, criteria for conditioning intensities, and GVHD prophylaxis) with cord blood transplants that did not adhere to cord blood guidelines.
3. Compare overall survival, treatment related mortality, relapse rate and disease free survival between double cord blood transplants with risk factors (minimal residual disease, p53 mutations, second allogeneic transplant) and that adhered to cord blood guidelines (TNC dose, CD34 dose, HLA matching, criteria for conditioning intensities, and GVHD prophylaxis) with cord blood transplants that did not adhere to cord blood guidelines and had the same risk factors.
4. Compare overall survival, treatment related mortality, relapse rate, disease free survival, and GRFS between double cord blood transplants that adhered to cord blood guidelines (TNC dose, CD34 dose, HLA matching, criteria for conditioning intensities, and GVHD prophylaxis) with haploidentical with PTCY, matched unrelated, mismatched unrelated with PTCY, and matched related donor transplants (we would only perform this aim if we detect an improvement in outcomes in the cord blood transplants that adhere to the guidelines vs. those that did not)

Q18. SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.

If our hypothesis is correct and the adherence to cord blood guidelines is associated with improved clinical outcomes, then prospective trials involving cord blood transplant should incorporate these guidelines. Additionally, if adhering to cord blood guidelines suggests a significant improvement in cord blood outcomes when compared to other graft sources, this may result in new prospective protocols comparing these graft sources.

Q19. SCIENTIFIC JUSTIFICATION: Provide a background summary of previous related research and their strengths and weaknesses, justification of your research and why your research is still necessary.

Umbilical cord blood (CB) is used as a source of stem cell in patients without a HLA- matched related or unrelated donors. The cell dose of total nucleated cell (TNC), CB34+ cells, and the degree of HLA disparities between cord blood donor and recipient are known to affect engraftment and clinical outcomes. The publication of cord blood guidelines on cord blood graft selection, conditioning intensity and GVHD prophylaxis offers an opportunity to separate out cord blood transplants (CBT) that adhered to these guidelines and compare outcomes with those that did not. Demonstrating that adherence to CB guidelines can improve outcomes is important for patient populations that have difficult to match haplo-types, those in need of a rapid transplant, or those of racial and ethnic minorities without HLA-matched donors.

Q19a. SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF)

N/A

Q20. PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.

Inclusion criteria:
1. Adult patients (≥ 18 years) with a diagnosis of Acute Myeloid Leukemia, Myelodysplasia, Acute Lymphocytic Leukemia.
2. Patients who have undergone allogeneic transplant with double cord blood transplant between 2010-2020
3. For Secondary Aim #4: Patients who have undergone haploidentical with PTCY, matched unrelated, mismatched unrelated with PTCY, and matched related donor transplants for the above malignancies

Exclusion Criteria:
1. For Secondary Aim #4: second allogeneic transplant not included in this analysis

Q21. Does this study include pediatric patients?

- No

Q21a. If this study does not include pediatric patients, please provide justification:

N/A

Q22. DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Data collection forms available at: http://www.cibmtr.org/DataManagement/DataCollectior Outline any supplementary data required. Additional data collection is extremely difficult and will make your proposal less feasible.

Patient Characteristics
- Patient age
- Patient gender
- Patient race / ethnicity
- KPS (<70, 70-90, > 90)
- Patient Comorbidity Index

Disease Characteristics
- Disease type (Acute Myeloid Leukemia, Myelodysplasia, Acute Lymphocytic Leukemia)
- Lines of prior therapies
- Evidence of minimal residual disease prior to transplant
- Disease state prior to allogeneic transplant
- Patient Disease Risk Index
- IPSS score for MDS patients
- ELN risk group for AML
- Type of ALL (T-cell vs. B-cell)
- Cytogenetics /mutations of disease and mutations
- Therapy related neoplasm (Y/N)

Transplant Characteristics
- Conditioning Chemotherapy (NMA vs. RIC vs. MAC)
- ATG use (Y/N) and dose
- Date transplant
- Cell dose of cord blood (CD34, TNC)
- HLA matching of donor to recipient,
- Graft type: bone marrow or peripheral blood (Secondary Aim #4)
- CMV positivity of donor / recipient
- Time from diagnosis to transplant
- GVHD prophylaxis

Clinical Outcomes
- Acute GVHD rate and grade and duration
- Chronic GVHD rate and grade and duration
- Disease-free survival 1 and 3 years
- Treatment Related Mortality 1 and 3 years
- Overall Survival 1 and 3 years
- Relapse Rate 1 and 3 years
- GVHD-free relapse-free survival 1 and 3 years

