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A G E N D A
CIBMTR WORKING COMMITTEE FOR GRAFT SOURCES & MANIPULATION
Orlando, FL
Thursday, February 20, 2020, 2:45 – 5:15 pm

Co-Chair:	**Asad Bashey, MD, PhD, Northside Hospital, Atlanta, GA** **Telephone: 404-255-1930; E-mail: abashey@bmtga.com**
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**
Scientific Director:	**Mary Eapen, MBBS, MS, CIBMTR Statistical Center, Milwaukee, WI;** **Telephone: 414-805-0700: E-mail: meapen@mcw.edu**
Statistical Director:	**Mei-Jie Zhang, PhD, CIBMTR Statistical Center, Milwaukee, WI;** **Telephone: 414-456-8375; E-mail: meijie@mcw.edu**
Statistician:	**Molly Johnson, MPH, CIBMTR Statistical Center, Milwaukee, WI;** **Telephone: 414-805-2258, E-mail: mhjohnson@mcw.edu**

Introduction

a. Minutes and Overview Plan from February 2019 meeting (Attachment 1)
b. Introduction of incoming Co-Chair:
Filippo Milano, MD, PhD; Fred Hutchinson Cancer Research Center;
Email: fmilano@fredhutch.org; Phone: 206-667-5925

Accrual summary (Attachment 2)

Presentations, published or submitted papers

a. **GS17-02** Solomon SR, St. Martin A, Shah NN, Fatobene G, Al Malki MM, Ballen KK, Bashey A, Bejanyan N, Bolaños Meade J, Brunstein CG, DeFilipp Z, Champlin RE, Fuchs EJ, Hamadani M, Hematti P, Kanakry CG, McGuirk JP, McNiece IK, Ciurea SO, Pasquini MC, Rocha V, Romee R, Patel SS, Vasu S, Waller EK, Wingard JR, Zhang M-J, Eapen M. Myeloablative vs reduced intensity T-cell-replete haploidentical transplantation for hematologic malignancy. ***Blood Advances.*** 2019 Oct 8;3(19):2836-2844.
b. **GS16-02** Perales M-A, Tomlinson B, Zhang M-J, St. Martin A, Beitinjaneh A, Gibson J, Hogan W, Kekre N, Lazarus H, Marks D, McGuirk J, Romee R, Solh M, Wagner JE, Weisdorf DJ, de Lima M, Eapen M. Alternative donor transplantation for acute myeloid leukemia in patients aged ≥50 years: Young HLA-matched unrelated or haploidentical donor? ***Haematologica.*** doi:10.3324/haematol.2018.215202. Epub 2019 May 17.
c. **GS18-03** Comparison of outcomes of reduced intensity transplantation in lymphoma patients using haploidentical related donors vs unrelated cord blood (G Fatobene/ V Rocha/ S Montoto) ***Journal of Clinical Oncology.*** **In Press.**

d. **GS18-04** Comparison of Outcomes with Haploidentical and Matched Unrelated Donors for Hematopoietic Stem Cell Transplantation in Myelodysplastic Syndromes (M Grunwald/ A Viswabandya/ B Tomlinson/ H Elmariah) ***ASH, December 2019.***
e. **GS19-01** Comparison of myeloablative haploidentical or umbilical cord blood transplantation for pediatric and adult patients with acute leukemia (J Wagner/K Ballen) ***TCT, February 2020.***

4. Studies in Progress (Attachment 3)

a. **GS18-01** Transplant outcomes after HLA Haploidentical donor transplantation with post-transplant cyclophosphamide (PTCy) vs matched unrelated donor transplantation with and without PTCy in AML, ALL, and MDS patients (R Romee et al) **Datafile prep**
b. **GS18-04** Comparison of Outcomes with Haploidentical and Matched Unrelated Donors for Hematopoietic Stem Cell Transplantation in Myelodysplastic Syndromes (M Grunwald et al) **Manuscript prep**
c. **GS19-01** Comparison of myeloablative Haploidentical or umbilical cord blood transplantation for pediatric and adult patients with acute leukemia (J Wagner et al) **Manuscript prep**
d. **GS19-02** Graft Failure in MDS and Acute Leukemia Patients After Allogeneic Stem Cell Transplantation Receiving Post Transplant Cyclophosphamide (C Hickey et al) **Protocol Development**
e. **GS19-03** Impact of G-CSF on in-vivo t-cell depleted allogeneic hematopoietic cell transplantation (N Orfali et al) **Datafile Prep**

5. Proposals

Future/proposed studies

a. **PROP 1910-10** Optimal Source of Graft and Cell Dose for allogeneic hematopoietic cell transplantation in Patients with Myelofibrosis (Q Salas/V Gupta/ R Kumar) (Attachment 4)
b. **PROP 1911-06** Graft Failure Scoring Systems for Each UCB HCT and Haploidentical HCT (C Ustun/ S Nathan/ C Hickey/ R Romee/ C Brunstein) (Attachment 5)
c. **PROP 1911-13** Optimal donor selection for myeloid and lymphoid malignancies using the CIBMTR database as a part of Personalized Medicine (A Varma/ H Don Yun/ V Ustun) (Attachment 6)
d. **PROP 1911-170** Graft Source for Salvage or Rescue Hematopoietic Stem Cell Transplantation for Hematological Malignancies after Primary Graft Failure (N Ali/ L Metheny/ M de Lima) (Attachment 7)
e. **PROP 1911-20** Outcomes after Double Unrelated Umbilical Cord Blood (dUCB) versus HLA-Mismatched Unrelated (MMUD) Transplants using Post-Transplantation Cytoxan for Patients with Hematologic Malignancies (N Farhadfar/ J Wingard) (Attachment 8)
f. **PROP 1911-39** Reduced Intensity (RIC) Conditioning and Transplantation of Double Unrelated Umbilical Cord Blood (dUCB) versus HLA-Haploidentical Related Bone Marrow (BM) for Patients with Acute Leukemias: Comparison of Survival Outcomes from a Randomized Clinical Trial with Outcomes from a Contemporaneous Cohort from the CIBMTR Registry (P O'Donnell/ C Brunstein/ E Fuchs) (Attachment 9)
g. **PROP 1911-19 / PROP 1911-210** Impact of Cell Dose on Haploidentical Bone Marrow Stem Cell Transplantation Outcome /Optimal Stem Cell Dosing for Peripheral Blood Stem Cell Transplantation with Post-Transplant Cyclophosphamide (N Farhadfar/ H Murthy/ J Wingard/ H Elmariah/ N Benjanyan/ T Nishiori/ S McCurdy) (Attachment 10)

Dropped proposed studies

a. **PROP 1908-02** Comparison of the Impact of Minimal Residual Disease before Allogeneic Stem Cell Transplantation in Adult Patients with Acute Lymphoblastic Leukemia between Unrelated Cord Blood vs. Conventional Marrow and Blood Grafts Malignancies *Dropped due to overlap with existing study*

b. **PROP 1911-100** Comparison of outcomes post allogeneic hematopoietic cell transplantation using fresh versus cryopreserved peripheral blood stem cell grafts *Dropped due to low scientific impact*
c. **PROP 1911-137** Comparison of haploidentical HSCT with post-transplant cyclophosphamide (PTCy) and of HLA matched unrelated donor (MUD) HSCT for children, adolescents and young adults with hematologic malignancies *Dropped due to small sample size*
d. **PROP 1911-236** Comparison of outcomes in adults with hematological malignancies undergoing single versus double cord blood transplantation *Overlap with recent publication*
e. **PROP 1911-250** Impact of CD34 cell dose on the outcomes after HLA-matched allogeneic hematopoietic cell transplantation for acute leukemia, myelodysplastic syndromes, and myeloproliferative neoplasms *Overlap published study BBMT 2014 20 (9):1418-1425*
f. **PROP 1911-262** Haploidentical Transplant with Posttransplant Cyclophosphamide vs. HLA-Matched Unrelated Donor Transplant for Adult Acute Lymphoblastic Leukemia *Dropped due to overlap with current study*

6. Other Business

MINUTES AND OVERVIEW PLAN
CIBMTR WORKING COMMITTEE FOR GRAFT SOURCES & MANIPULATION
Houston, TX
Thursday, February 21, 2019, 2:45 – 5:15 pm

Co-Chair:	**Asad Bashey, MD, PhD, Northside Hospital, Atlanta, GA;** **Telephone: 404-255-1930; E-mail: abashey@bmtga.com**
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**
Scientific Director:	**Mary Eapen, MBBS, MS, CIBMTR Statistical Center, Milwaukee, WI;** **Telephone: 414-805-0700: E-mail: meapen@mcw.edu**
Statistical Director:	**Mei-Jie Zhang, PhD, CIBMTR Statistical Center, Milwaukee, WI;** **Telephone: 414-456-8375; E-mail: meijie@mcw.edu**
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1. Introduction

Dr. Brunstein opened the meeting at 2:45 pm by welcoming the working committee members for attending the Graft Sources and Manipulation Working Committee (GSWC) meeting. He introduced the GSWC's leadership, and disclosed their conflicts of interest per CIBMTR policy. The minutes from the 2018 GSWC Tandem meeting were approved. Dr. Brunstein then presented the GSWC's membership guidelines, goals and expectations, as well as a brief reminder about the CIBMTR's rules of authorship. He also presented information on data sources (TED vs CRF), showed US transplant trends by donor type, and highlighted the Advisory Committee metrics for the committee. Members in the audience were directed to the CIBMTR's website for additional information. Dr. Brunstein concluded the introduction by referring the committee to Attachment 3 in the materials for a detailed description of current studies in progress.

2. Published/submitted papers and studies in progress

Dr. Brunstein then invited Dr. Bashey to present GS17-02: *T-replete haploidentical cell transplantation using post-transplant cyclophosphamide for AML, ALL, and MDS: Effect of transplant conditioning regimen intensity on outcomes* (oral presentation at ASH 2018, manuscript preparation). Dr. Eapen then presented the results of GS18-02: *Impact of race on relapse after haploidentical transplantation with post-transplant cyclophosphamide compared to cord blood (manuscript preparation).*

3. Future/proposed studies

a. **PROP 1809-05** This proposal was seeking to compare outcomes between haploidentical transplants with post-transplant cyclophosphamide and cord blood transplants for adult and pediatric patients with acute leukemia or MDS receiving myeloablative conditioning. Dr. Karen Ballen presented the proposal.
The CIBMTR identified 1212 haploidentical transplants with post-transplant cyclophosphamide (434 BM, 778 PBSC) and 1793 cord blood transplants occurring between 2008 and 2018. These transplants were all myeloablative conditioning.

The primary objective of this proposal was to compare leukemia-free survival between haploidentical and cord blood transplants. Secondary objectives included hematopoietic recovery, acute and chronic GVHD, relapse, treatment related mortality, and overall survival.

There was some discussion about the age cutoff, as patients older than 55 were excluded. It was mentioned that since this proposal was including myeloablative conditioning only, there would be very few patients older than 55 who would be eligible, though possibly expanding to include patients up to 60 years old was suggested. Additionally, it was recommended that high resolution HLA typing be used for the cords, as prior work has shown this to be an important factor. However, high resolution typing will only be available in a subset of the cords, and it may not be feasible. Finally, there were comments on incorporating data on donor specific antibodies and recipient parity, which unfortunately is unavailable.

A comment was made that this proposal might be a significant overlap to work done by Dr. Rohtesh Mehta with the Graft vs Host Disease Working Committee. That study was GV16-01. It did not compare haploidentical to cord blood transplants in children. Among the adults, there was a comparison between haploidentical and cord blood transplants. However, GV16-01 included ~140 haploidentical transplants and ~40 used myeloablative regimen and haploidentical transplants were considered as a single group. The purpose of PROP 1809-05 is to compare outcomes after myeloablative haploidentical and cord blood transplants in young adults. As such we confirm there is minimal overlap between GV16-01 and PROP 1809-05.

This proposal received a high priority score from the committee and was accepted.

b. **PROP 1811-01** This proposal was looking to compare the incidence of graft failure in the setting of post-transplant cyclophosphamide between haploidentical, matched sibling, and matched unrelated donor HCT in acute leukemia and MDS. Dr. Cindy Lynn Hickey presented the proposal.

The CIBMTR identified 1018 adults transplanted for AML, ALL, or MDS with a haploidentical donor, 105 transplanted with a matched sibling donor, and 178 transplanted with a matched unrelated donor. These transplants occurred from 2012 to 2018 and had uniform GVHD prophylaxis of post-transplant cyclophosphamide, calcineurin inhibitor, and mycophenolate or methotrexate.

The primary objective of this proposal was to determine the incidence of graft failure in haploidentical donor HCT recipients compared to matched sibling and matched unrelated

donor HCT recipients. Secondary objectives included determining the effect of post-transplant cyclophosphamide on the need for CD34+ selected stem cell boosts, identifying risk factors for graft failure, overall survival for patients with graft failure, efficacy of stem cell boosts as a treatment for graft failure, and second transplant compared to stem cell boosts as treatment for graft failure.

The main discussion around this proposal was the definition of graft failure. It was mentioned that chimerism data could be used to identify graft failures when available, and consulting with centers when it was unclear whether a graft failure had occurred. It was also mentioned that primary and secondary graft failures would both be considered.

It was again suggested that data on donor specific antibodies would strengthen the study, and it was mentioned that centers could be contacted to determine if they have any DSA data available for the study.

This proposal received a high priority score and was accepted.

c. **PROP 1811-52** This proposal was seeking to compare outcomes following bone marrow and peripheral blood grafts from matched sibling or matched unrelated donors in the post-transplant cyclophosphamide setting. Dr. Rotesh Mehta presented the proposal.

The CIBMTR identified 250 bone marrow and 589 peripheral blood grafts from matched sibling and matched unrelated donors from 2012 to 2018. These transplants all had uniform GVHD prophylaxis of post-transplant cyclophosphamide, calcineurin inhibitor, and mycophenolate or methotrexate. The diseases included AML and ALL in complete remission, and MDS.

The primary objectives of this proposal was to compare acute and chronic GVHD, relapse, treatment-related mortality, progression-free survival, overall survival, GRFS, and CRFS between bone marrow and peripheral blood grafts. Secondary objectives included incidence of infection, engraftment, and donor chimerism.

The main concern raised regarding this proposal was the potential overlap with an accepted graft sources study, GS18-01. That study is a comparison of haploidentical and matched unrelated donor transplants with post-transplant cyclophosphamide. As this proposal is comparing bone marrow and peripheral blood in the setting of post-transplant cyclophosphamide with wither matched sibling or matched unrelated donors, there overlap is not substantial.

Dr. Bashey asked Dr. Mehta what the standard of care or the baseline would be in this analysis, which Dr. Mehta asserted would be the bone marrow grafts from the matched sibling donors.

This proposal was not accepted.

d. **PROP 1811-119** This proposal was seeking to determine the impact of G-CSF on *in-vivo* T-cell depleted allogeneic hematopoietic cell transplantation. Dr. Nina Orfali presented the proposal.

The CIBMTR identified 1325 patients who received prophylactic G-CSF and 1350 patients who did not receive prophylactic G-CSF from 2007 – 2018. Prophylactic G-CSF was defined as administration -3 to +10 days from transplant. All of these patients received ATG, and were transplanted for AML, ALL, or MDS. Donor type included matched sibling, matched unrelated, and mis-matched unrelated donors.

The primary objective of this proposal was to compare the effect of G-CSF on relapse and relapse-related mortality between patients who received ATG. Secondary objectives included treatment-related mortality, overall and event-free survival, acute and chronic GVHD, and infection.

The only question raised during the discussion was whether data on the source and dose of ATG was available, which was confirmed that it is available.

This proposal received a high priority score from the committee and was accepted.

e. **PROP 1811-133/1811-121** These two proposals were both seeking to compare alternative donor selection for transplantation for aplastic anemia, and were presented as a single proposal. Dr. Queralt Salas presented the proposal.
The CIBMTR identified 67 haploidentical donor transplants with post-transplant cyclophosphamide, 299 matched unrelated donor transplants, and 52 cord blood transplants for aplastic anemia between 2008 and 2018.