Q23. **PATIENT REPORTED OUTCOME (PRO) REQUIREMENTS: If the study requires PRO data collected by CIBMTR, the proposal should include: 1) A detailed description of the PRO domains, timepoints, and proposed analysis of PROs; 2) A description of the hypothesis specific to PROS.**

For additional information on what PRO measures have been collected and timepoints of collection, please reach out to the Late Effects and Quality of Life or Health Services Working Committee leadership: https://www.cibmtr.org/About/WhoWeAre/Com

None required

Q24. **SAMPLE REQUIREMENTS: If the study requires biologic samples from the CIBMTR Repository, the proposal should also include: 1) A detailed description of the proposed testing methodology and sample requirements; 2) A summary of the investigator's previous experience with the proposed assay systems. PIs should be encouraged to review the inventory details, sample types collected and reach out to research_repos@nmdp.org with any questions.**

More information can be found at: https://www.cibmtr.org/Samples/Inventory/Pages/index

None required

Q25. **NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required, i.e., neither database contains all the data required to answer the study question.**

NA

Q26. **REFERENCES:**

N/A

Q27. **CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning:**

1. Employment (such as an independent contractor, consultant or providing expert testimony)?
2. Relationships (such as executive and advisory committee positions, medical consultant, speaker's bureau)?
3. Ownership (such as equity, ownership or financial interests)?
4. Transactions (such as honoraria, patents, royalties and licenses)?
5. Legal (such as pending or current arbitration or legal proceedings)?

- No, I do not have any conflicts of interest pertinent to this proposal

Q27a. **If yes, provide detail on the nature of employment, name of organization, role, entity, ownership, type of financial transaction or legal proceeding and whether renumeration is >$5000 annually.**

N/A

BEFORE FINAL SUBMISSION, please review the PI checklist to ensure that you have completed all necessary steps. This will increase the likelihood of submitting a feasible and successful proposal.

Embedded Data:

N/A

Characteristics of patients who underwent first allo HCT for AML, ALL, or MDS with a UCB graft reported to the CIBMTR 2005-2019 by guideline

	Guidelines Followed		
Characteristic	**No**	**Yes**	**Not Reported**
No. of patients	257	270	233
No. of centers	70	65	59
Age (years) - no. (%)			
18-29	69 (27)	67 (25)	53 (23)
30-39	33 (13)	37 (14)	33 (14)
40-49	50 (19)	49 (18)	50 (21)
50-59	50 (19)	65 (24)	57 (24)
60-69	43 (17)	44 (16)	34 (15)
70+	12 (5)	8 (3)	6 (3)
Race - no. (%)			
White	192 (75)	208 (77)	132 (57)
Black or African American	33 (13)	26 (10)	5 (2)
Asian	13 (5)	24 (9)	13 (6)
Native Hawaiian or other Pacific Islander	0 (0)	1 (0)	0 (0)
American Indian or Alaska Native	0 (0)	1 (0)	1 (0)
More than one race	2 (1)	3 (1)	0 (0)
Missing	17 (7)	7 (3)	82 (35)
Primary disease - no. (%)			
AML	164 (64)	152 (56)	131 (56)
ALL	63 (25)	69 (26)	55 (24)
MDS	30 (12)	49 (18)	47 (20)
Donor type - no. (%)			
Unrelated single CB, 6/6	23 (9)	20 (7)	4 (2)
Unrelated single CB, 5/6	87 (34)	81 (30)	29 (12)
Unrelated single CB, LE4/6	119 (46)	136 (50)	49 (21)
Unrelated single CB, degree of match Unknown	28 (11)	33 (12)	151 (65)
CD34 cell doses (1st cord, x 10^5/kg) - no. (%)			
<1.5 x 10/kg	146 (57)	0 (0)	0 (0)
>=1.5 x 10/kg	35 (14)	183 (68)	0 (0)
Not reported	76 (30)	87 (32)	233 (100)
Nucleated cell doses (1st cord, x 10^7/kg) - no. (%)			
<2.5 x 10/kg	171 (67)	0 (0)	0 (0)
>=2.5 x 10/kg	72 (28)	260 (96)	0 (0)
Not reported	14 (5)	10 (4)	233 (100)

	Guidelines Followed		
Characteristic	**No**	**Yes**	**Not Reported**
Conditioning regimen intensity - no. (%)			
MAC	184 (72)	166 (61)	175 (75)
RIC	16 (6)	26 (10)	21 (9)
NMA	30 (12)	54 (20)	14 (6)
TBD	16 (6)	18 (7)	18 (8)
Missing	11 (4)	6 (2)	5 (2)
Year of transplant - no. (%)			
2005 - 2009	85 (33)	65 (24)	52 (22)
2010 - 2014	100 (39)	89 (33)	107 (46)
2015 - 2019	72 (28)	116 (43)	74 (32)

Characteristics of patients who underwent first allo HCT for AML, ALL, or MDS with a dUCB graft reported to the CIBMTR 2005-2022 by guideline

	Guideline Followed		
Characteristic	**No**	**Yes**	**Not Reported**
No. of patients	1287	596	949
No. of centers	114	69	143
Age (years) - no. (%)			
18-29	226 (18)	116 (19)	212 (22)
30-39	266 (21)	90 (15)	148 (16)
40-49	218 (17)	91 (15)	185 (19)
50-59	261 (20)	132 (22)	233 (25)
60-69	287 (22)	148 (25)	151 (16)
70+	29 (2)	19 (3)	20 (2)
Race - no. (%)			
White	889 (69)	450 (76)	638 (67)
Black or African American	134 (10)	47 (8)	103 (11)
Asian	135 (10)	51 (9)	101 (11)
Native Hawaiian or other Pacific Islander	11 (1)	7 (1)	5 (1)
American Indian or Alaska Native	16 (1)	1 (0)	5 (1)
More than one race	17 (1)	9 (2)	3 (0)
Missing	85 (7)	31 (5)	94 (10)
Primary disease - no. (%)			
AML	787 (61)	362 (61)	563 (59)
ALL	324 (25)	148 (25)	261 (28)
MDS	176 (14)	86 (14)	125 (13)
Donor type (US AlloHCT activity report) - no. (%)			
Unrelated double CB, 6/6	41 (3)	24 (4)	28 (3)
Unrelated double CB, 5/6	375 (29)	152 (26)	190 (20)
Unrelated double CB, LE 4/6	671 (52)	353 (59)	462 (49)
Unrelated double CB, degree of match Unknown	200 (16)	67 (11)	269 (28)
CD34 cell doses (1st cord, x 10^5/kg) - no. (%)			
<1.0 x 10/kg	832 (65)	0 (0)	103 (11)
>=1.0 x 10/kg	446 (35)	590 (99)	64 (7)
Not reported	9 (1)	6 (1)	782 (82)
CD34 cell doses (2nd cord, x 10^5/kg) - no. (%)			
<1.0 x 10/kg	868 (67)	0 (0)	80 (8)
>=1.0 x 10/kg	406 (32)	589 (99)	26 (3)
Not reported	13 (1)	7 (1)	843 (89)

	Guideline Followed		
Characteristic	**No**	**Yes**	**Not Reported**
Nucleated cell doses (1st cord, x 10^7/kg) - no. (%)			
<1.5 x 10/kg	274 (21)	0 (0)	48 (5)
>=1.5 x 10/kg	1008 (78)	594 (100)	200 (21)
Not reported	5 (0)	2 (0)	701 (74)
Nucleated cell doses (2nd cord, x 10^7/kg) - no. (%)			
<1.5 x 10/kg	323 (25)	0 (0)	25 (3)
>=1.5 x 10/kg	961 (75)	596 (100)	119 (13)
Not reported	3 (0)	0 (0)	805 (85)
Conditioning regimen intensity - no. (%)			
MAC	672 (52)	268 (45)	490 (52)
RIC	87 (7)	28 (5)	42 (4)
NMA	347 (27)	193 (32)	256 (27)
TBD	120 (9)	65 (11)	88 (9)
Missing	61 (5)	42 (7)	73 (8)
Year of transplant - no. (%)			
2005 - 2009	195 (15)	109 (18)	180 (19)
2010 - 2014	653 (51)	248 (42)	534 (56)
2015 - 2019	439 (34)	239 (40)	235 (25)

Response Summary:

This form is intended to be completed by a physician/researcher for the purpose of proposing a study. Content should not include Personal Identifiable Information (PII) or Protected Health Information (PHI). If you are a patient, do not complete this form. Patients: Contact your healthcare provider immediately for reports of problems with your treatment or problems with products received for your treatment. The CIBMTR uses de-identified data and is unable to associate reported treatment problems, adverse events, or corrections of information with a center, clinical trial, or healthcare provider.