The primary objective of this proposal was to compare overall survival between haploidentical donor, matched unrelated donor, and cord blood transplants. Secondary objectives included non-relapse mortality, graft failure, acute and chronic GVHD, and engraftment.

There were two main concerns raised regarding this proposal. First, there were substantial discrepancies in the year of transplants between the donor types such that a direct comparison of the 3 donor types would be difficult. While the MUD transplants were relatively consistent from 2008 to 2018, the cord blood transplants occurred in the early time period and tapered off, whereas the haploidentical transplants occurred in the later years. Dr. Zhang commented that adjustment for transplant period could not be done. The second main concern was the low number of patients eligible for the study. It would be difficult to adjust for confounders in the multivariable analysis, and the analysis would be underpowered.

This proposal was not accepted.

f. **PROP 1811-143** This proposal was seeking to identify factors influencing poor graft function following allogeneic bone marrow transplantation. Dr. Ashish Bajel presented the proposal on behalf of Dr. Emma Leitinger, who could not be in attendance.
The CIBMTR identified 2160 adults transplanted for acute leukemia in complete remission from HLA-identical siblings or unrelated donors. These transplants occurred over the time period between 2013 and 2017.

The primary objective of this proposal was to document the incidence of poor graft function in the presence of full donor chimerism. The secondary objective was to identify risk factors associated with poor graft function.

Dr. McNiece suggested that including graft quality data would strengthen the analysis, such as TNC and CD34 counts. Someone mentioned that the analysis may be difficult with the definition of poor graft function presented due to underlying cytopenias. It was also brought up that the timing of chimerism reported is not consistent and donor chimerism at day 30 may not be available for all patients. Additionally, there was a question about whether data on interventions is available, which Dr. Eapen confirmed was not available.

This proposal was not accepted.

g. **PROP 1811-173** This proposal was looking to compare alternative donor transplants and matched unrelated donor transplants for AML and MDS among patients with a high comorbidity-age composite index. Dr. Shivaprasad Manjappa presented the proposal. The CIBMTR identified 2186 haploidentical transplants with post-transplant cyclophosphamide, 4783 matched unrelated donor transplants, and 1053 cord blood transplants for AML and MDS. These transplants were all for adults older than 40 years, and occurred between 2008 and 2018.

The main objective of this proposal was to compare overall survival between alternative donors and matched unrelated donors for patients with a high comorbidity-age index. Secondary objectives non-relapse mortality, progression-free survival, relapse, engraftment, GVHD, and graft failure.

One of the discussion points raised was that disease severity would need to be adjusted for, and it was recommended that DRI either be incorporated in the comorbidity index itself, or adjusted for in the multivariable analysis. Additionally, it was brought up that this proposal might overlap with previous work done by the Acute Leukemia Working Committee.

This proposal was not accepted.

h. **PROP 1811-176** This proposal was seeking to study the impact of cell dose on outcomes following haploidentical bone marrow transplants. Dr. Nosha Farhadfar presented the proposal.

The CIBMTR 543 haploidentical donor transplants with post-transplant cyclophosphamide for hematologic malignancies between 2008 and 2018.

The primary objective was the impact of bone marrow cell dose on overall survival. Secondary objectives included the impact of cell dose on engraftment, acute and chronic GVHD, non-relapse mortality, relapse, and progression-free survival.

The main concern raised about this proposal was that John's Hopkins recently published on the effect of bone marrow cell dose for haploidentical donor transplantation, and there was concern about how much this analysis would add to the field. Additionally, there was

concern that some of the Hopkins patients from that publication might be included in this proposal.

There were several suggestions to strengthen the study, including looking at donor age and other donor factors, as well as ABO incompatibility. Someone also suggested adding peripheral blood transplants to the analysis.

This proposal was not accepted.

i. **PROP 1812-03** This proposal was seeking to compare conditioning intensities in adult cord blood transplants for AML, ALL, and MDS. Dr. Ioannis Politikos presented the proposal.

The CIBMTR identified 548 adult cord blood transplants with TBI200/Cy/Flud as conditioning, 127 transplants with TBI400/Cy/Flud/Thio as conditioning, and 415 transplants with TBI1320-1375/Cy/Flud as conditioning. These transplants occurred from 2008 to 2018.

The main objective of this proposal was to compare progression-free survival between the different conditioning regimens. Secondary objectives included hematopoietic recovery, acute and chronic GVHD, relapse, transplant-related mortality, and overall survival.

The only suggestion from the committee was to limit the study population to the double cord blood unit transplants, as the single cords were limited in numbers.

This proposal was not accepted.

j. **PROP 1812-09** This proposal was looking to compare haploidentical donors with unrelated donors as second allogeneic transplants following relapse or progression of AML, ALL, or MDS. Dr. Vanderson Rocha presented the proposal.

The CIBMTR identified 225 haploidentical donor transplants with post-transplant cyclophosphamide and 140 unrelated donor transplants. These were all second allogeneic transplants following relapse or progression, and occurred between 2013 and 2018.

The primary objective of this proposal was to compare overall survival following second haploidentical and matched unrelated donor transplants for relapse or progression. Secondary objectives included relapse, non-relapse morality, disease-free survival, acute and chronic GVHD, and graft failure.

A main discussion point was how to address the haploidentical patients who had a different donor for the second transplant compared to those who had the same donor for both transplants. It was recommended that the haploidentical donor group be split into two groups: those with the same haplo donors for the first and second allogeneic transplants and those with different haplo donors for the first and second transplants. Dr. Fuchs reported that the policy at Hopkins is to automatically use a different donor if the patient relapsed or progressed, and that the decision of whether to use the same donor may be center driven.

It was asked what the role of haploidentical DLI would be in this study. Dr. Rocha suggested that since DLI's typically don't involve conditioning, haplo DLI's would not be considered for this analysis. It was also recommended to exclude the MDS due to small numbers, which Dr. Rocha agreed with. Finally, it was mentioned that it would be important to know when the relapse occurred following the first transplant, as that will be an important factor in the outcomes following the second transplant.

This proposal was not accepted.

Meeting adjourned at 5:00 pm

Working Committee Overview Plan for 2019-2020							
Study number and title	**Current status**	**Goal with date**	**Total hours to complete**	**Total hours to goal**	**Hours allocated to 6/30/2018**	**Hours allocated 7/1/2018-6/30/2019**	**Total Hours allocated**
GS16-02: Haploidentical vs MUD HCT in older patients	Submitted	Published – May 2019	10	**10**	10	0	**10**
GS17-02: Myeloablative vs reduced intensity conditioning in Haploidentical transplantation	Manuscript preparation	Published – June 2019	10	**10**	10	0	**10**
GS18-01: Comparison of outcomes after HCT from haploidentical donor with PT-Cy, MUD with PT-Cy, and MUD with CNI	Protocol development	Submitted – April 2020	310	**310**	0	310	**310**
GS18-02: Impact of race on relapse after haploidentical with PT-Cy vs cord blood	Manuscript preparation	Submitted – August 2019	80	**70**	70	10	**80**
GS18-03: Comparison of outcomes of	Manuscript preparation	Submitted – July 2019	80	**70**	70	10	**80**

reduced intensity transplantation in lymphoma patients using haploidentical related donors versus unrelated cord blood							
GS18-04: Haploidentical donor with PT-Cy vs MUD for MDS	Data file preparation	Submitted – October 2019	200	**200**	130	70	**200**
GS19-01: Comparison of myeloablative haplo or CB in Acute Leukemia	Protocol pending	Manuscript preparation – January 2020 Submitted – July 2020	330	**330**	0	330	**330**
GS19-02: Graft Failure in MDS and Acute Leukemia with PT-Cy	Protocol pending	Data file preparation – June 2020	330	**100**	0	100	**100**
GS19-03: Impact of G-CSF on in-vivo T-cell depleted Allogeneic Hematopoietic Cell Transplantation	Protocol pending	Data file preparation – April 2020	330	**100**	0	100	**100**

Oversight Assignments for Working Committee Leadership (March 2019)	
Ian McNiece	**GS16-02:** Donor selection: Biologic child vs. HLA-matched sibling or Haplo-identical relative vs. HLA-matched sibling. Can post-transplant cyclophosphamide overcome the HLA barrier?
Asad Bashey	**GS17-02:** Myeloablative versus reduced intensity conditioning in haploidentical transplantation.
Ian McNiece	**GS18-01:** Comparison of outcomes after HCT from haploidentical donor with PT-Cy, MUD with PT-Cy, and MUD with CNI.
Asad Bashey	**GS18-02:** Impact of race (African Americans vs. Caucasians) on relapse after haploidentical with PT-Cy vs cord blood
Claudio Brunstein	**GS18-03:** Comparison of Outcomes of Reduced Intensity Transplantation in Lymphoma Patients Using Haploidentical Related Donors vs. Unrelated Cord Blood (joint study with EBMT)
Asad Bashey	**GS18-04:** Haploidentical donor with PT-Cy vs MUD for MDS.
Claudio Brunstein	**GS19-01:** Comparison of myeloablative haplo or CB in Acute Leukemia
Asad Bashey	**GS19-02:** Graft Failure in MDS and Acute Leukemia with PT-Cy
Ian McNiece	**GS19-03:** Impact of G-CSF on in-vivo T-cell depleted Allogeneic Hematopoietic Cell Transplantation

Accrual Summary for Graft Sources and Manipulation Working Committee

Characteristics of patients reported to the CIBMTR between 2000 and 2019

Characteristics	Registration N (%)	Research N (%)
Number of cases	**193675**	**67670**
Donor type		
HLA-identical sibling donor HCT	80712	20998
Bone marrow	22659 (28)	6059 (29)
Peripheral blood	57468 (71)	14686 (70)
Umbilical cord blood	585 (1)	253 (1)
Identical twin donor HCT	1078	516
Bone marrow	160 (15)	80(16)
Peripheral blood	913 (85)	434 (84)
Umbilical cord blood	5 (<1)	2 (<1)
HLA mismatched related donor HCT	15500	5978
Bone marrow	5050 (33)	1964 (33)
Peripheral blood	10024 (65)	3769 (63)
Umbilical cord blood	426 (2)	245 (4)
Unrelated donor HCT	96385	40178
Bone marrow	24591 (26)	11273 (28)
Peripheral blood	57996 (60)	19912 (50)
Umbilical cord blood	13798 (14)	8993 (22)

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TO: Graft Sources and Manipulation Working Committee Members

FROM: Mary Eapen, MBBS, MS; Scientific Director for the Graft Sources Working Committee

RE: Studies in Progress Summary

GS18-01: Transplant outcomes after HLA haploidentical donor transplantation with post-transplant cyclophosphamide (PTCy) vs matched unrelated donor transplantation with and without PTCy in AML, ALL, and MDS patients (R Romee et al): The aim of this study is to compare outcomes following haploidentical donor and matched unrelated donor transplantation in the setting of a uniform GVHD prophylaxis with post-transplant cyclophosphamide. We delayed starting this study to allow for further accrual of MUD's with PTCy. The Study is currently in protocol development and datafile prep, we plan to have a dataset finalized by June 2020 and a submission to ASH.

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 outcomes of haploidentical with PTCy, matched donor with PTCy and matched donor without PTCy transplants. We plan to have a protocol by June 2020 and complete the study by June 2021.

GS19-03: Impact of G-CSF on In-Vivo T-Cell Depleted Allogeneic Hematopoietic Cell Transplantation (N Orfali et al): The aim of this study is to compare outcomes following T-cell depleted allo HCT with or without G-CSF. The study is currently in protocol development and datafile prep, we plan to begin the analysis in June 2020 and a submission to ASH.

Proposal: 1910-10

Title:
Optimal Source of Graft and Cell Dose for allogeneic hematopoietic cell transplantation in Patients with Myelofibrosis

M. Queralt Salas MD, queralt.salas87@outlook.es / Queralt.salasgay@uhn.ca, Princess Margaret Cancer Center, University of Toronto
Vikas Gupta, MD, FRCP, FRCPath, vikas.gupta@uhn.ca, University of Toronto, Princess Margaret Cancer Centre
Rajat Kumar, MD, FRCPC, rajat.kumar@uhn.ca, Princess Margaret Cancer Center, University of Toronto

Hypothesis and scientific justification:
Primary myelofibrosis (MF) and the advanced forms of post-essential thrombocythemia (post-ET) and post-polycythemia vera (post-PV) MF, are chronic hematological malignancies characterized by clonal proliferation of hematopoietic stem cells with marrow fibrosis, cytopenias, splenomegaly, and systemic symptoms resulting from excessive cytokine production (1). Allogeneic hematopoietic stem cell transplantation (allo-HCT) is the only potentially curative strategy for patients with MF. However, despite of the use of reduced-intensity conditioning (RIC) regimens and the refinement of graft-versus-host disease (GVHD) prophylaxis, there remains significant morbidity and mortality in recipients with MF (2).
The use of peripheral blood stem cell (PBSC) grafts is becoming more predominant especially in patients diagnosed with hematological malignancies. In myelofibrosis, the use of PBSC grafts could be beneficial secondary to the higher efficacy of peripheral blood by reducing the time of engraftment and the increased graft-versus leukemia effect compared with bone marrow (BM) sources. However, there are not specific studies supporting this practice.
An adequate cell dose is crucial to achieve a sustained engraftment. However, the infusion of high cell dose containing grafts seems to be associated with an increased incidence of GVHD and worse overall survival (OS). Several studies have investigated the effect of CD34+ cell dose on allo-HCT outcomes and have reported inconsistent results. These discrepancies may be explained by differences in disease categories, donor type, conditioning regimen and GVHD prophylaxis (4-6).
First, because the use PBSC is becoming the standard of care in patients diagnosed with MF, to explore the outcome between the infusion of BM and PBSC grafts in this setting will provide valuable clinical information.
Secondary, myelofibrosis has been associated with higher rates of graft failure because the impairment of the bone marrow niche and the presence of enlarged spleen. The strategy of infusing higher cell dose containing grafts (nucleated cells in BM grafts or CD34+ cells in PBSC grafts) can be questioned to overcome this complication.
Finally, the impact of CD34+ cell dose on RIC allo-HCT outcomes remains controversial secondary to the fact that the curative potential effect of RIC regimens relies on the immunological effects of the graft rather than the cytotoxic power of the preparative regimen.

- The aim of the present study is to investigate the impact of the source of graft in patients diagnosed with MF.
- We hypothesize that patients diagnosed with MF may need different cell dose containing grafts depending on the intensity of the conditioning regimen, and donor type.

The **innovation**: The use of peripheral blood stem cell grafts (PBSC) is becoming more predominant in myelofitrosis however there are no studies comparing both sources of graft. There are no research studies on the optimal cell dose in patients with MF.
The **clinical significance**: Because the source of graft and cell douse count from the product are two parameters that can be adjusted in order to improve survival and reduce transplant-related complications, we think that to explore this two parameters in myelofibrosis has value in informing clinical practice.
To explore if the optimal source of graft and cell dose count varies among the intensity of the conditioning regimen, donor source or spleen size will be relevant information in patients with MF.

Objectives:
Primary objective:

- To explore the impact of the stem cell source (bone marrow vs peripheral blood) on overall survival in patients diagnosed with myelofibrosis.