Q1. Study Title

Does use of ex vivo expanded cord blood lead to improved outcomes compared to unmanipulated umbilical cord blood or haploidentical graft in myeloablative hematopoietic cell transplant?

Q2. Key Words

Umbilical cord blood, haploidentical, ex vivo, expanded, myeloablative, stem cell transplant

Q3. PRINCIPAL INVESTIGATOR

Provide the following information for each investigator:

Principal Investigator #1:

First and last name, degree(s):	Andrew Trunk, MD
Email address:	trunka@ccf.org
Institution name:	Cleveland Clinic Foundation
Academic rank:	Fellow

Q4. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- Yes

Q5. Do you identify as an underrepresented/minority?

- No

Q6. Principal Investigator #2 (If applicable):

First and last name, degree(s):	Claudio Brunstein, MD PhD
Email address:	brunstc@ccf.org
Institution name:	Cleveland Clinic Foundation
Academic rank:	Vice Chair of Hematology and Oncology

Q7. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- No

Q8. Do you identify as an underrepresented/minority?

- No

Q9. We encourage a maximum of two Principal Investigators per study. If more than one author is listed, please indicate who will be identified as the corresponding PI below:

N/A

Q10. If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:

N/A

LETTER OF COMMITMENT:

Please note: *A letter of commitment will be signed by Lead and Last authors as it describes the expectations for filling that role. By signing the letter of commitment, the authors accept their responsibilities and will be held accountable for timely completion of all steps in the project. More details regarding author responsibilities can be found here:* *https://www.cibmtr.org/Studies/Observational/StudyManagement/p*

Q12. CURRENT ONGOING WORK WITH CIBMTR: Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.

N/A.

Q13. PROPOSED WORKING COMMITTEE:

- Graft Sources and Manipulation

Q14. Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.

- No

Q15. RESEARCH QUESTION:

Does the use of ex vivo expanded cord blood lead to improvements in disease-free and overall survival when compared to standard cord blood and haploidentical myeloablative allogeneic stem cell transplants?

Q16. RESEARCH HYPOTHESIS:

Ex vivo expanded cord blood improves time to engraftment and reduces morbidity and mortality after HCT resulting in better outcomes as compared to unmanipulated umbilical (single and double) cord blood and haploidentical hematopoietic cell transplant in the myeloablative setting.

Q17. SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.)

Suggested word limit of 200 words:

Primary: Our primary aim is to determine if the use of ex vivo expanded cord blood results in improved overall survival (OS) compared to unmanipulated umbilical cord blood or haploidentical grafts in myeloablative HCT.
Secondary: Our secondary aims are to determine if the use of ex vivo expanded cord blood results in improvements in the following variables: Progression free survival (PFS), incidence non-relapse mortality (NRM), incidence of relapse, time in hospital in first 100 days, and time to and incidence hematopoietic recovery (ANC>1000, platelets >20,000).

Q18. SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.

The use of umbilical cord blood (CB) represents an appealing option to counteract the issue of finding a well-matched unrelated donor for hematopoietic stem cell transplant, particularly in ethnic minority populations. However, in the myeloablative setting CB transplants have been associated with a high early transplant related mortality (TRM). Conversely, the lower incidence of relapse typically leads to similar disease-free and overall survival. Novel approaches such ex vivo CB expansion are meant to improve early outcomes, while at the same time preserving the potent graft-versus-leukemia effect attributed to CB [1]. Demonstration of reduced TRM and improved OS with the use of ex vivo expanded umbilical CB would support further investigation in prospective trials against unmanipulated grafts of CB and adult donor origin.

Q19. SCIENTIFIC JUSTIFICATION: Provide a background summary of previous related research and their strengths and weaknesses, justification of your research and why your research is still necessary.