Secondary objectives:

- To explore the impact of the stem cell source (bone marrow vs peripheral blood) among other relevant variables:
    - Time to engraftment
    - Primary Graft Failure
    - Progression free survival (PFS).
    - Non-relapse mortality (NRM)
    - Cumulative incidence of relapse (CIR)
    - GVHD-Free / RFS (GRFS)
    - Cumulative incidence of clinically relevant GVHD (grade II-IV acute GVHD, grade III-IV acute GVHD, and extensive chronic GVHD)

- To explore if the cell dose infused has an impact overall survival in patients diagnosed with myelofibrosis
  This variable would be explored separately among patients who received bone marrow grafts (total nucleated cell dose/kg) and among those recipients who received peripheral blood stem cell grafts (CD34+/kg).
  To explore if the nucleated cells infused has an impact in survival
  To explore if cell dose has an impact in other relevant variables:
    - Time to engraftment
    - Progression free survival (PFS).
    - Non-relapse mortality (NRM)
    - GVHD-Free / RFS (GRFS)
    - Graft failure
    - Cumulative incidence of clinically relevant GVHD (grade II-IV acute GVHD, grade III-IV acute GVHD, and extensive chronic GVHD)

- To determine an ideal cut-off of CD34+ cell dose and nucleated cell dose /kg for patients with MF who undergo allo-HCT to achieve a maximum OS.
  Is there a universal cut-off or it should be modified according to donor type (conditioning regimen (MAC vs RIC) and prior splenectomy or spleen size (10cm / 11to22 / >22/ No spleen).

Study population:
Adult patients diagnosed with post-PV MF, post-ET MF and PMF who underwent allo-HCT between 2001 to 2017.
Inclusion criteria:

- Adults diagnosed with post-PV MF, post-ET MF and PMF, age ≥18 years, undergoing first allo-HCT between 2001-2017
- Eligible donors include HLA-identical donors and unrelated donors (HLA 10/10 and 9/10).
- Donor source: Peripheral blood and bone marrow
- Myeloablative (MAC) and reduced intensity (RIC) conditioning regimen will be permitted.

Exclusion criteria:

- Non eligible donors include umbilical cord blood and haploidentical donor source.
- Transformation to AML prior to first HCT

Outcomes:
The main variable of interest will be overall survival (OS). Other relevant variables would be relapse-free survival (RFS), therapy-related mortality (TRM), cumulative incidence (cum.Inc) of GVHD, cumulative incidence of relapse (CIR) and GVHD-free / RFS.

Main Definitions:

- OS: Time to death. Death from any cause will be considered an event. Surviving patients will be censored at time of last follow-up.
- RFS: Time to death or relapse . Death from any cause or relapse will be considered as event. Surviving patients will be censored at time of last follow-up.
- TRM: Cumulative incidence of TRM will be estimated at day +100 and 1, 2 and 5 year. TRM is defined as death without preceding disease relapse/progression.
- CIR: Cumulative incidence of relapse will be estimated at 1 and 2 years after HCT. is defined as death preceding disease relapse/progression.
- GFRS: Time to death, relapse, and present clinically relevant GVHD at 1 and 2 years. Death from any cause, relapse and to present grade III-IV aGVHD and extensive (moderate/severe) cGVHD will be considered an event. Surviving patients will be censored at time of last follow-up.
- Cum.Inc of acute GVHD: Cum.Inc of aGVHD will be assessed considering death and relapse as competing events. Percentages would be calculated at day +100 allo-HSCT.
- Cum.Inc of chronic GVHD: Cum.Inc of cGVHD will be assessed considering death and relapse as competing events. Percentages would be calculated at 1 year post allo-HSCT.
- Graft failure: Primary graft failure (GF) will be defined as peripheral blood ANC < 0.5×10^9/L in the first 6 weeks in the absence of relapse.
- Hematopoietic recovery:
    - Time to neutrophils (ANC) > 0.5 x109/L sustained for three consecutive days. This endpoint will be evaluated at 28-day and 100-day after HCT.
    - Time to achieve a platelet count of >20 x 109/L independent of platelet transfusions for 7 consecutive days within 28 and 100 days post-transplant.
    - This endpoint will be evaluated at 28-day and 100-day after HCT.

Data requirements:

Utilizing data collected by the CIBMTR organization from patients diagnosed primary of post-PV and post-TE MF that underwent allo-HCT between 2012 and 2017. This proposed study will require no supplemental data to be collected. No biological samples are required for this study. The parameters to be assessed are outlined in **Table 1** below.

Type of data	**Data point**	**Specific data**
Patient Specific	Patient specific characteristics	Age at transplant (Date of birth) Sex Country of transplant HCT-CI (if available) Variant of MF: Primary, post-ET MF and post-PV MF Date of diagnosis Interval from diagnosis to transplant Baseline Characteristics: Cytogenetic molecular profile (JAK2/CALR/MPL positive or negative where available) Number of blasts in peripheral blood Hemoglobin level WBC count Platelet count Requirement of transfusional support Constitutional symptoms DIPSS Prior use of Ruxolitinib. Response to Ruxolitinib (yes/no) Spleen size (if available). Pre-alloHCT splenectomy yes/no.
-	Transplant date	Transplant date
	Transplant information	Donor type HLA match -mismatch degree Donor-recipient gender match Donor-recipient ABO mismatch Donor age (if available)
	Conditioning regimen	MAC vs RIC Conditioning regimen description
	GVHD prophylaxis	Calcineurin based T cell depletion Others
	Graft characteristic	**Source of graft**

		CD34+ cell dose (PBSC) / Nucleated cell dose (BM) CD3+ cell dose
Outcome Measures	Engraftment	Neutrophil engraftment date Platelet engraftment date Graft failure Date of the graft failure Second transplant: Yes/No. Date of the second transplant
	Post-transplant complications	VOD: Yes/No. Grade if available. Resolved: Yes/no CMV reactivation: yes/no. EVB reactivation: yes/no.
	GVHD	Acute GVHD (aGVHD) overall percentages and according to grade Cum.Inc of grade II-IV and grade III-IV acute GVHD (aGVHD) Chronic GVHD (cGVHD) overall percentages and according to grade Cum.Inc of moderate/severe chronic GVHD (cGVHD)
	Relapse	Disease status after HCT Relapse Date of relapse Second transplant (yes/no) and date of second HCT (if applicable)
	Last follow/up or death	Disease status last follow-up Death yes/no Date of death Cause of Death

Study design:

Study characteristics: retrospective and observational.

The CIBMTR data base would provide data for the variables of interest. Baseline characteristics will be reported using descriptive statistics (counts and percentages). Comparisons between categorical variables would be done using x2 test.

The main variable of interest will be overall survival (OS) and it will be calculated from the date of transplant to the date of death or last date of follow-up. OS and RFS would be calculated using the Kaplan-Meier product-limit method and the impact of variables will be assessed using the Log-rank test. NRM would be estimated using the cum.Inc method accounting death because relapse as competing event. CIR would be estimated using the cum.Inc method accounting death without relapse as competing event. Cumulative incidence analysis will be done utilizing the cumulative incidence procedure to account for competing risks, and comparison will be performed utilizing the Fine-Gray test. Prognostic variables (will be evaluated for their impact on OS and RFS utilizing univariate and multivariate analysis by cox proportional hazards analysis. Variables found to be significant in the univariate analysis would be included in the multivariate analysis. Results will be expressed as hazard ratio (HR). All P-values will be 2-sided and for the statistical analyses, $P < 0.05$ will be considered to indicate a statistically significant result.

The impact of the source of graft would be explored in the entire cohort of patients. OS, RFS, CIR, NRM, GRFS, and the cumulative incidence of GVHD and GF would be analyzed in the entire cohort and according to the source of graft. A univariate analysis would be done to explore relevant variables in OS and RFS. A multivariate analysis will be conducted including those variables found to be significant in the univariate analysis. Source of graft (BM vs PB) would be included in the multivariate model irrespective of the p value found in the univariate analysis.
The optimal cell dose count would be explored separately in the cohort who received PBSC grafts and in the group of patients who received BM grafts. The impact of the cell dose in OS, RFS, NRM, GRFS, cum. Inc of GVHD and GF would be explored as a continuous variable using cox proportional hazards analysis/Fine-Gray test. An optimal cut-off of CD34+/nucleated cell dose cut-off for OS would be explored based on the binary partitioning method for the entire cohort, according to the type of conditioning regimen, donor source (haplo vs other) and prior splenectomy / spleen size.

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Characteristics of patients who underwent allogeneic HCT with peripheral blood for MF and reported to CIBMTR. 2008-2018

Characteristic	PB
No. of patients	621
Patient age -	
Median (min-max)	62 (40-78)
40-49 yrs	54 (9)
50-59 yrs	215 (35)
60-69 yrs	313 (50)
≥70 yrs	39 (6)
Donor type - no. (%)	
HLA-identical sibling	200 (32)
HLA-matched other relative	10 (2)
HLA mismatched other relative	2 (<1)
HLA-matched unrelated Donor	365 (59)
HLA-mismatched unrelated Donor	44 (7)
Conditioning regimen intensity - no. (%)	
MAC	266 (43)
RIC/NMA	355 (57)
Year of transplant - no. (%)	
2008-2012	67 (11)
2013-2018	554 (89)
CD34 infused cells x 10^8/ weight - median (25^{th}, 75^{th} quartiles)*	6 (4-8)
CD34 infused cells x 10^8/ ideal weight - median (25^{th}, 75^{th} quartiles)	7 (5-10)
Follow-up - median (min-max)	24 (3-123)

*Missing CD34 information for n=148 cases (not included in table).

Footnote: CD3 infusion information available (n=511).

Proposal: 1911-06

Title:
Graft Failure Scoring Systems for Each UCB HCT and Haploidentical HCT

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Cindy Hickey, Dana Farber Cancer Institute
Rizwan Romee, Dana Farber Cancer Institute
Claudio Brunstein, University of Minnesota

Hypothesis:
Developing scoring systems for primary graft (PGF) failure after UCB and haploidentical HCT will be useful to identify high risk patients.

Primary objective:
To create 2 scoring systems to predict PGF following UCB HCT and Haploidentical HCT with PTCy Given the risk of PGF is still markedly high (5-12%) and more importantly associated with very high mortality/morbidity? (70%), it would be very useful to have a scoring system to predict PGF.

Secondary objective:
To evaluate the effect of disease type (lymphoid vs. myeloid) and thus their treatment before transplantation on PGF. In another word, immunosuppressive chemotherapies vs. nonimmunosuppresive chemotherapies

Scientific justification:
Umbilical cord blood (UCB) and haploidentical donors are important source of hematopoietic cell transplantation (HCT).[1] This is particularly important for minority ethnic groups or patients who do not have HLA-full matched donor. Moreover, these alternative donors may have additional advantages over other conventional donor sources (matched siblings or unrelated donors). For example, UCB is associated with a strong graft-versus- leukemia (GVL) effect and less chronic graft-versus-host disease (GVHD).[2] Haploidentical HCT is associated with less chronic GVHD and a lower NRM.[3, 4]
However, alternative donors are associated with a higher rate of PGF. PGF is about 7-14% after UCBT[5-7] and is associated with severe consequences, such as increased mortality rates. [7] Salvaging patients with PGF is very difficult, stem cell rescue (for only haploidentical HCT) or second HCT. However, only 25% of patients may undergo a second alloHCT.[8] In patients who undergo allogeneic HCT, overall survival (OS) has been reported to be 40% at year 1, and 23% at year 3. Therefore, the focus should be directed to prevent PGF and determine high risk patients prior to UCBT. Therefore, identifying risk factors of PGF is important in this population. Already established risk factors include, TNCs, CD34+, CD3+ cell counts at cryopreservation, viability of CD34+ after thaw, and HLA-match status. Several factors like conditioning intensity, donor-relation with the patient, the presence of DSA have been also found to be associated PGF after UCB[9] and haploidetical HCT.[10]
As a secondary point, we hypothesize that disease type for which patient undergoing an HCT is also critical to develop PGF. Patients with lymphoid diseases, including acute lymphoblastic leukemia, high grade lymphomas will receive various lympholytic drugs (methotrexate, steroids, vincristine, fludarabine) in different regimens/ lines before HCT. Therefore, these patients are exposed to more lymphocytic/immunosuppressive drugs even before HCT compared with MDS or AML patients who receive mostly antimyeloid drugs (in fact, some of them only receive an hypomethylating agent.

Moreover, new patients might be only receiving only targeted drugs (antiIDH1 or 2, FLT3, antibcl2) before HCT and morphologically have <5% blasts (in morphologic CR, but most patients continue to have leukemic clone due to maturation/differentiation. The rate of PGF in these patients is unknown?

Patient population:

- Any age (would you just focus on adult population, age >/= 18? Treatment regimens are significantly different in peds population)
- Hematologic malignancy a) myeloid and b)lymphoid
- Receiving single or double UCBT or Hapolidentical HCT
- Between 2005-2019
- First HCT

Outcome:

PGF

Variables to be described:

Patient related:

- Age at HCT
- 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 related:

- Myeloid vs lymphoid
- Last 2 lines of Treatment type (over the last 4 months): immunosuppressive (MTX, Cy, Lasparaginase, vincristine, fludarabine-FLAG, cladribine) vs. nonimmunosuppresive1 (HMA-based, targeted therapies-e.g., IDH1/2 inhibitors, FLT3 inihitor alone vs conventional chemo) vs. intermediate (conventional AML combinations-e.g., 7+3, HidAC)
- Time from last chemo to HCT
- CR1 vs. CR2 vs. >CR2

Transplant related:

- Consolidation prior to transplant
- Conditioning regimen (MAC or RIC vs NMA)
- In vivo or in vitro T-cell depletion
- Donor age (for Haplo)
- Donor-recipient gender match: M-M vs. M-F vs. F-M vs. F-F
- Donor-recipient CMV status: +/+ or -/+ vs. +/- vs. -/-
- Donor type (related (RD), unrelated (URD), UCB (single or double), and haploidentical)

- Donor ABO
- HLA match status (well-matched vs. partial-match vs. mismatched URD; 4/6 vs 5-6/6 UCB)
- Donor (parents, siblings are children for haploidentical HCT)
- GVHD prophylaxis ; CNI-based vs. sirolimus-based vs. PostCy
- Viable CD34+ cells/kg of recipient infused (if available)
- TNC/kg of recipient before thawing
- CD3+/kg of recipient before thawing
- Single vs. double units (for UCB)
- DSA present (Y/N)
- PBSCT vs BM (for haploidentical HCT)

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Characteristics of patients who underwent first HCT for lymphoma/leukemia and reported to CIBMTR 2014-2019- Research level data.

Characteristic	Haploidentical with PT-Cy	UCB	dUCB
No. of patients	1435	61	257
Patient age - no. (%)			
Median (min-max)	58 (18-88)	48 (18-74)	51 (19-74)
18-29 yrs	188 (13)	10 (16)	39 (15)
30-39 yrs	133 (9)	5 (8)	40 (16)
40-49 yrs	180 (13)	22 (36)	46 (18)
50-59 yrs	338 (24)	10 (16)	63 (25)
60-69 yrs	450 (31)	10 (16)	62 (24)
≥70 yrs	146 (10)	4 (7)	7 (3)
Disease - no. (%)			
AML	635 (44)	28 (46)	130 (51)
ALL	227 (16)	19 (31)	52 (20)
MDS	412 (29)	11 (18)	39 (15)
Non-Hodgkin lymphoma	110 (8)	3 (5)	32 (13)
Hodgkin lymphoma	51 (4)	0	4 (2)
Graft source - no. (%)			
Bone marrow	443 (31)	0	0
Peripheral blood	992 (69)	0	0
Umbilical cord blood	0	61	257
Conditioning regimen intensity - no. (%)			
MAC	538 (38)	44 (72)	129 (50)
RIC/NMA	897 (63)	17 (28)	128 (50)
Neutrophil recovery - no. (%)			
No	62 (4)	5 (8)	13 (5)
Yes	1365 (95)	54 (89)	243 (95)
Unknown	8 (1)	2 (3)	1 (<1)
Year of transplant - no. (%)			
2014	162 (11)	1 (2)	3 (1)
2015	234 (16)	2 (3)	7 (3)
2016	291 (20)	14 (23)	55 (21)
2017	326 (23)	27 (44)	109 (42)
2018	419 (29)	14 (23)	71 (28)
2019	3 (<1)	3 (5)	12 (5)
Follow-up - median (min-max)	24 (3-63)	13 (3-57)	13 (3-60)

Proposal: 1911-13

Title:
Optimal donor selection for myeloid and lymphoid malignancies using the CIBMTR database as a part of Personalized Medicine.