Cord blood stem cell transplantation has been used successfully for over two decades for the treatment of pediatric and adult patients with acute leukemia and myelodysplastic syndrome (MDS). Outcomes historically have been similar to matched related and unrelated donor grafts [2], though many of these studies include myeloablative and reduced-intensity conditioning regimens. Moreover, in patients who were minimal residual disease (MRD) positive at the time they were taken to transplant and received myeloablative regimens with a cord blood graft, there seemed to be better disease control [1]. Thus, the use of cord blood grafts represents a viable stem cell source to treat patient with high risk disease who need allogeneic transplants.
In the last 10 years, haploidentical transplantation with post-transplant cyclophosphamide (ptCy) has been widely used as an alternative source of hematopoietic stem cells for HCT. Cord blood and haploidentical donors with ptCy HCT share many of the same advantages of rapid availability, ability to be used across HLA barriers, and relatively low risk of GVHD. However, recent data support haploidentical donors with ptCy, with similar or better outcomes, and at a lower cost. The difference in survival between these two donor types seems driven by TRM, whereas the difference in cost is driven by the longer hospitalization, which is largely driven by the longer time to ANC recovery.
For many years we have been investigating ex vivo cord blood expansion as a strategy to improve time to ANC recovery, expecting to reduce the risk of TRM and improving the overall survival [3-6]. Despite consistently demonstrating a time to neutrophil engraftment between 11-19 days (as compared to 24-26 days in unmanipulated grafts), most ex-vivo cord blood expansion studies have been relatively small pilots or Phase1/2 studies. Individually, these studies had no power to evaluate the impact of the improved time to engraftment on survival, as compared to unmanipulated grafts.
Thus, we propose studying if these ex vivo expanded cord blood transplants result in improved patient outcomes as compared to unmanipulated cord blood and haploidentical donors with ptCy HCT. We propose using days in the hospital in the first 100 days post-HCT as a surrogate measure of resource utilization.

Q19a. SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF)

N/A

Q20. PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.

- Myeloablative conditioning regimen
- Age >/ 12 years
- Allogeneic transplant with unmanipulated single or double umbilical cord blood graft
- Allogeneic transplant with any ex vivo cord blood expansion (NOTCH, MSC, SR1, nicotinamide U171, carlecortemcel-L) in single or combined with unmanipulated unit
- Haploidentical donors with ptCy HCT with peripheral and (if enough cases, include BM)
- Transplanted between 2005 and 2021 (pending data review)
- Primary malignant hematologic condition

Q21. Does this study include pediatric patients?

- Yes

Q22. DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Data collection forms available at: http://www.cibmtr.org/DataManagement/DataCollectior Outline any supplementary data required. Additional data collection is extremely difficult and will make your proposal less feasible.

- Required Forms
  - Recipient baseline data (2000)
  - Hematopoietic stem cell transplant (HCT) infusion (2006)
  - Acute myelogenous leukemia (AML) pre-HCT data (2010)
  - Acute lymphoblastic leukemia (ALL) pre-HCT data (2011)
  - Myelodysplastic syndrome (MDS) pre-HCT data (2014)
  - Post-HCT data (2100)
  - Acute myelogenous leukemia (AML) post-HCT data (2110)
  - Acute lymphoblastic leukemia (ALL) post-HCT data (2111)
  - Myelodysplastic syndrome (MDS) post-HCT data (2114)
- Patient Characteristics
  - Age
  - Gender
  - Race
  - Karnofsky performance status
- Disease Characteristics
  - Disease
  - Date of diagnosis
  - Disease stage
  - Cytogenetic studies
  - Molecular studies
- HCT Characteristics
  - Date of conditioning chemotherapy
  - Pre-allogeneic HCT chemotherapy regimen
  - Cell dose
- Outcomes
  - Time to neutrophil, platelet, hemoglobin recovery
  - Rate of complete response
  - Rate of partial response
  - Time to relapse
  - Time to progression
  - Date of last follow up and status
  - Date and cause of death

Q23. **PATIENT REPORTED OUTCOME (PRO) REQUIREMENTS: If the study requires PRO data collected by CIBMTR, the proposal should include: 1) A detailed description of the PRO domains, timepoints, and proposed analysis of PROs; 2) A description of the hypothesis specific to PROS.**

For additional information on what PRO measures have been collected and timepoints of collection, please reach out to the Late Effects and Quality of Life or Health Services Working Committee leadership: https://www.cibmtr.org/About/WhoWeAre/Com

N/A

Q24. **SAMPLE REQUIREMENTS: If the study requires biologic samples from the CIBMTR Repository, the proposal should also include: 1) A detailed description of the proposed testing methodology and sample requirements; 2) A summary of the investigator's previous experience with the proposed assay systems. PIs should be encouraged to review the inventory details, sample types collected and reach out to research_repos@nmdp.org with any questions.**

More information can be found at: https://www.cibmtr.org/Samples/Inventory/Pages/index

N/A

Q25. NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required, i.e., neither database contains all the data required to answer the study question.