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Research hypothesis:
Optimal donor selection for myelodysplastic syndrome (MDS), acute myeloid leukemia (AML), and acute lymphoblastic leukemia (ALL) plays a key role in its outcome after allogeneic transplant and is a critical element of personalized medicine in the modern era. For example, the optimal donor source would be different for a 10-year-old female with AML in CR2 with an HCT-CI of 0 from a 70-year-old male with slowly progressing MDS with an HCT-CI of 4. We believe that each donor source has its own pros and cons and can be selected (i.e., optimal) for a specific aim for a specific patient. In this example, the goal for the first patient is cure without chronic GVHD while for the latter is less NRM with prolonged survival.

Specific aims:
- To find out the optimal donor for a specific patient with MDS, AML or ALL
- To evaluate the disease-free survival (DFS), overall survival (OS) and non-relapse mortality rate (NRM) with the use of different donor types following a myeloablative (MAC) or reduced intensity conditioning (RIC) in patients of AML/MDS, ALL of any age
- To evaluate the incidence of acute GVHD at 6 months and 2 years; chronic GVHD at 1 year and 2 years.

Scientific impact:
Each donor type has advantages over the other and many studies have compared one donor type to another for different hematological malignancy over decades. Although these give us tremendous data/knowledge for gross comparisons; however, the results of these studies are tough to extrapolate to an individual patient as the outcome not only depends on the donor type but an interplay of many other related factors. Our study will allow physicians to choose the optimal donor for a patient in a specific clinical scenario paving the way for personalized medicine and not generalized medicine.

Scientific justification:
Donor type is an incredibly important factor for the success of allogeneic hematopoietic cell transplantation (alloHCT). This has become much more critical as we now have seven donor options *(e.g., Table 1: peripheral blood vs bone marrow: sibling, unrelated, haploidentical, umbilical cord blood)*. Per the NMDP registry study, less than 30% of all the patients will have a sibling donor and they will depend on alternate donor sources[1].
Donor selection for a patient is not just a category (sibling or unrelated), but a more complex process which involves the interplay of many factors like the type of hematological malignancy, disease status at transplant, age/comorbidities of the patient, intensity of the conditioning regimen (myeloablative versus reduced intensity conditioning)etc. Each donor type has its own advantages[2] and though HLA identical sibling donors are readily available and have low chances of graft failure and GVHD[3], they have a higher occurrence of relapse. Unrelated donor also has its own advantage (strong graft versus tumor (GVT)

effect) and many studies have shown comparable outcomes of MUD and HLA identical sibling donors[4,5] but there is an increased risk of acute and chronic GVHD with unrelated donors and often the urgency of the clinical situation, dictates alternate donor choices (umbilical cord blood (UCB), haploidentical). UCB requires less restrictive HLA matching [6] than the HLA identical siblings/unrelated donors and is readily available[7] but has a higher risk of graft failure and NRM and it might not be an ideal donor source for patients with advanced age. Haploidentical donors just like the HLA identical sibling/UCB donors are readily available, have less NRM and chronic GVHD[8] but have increased incidence of graft failure and might have a lower GVT effect in myeloid malignancy when compared to lymphoid malignancy[9]. Moreover, each donor type comes with a different donor source (i.e., peripheral blood or bone marrow), and we know that this makes the difference even further. For example, PBSCT has a stronger GVL effect but more cGVHD. In this proposal, we would like to use these differences between donor type/donor source combinations as an advantage to find best option for a patient (precise, personalized medicine).

The three outcomes that determine the success of alloHCT are relapse rate, NRM, and chronic GVHD. Ideally, the goal of any alloHCT is no relapse, no NRM, no chronic GVHD and 100% GVHD free relapse free survival (GFRS). However, GFRS gives equal weight to GVHD, relapse, and survival and in reality, for a patient you either get less relapse with high NRM or high relapse with less NRM. Depending on the age, co-morbidities and disease status at transplant/ disease risk index (DRI) the goals for each alloHCT is different. For a younger patient with low HCT-CI, the goal is to choose a donor source which has the least relapse > less chronic GVHD > less NRM and for an older patient or patients with high HCT-CI the goal is least NRM > less relapse > less chronic GVHD. We wanted to create a model where were we compared the NRM, relapse rate and chronic GVHD of AML/MDS and ALL patients depending on the donor type and stratify it by disease risk index (high vs low) (table 1). We plan to repeat this analysis for both myeloablative (Table 1) and reduced intensity conditioning regimens (Table 2). This analysis will help the physician and their patients to choose what is most important for them: least relapse rate, least NRM or least chronic GVHD in any order or an intermediate relapse rate, NRM and chronic GVHD

Table 1: AML/MDS, ALL donor selection: Hazard ratio for **myeloablative conditioning regimen.**

	High Risk DRI			Low Risk DRI		
	NRM	**Relapse**	**cGVHD**	**NRM**	**Relapse**	**cGVHD**
MRD BM						
MRD PBSC						
MUD BM						
MUD PBSC						
Haplo BM						
Haplo PBSC						
UCB						

Table 2: AML/MDS, ALL donor selection: Hazard ratio for **reduced intensity conditioning regimen.**

	High Risk DRI			Low Risk DRI		
	NRM	**Relapse**	**cGVHD**	**NRM**	**Relapse**	**cGVHD**
MRD BM						
MRD PBSC						
MUD BM						
MUD PBSC						
Haplo BM						
Haplo PBSC						
UCB						

For example:
In the younger patient relapse is the main concern (in another word, main goal is to prevent relapse), followed by less cGVHD that is followed by less NRM.
In the older patient, the first goal "do not kill" (lower NRM), followed by less relapse and that is followed by less cGVHD.
Hazard ratios comparing each donor option to others for each outcome can be computed to find which donor option provides the best possibility to reach this goal for that patient. And also, the second-best option and so on so forth for the 7 donor options can be figured out with this model.

Patient eligibility population:
Any age who underwent allogeneic transplant for AML/MDS and ALL in between 2000-2015

Date requirements:
- Pre HSCT data for AML, MDS, ALL,
- Post HSCT data for AML, MDS, ALL
- Post-Transplant Essential Data
- Recipient Death Data

Sample requirements:
N/A

Study design:
Retrospective analysis

Variables to be analyzed:
Patient related variables:
- Age at transplantation
- Gender: Female vs. male
- Karnofsky performance score: < 80% vs. ≥ 80%
- Hematopoietic stem cell transplantation-specific comorbidity index (HCT-CI)

Disease related variables at diagnosis and treatment prior to alloHCT
- DRI
- Disease status at HCT
    - CR1 or CR2
    - >CR2
    - Active disease

Transplant related variables:
- Donor type: HLA matched sibling vs. HLA matched unrelated donor (matched for HLA –A, B, C, DRB1) vs UCB vs. haploidentical donor.
- Donor-Recipient Sex M-M vs. M-F vs. F-M vs. F-F (for dUCB, dominant cord)
- Donor Age (for dUCB, dominant cord)
- Donor-recipient CMV serostatus: -/- vs. -/+ vs. +/- vs. +/+ (for dUCB, dominant cord)
- GVHD prophylaxis: CSA or Tac plus MTX vs. MMF+ others vs. ex vivo T cell depletion vs. post-HCT Cy
- Transplant period: 2000-2007 vs. 2008-2015
- Conditioning regimen: myeloablative vs.reduced intensity

- Source of stem cells: Bone marrow (BM) vs. peripheral blood stem cell (PBSC) vs. UCB
- CD34+ cell dose (for PBSC and UCB)
- Nucleated cell dose (for BM)
- Time to CR from diagnosis
- Duration of CR1 for patients in CR2

Post-Transplant variables:

- Cumulative incidence of Acute GVHD at 6 months and year 2
- Cumulative incidence of chronic GVHD at year 1 and year 2
- NRM at day 100 and 180
- Secondary malignancy at year 5
- GVHD free relapse free survival (GFRS) at year 2 and 5

Study end points and outcomes:

- NRM at day 100 and day365, relapse is a competing risk.
- Relapse at 2-year. This event will be summarized by cumulative incidence estimate with NRM as the competing risk.
- DFS at 2 years: Time to death or relapse, patients censored at last follow-up.
- Secondary malignancy at year 5
- GFRS at year 2 and 5
- OS at 2-years: Time to death, patients censored at last follow-up.
- Stratify the NRM, relapse, DFS and OS at 2 yr by MAC vs RIC for each donor type

Study design: (scientific plan)

Kaplan and Meier will be used to estimate the median survivals and create survival plots and the survival curves will be compared using the log rank tests. Cox proporational hazard will be used for univariate and multivariate analysis. OS will be calculated from the date of transplantation to the date of death or date of last follow-up. DFS will be calculated from the date of transplantation to the date of first disease progression, date of death, or date of last follow-up. Patients who are alive and who didn't experience disease progression at their last evaluation will be censored. Non relapse morality will be calculated considering disease progression as a competing event. Hazard ratio will be used to compare the NRM, relapse and chronic GVHD for each donor type.