N/A

Q26. REFERENCES:

Milano F, Gooley T, Wood B, et al. Cord-blood transplantation in patients with minimal residual disease. N Eng J Med. 2016; 375(10):944-953.
Brunstein CG, Gutman JA, Weisdorf DJ, et al. Allogeneic hematopoietic cell transplantation for hematologic malignancy: relative risks and benefits of double umbilical cord blood. Blood. 2010; 116(22):4693-4699.
Horwitz ME, Wease S, Blackwell B, et al. Phase I/II study of stem-cell transplantation using a single cord blood unit expanded ex vivo with nicotinamide. J Clin Oncol. 2019; 37(5):367-375.
Wagner JE, Brunstein CG, Boitano AE, et al. Phase I/II trial of StemRegenin-1 expanded umbilical cord blood hematopoietic stem cells supports testing as a stand-alone graft. Cell Stem Cell. 2016; 18(1):144-155.
Cohen S, Roy J, Lachance S, et al. Hematopoietic stem cell transplantation using single UM171-expanded cord blood: a single arm, phase 1-2 safety and feasibility study. Lancet Haematol. 2020; 7(2):E134-E145.
Stiff PJ, Montesinos P, Peled T, et al. Cohort-controlled comparison of umbilical cord blood transplantation using carlecortemcel-L, a single progenitor-enriched cord blood, to double cord blood unit transplantation. Biol Blood Marrow Transplant. 2018; 24(7):1463-1470.

Q27. CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning:

1. Employment (such as an independent contractor, consultant or providing expert testimony)?
2. Relationships (such as executive and advisory committee positions, medical consultant, speaker's bureau)?
3. Ownership (such as equity, ownership or financial interests)?
4. Transactions (such as honoraria, patents, royalties and licenses)?
5. Legal (such as pending or current arbitration or legal proceedings)?

- No, I do not have any conflicts of interest pertinent to this proposal

Q27a. If yes, provide detail on the nature of employment, name of organization, role, entity, ownership, type of financial transaction or legal proceeding and whether renumeration is >$5000 annually.

N/A

BEFORE FINAL SUBMISSION, please review the PI checklist to ensure that you have completed all necessary steps. This will increase the likelihood of submitting a feasible and successful proposal.

Embedded Data:

N/A

Characteristics of patients who underwent UCB or Haplo HCT for any malignant disease reported to the CIBMTR 2005-2019

Characteristic	UCB	dUCB	UCB-EX	dUCB-EX	Haplo
No. of patients	1397	4158	115	165	6586
Age group - no. (%)					
18-29	591 (42)	1071 (26)	40 (35)	46 (28)	1200 (18)
30-39	183 (13)	680 (16)	12 (10)	34 (21)	733 (11)
40-49	182 (13)	709 (17)	25 (22)	31 (19)	881 (13)
50-59	247 (18)	887 (21)	19 (17)	28 (17)	1468 (22)
60-69	164 (12)	731 (18)	15 (13)	23 (14)	1806 (27)
70+	30 (2)	80 (2)	4 (3)	3 (2)	498 (8)
Disease - no. (%)					
AML	593 (42)	1934 (47)	49 (43)	79 (48)	2811 (43)
ALL	366 (26)	910 (22)	35 (30)	34 (21)	1127 (17)
Other leukemia	25 (2)	96 (2)	1 (1)	8 (5)	130 (2)
CML	49 (4)	149 (4)	3 (3)	5 (3)	236 (4)
MDS	169 (12)	439 (11)	17 (15)	18 (11)	1025 (16)
Other acute leukemia	33 (2)	78 (2)	2 (2)	2 (1)	98 (1)
NHL	114 (8)	385 (9)	7 (6)	13 (8)	642 (10)
HD	31 (2)	119 (3)	1 (1)	6 (4)	262 (4)
MPN	17 (1)	48 (1)	0 (0)	0 (0)	255 (4)
Graft type - no. (%)					
Bone marrow	0 (0)	0 (0)	0 (0)	0 (0)	1852 (28)
Peripheral blood	0 (0)	0 (0)	0 (0)	0 (0)	4734 (72)
Umbilical cord blood	1397 (100)	4158 (100)	115 (100)	165 (100)	0 (0)
Year of transplant - no. (%)					
2005 - 2009	506 (36)	856 (21)	18 (16)	51 (31)	0 (0)
2010 - 2014	482 (35)	2095 (50)	37 (32)	83 (50)	549 (8)
2015 - 2019	409 (29)	1207 (29)	60 (52)	31 (19)	6037 (92)