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Characteristics of patients who underwent first allo HCT with AML, ALL, and MDS and reported to CIBMTR 2012-2018

Characteristic	MAC	RIC/NMA
No. of patients	3832	3233
Patient age - no. (%)		
Median (min-max)	49 (18-88)	63 (18-81)
18-29 yrs	700 (18)	125 (4)
30-39 yrs	625 (16)	142 (4)
40-49 yrs	793 (21)	280 (9)
50-59 yrs	1107 (29)	740 (23)
60-69 yrs	546 (14)	1515 (47)
≥70 yrs	61 (2)	431 (13)
Disease - no. (%)		
AML	2337 (61)	2089 (65)
ALL	978 (26)	402 (12)
MDS	517 (14)	742 (23)
Donor, graft and DRI grouping- no. (%)		
Matched sibling/BM/low/intermediate DRI	96 (3)	13 (<1)
Matched sibling/BM/high/very high DRI	15 (<1)	3 (<1)
Matched sibling/PB/low/intermediate DRI	674 (18)	496 (15)
Matched sibling/PB/high/very high DRI	183 (5)	119 (4)
Haploidentical with PT CY/BM/low/intermediate DRI	66 (2)	201 (6)
Haploidentical with PT CY/BM/high/very high DRI	36 (1)	39 (1)
Haploidentical with PT CY/PB/low/intermediate DRI	276 (7)	256 (8)
Haploidentical with PT CY/PB/high/very high DRI	100 (3)	79 (2)
Matched URD/BM/low/intermediate DRI	288 (8)	68 (2)
Matched URD/BM/high/very high DRI	76 (2)	39 (1)
Matched URD/PB/low/intermediate DRI	929 (24)	965 (30)
Matched URD/PB/high/very high DRI	270 (7)	236 (7)
Mismatched URD/BM/low/intermediate DRI	71 (2)	41 (1)
Mismatched URD/BM/high/very high DRI	19 (1)	15 (1)
Mismatched URD/PB/low/intermediate DRI	164 (4)	145 (5)
Mismatched URD/PB/high/very high DRI	66 (2)	43 (1)
UCB/low/intermediate DRI	386 (10)	396 (12)
UCB/high/very high DRI	117 (3)	79 (2)
Year of transplant - no. (%)		
2012-2014	1610 (42)	1157 (36)
2015-2018	2222 (58)	2076 (64)
Follow-up - median (min-max)	37 (2-77)	36 (2-78)

Proposal: 1911-170

Title:
Graft Source for Salvage or Rescue Hematopoietic Stem Cell Transplantation for Hematological Malignancies after Primary Graft Failure

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Research hypothesis:
Salvage (or rescue) hematopoietic cell transplantation (HCT) is the only potential therapeutic option for primary graft failure. Clinical outcomes (overall survival, relapse mortality and non-relapse mortality) differ based on various graft sources (sibling donor, same unrelated donor, different unrelated donor, haploidentical and umbilical cord blood) for salvage HCT. Time to salvage HCT is an important parameter which determines outcomes in these patients.

Specific aims:
Primary objective:
To determine 100-day and 1-year overall survival following salvage HCT after primary graft failure based on the graft source (sibling donor, same unrelated donor, different unrelated donor, haploidentical and umbilical cord blood)

Secondary objectives:
- To study the time to second or salvage HCT after primary graft failure
- To determine the optimal conditioning regimen for salvage HCT
- To determine relapse and non-relapse mortality after salvage HCT

Scientific impact:
The proposed CIBMTR study will help determine the best graft source (sibling donor, same unrelated donor, different unrelated donor, haploidentical and umbilical cord blood) for salvage HCT after primary graft failure. In addition, this study will help determine the outcomes of alternative donors (umbilical cord blood and haploidentical) when used as graft sources for salvage HCT.

Scientific justification:
Primary graft failure is a serious complication of allogeneic hemopoietic cell transplantation (HCT) associated with a high mortality rate. It is characterized by lack of donor progenitor cells to engraft and recover from neutropenia induced by the conditioning regimen i.e. failure to achieve neutrophil count of $\geq 0.5 \times 10^9$/L. The incidence of primary graft failure is reported to be 5-10% [1, 2]. Use of myeloid growth factors, choice of conditioning regimen and immunosuppression, total nucleated cell or CD34+ cell count and improved HLA matching are strategies to mitigate the risk of primary graft failure. Despite, primary graft failure remains a feared complication of HCT.
Various risk factors for primary graft failure have been identified including the degree of HLA match, hematopoietic progenitor cell dose and viral infections. It is mediated by the recipient cellular and humoral immune responses such as donor CD34+/ PDGFR-2+ cell specific antibodies [3]. A study identified myeloproliferative disorders, recipient age < 30, HLA mismatch, ABO incompatibility,

busulfan/ cyclophosphamide condition and cryopreservation as major risk factors for primary graft failure [4].
Salvage or rescue transplantation is the only potential life-saving therapy for patients with primary graft failure. However, it is complicated because of protracted pancytopenia, infections and poor performance status. In addition, selection of donor is particularly challenging. In one study, one-year overall survival after salvage allogeneic HCT was found to be 11%. Graft source for the second HCT was bone marrow (BM) in 51% of the patients, with the remaining receiving peripheral blood stem cells (PBSC). Eighty percent of the patients received HCT from the same donor. Although engraftment rate was reported to be 74% at day 100, outcomes based on graft source (BM vs PBSC) were not reported [5]. Another recent study reported outcomes following second HCT after primary graft failure. Graft sources were reported to be sibling donor (6%), unrelated donor (49%), haploidentical (7%) and umbilical cord blood (33%). One-year overall survival was reported to be 27% after second HCT but outcomes based on graft source were not reported [6]. Therefore, choice of the best donor for salvage HCT after primary graft failure is currently unknown.
We propose to conduct a study utilizing CIBMTR database to evaluate various graft sources (sibling donor, same unrelated donor, different unrelated donor, haploidentical and umbilical cord blood) for salvage HCT after primary graft failure. We believe that such a study would be important to conduct for various reasons. First, our literature search did not identify any study to answer this critical question. Second, prior studies excluded patients who received umbilical cord blood grafts. Third, prior two CIBMTR studies on primary graft failure included patients till 2005 in one [5] and till 2008 in the other study [4]. Since then, the number of potentially evaluable patients has grown substantially. And finally, haploidentical transplant has gained popularity and has been adopted increasingly in recent years. Therefore, it would be important to include haploidentical transplant in the study which has not been included in the previous studies.

Patient eligibility population:
Inclusion criteria:

- Recipients of allogeneic hematopoietic cell transplantation for hematological malignancies between 2000 to 2018
- All donor types including sibling donor, unrelated donor, haploidentical and umbilical cord blood would be included
- Age ≥ 18 years

Exclusion criteria:
Recipients of allogeneic hematopoietic cell transplantation for non-malignant disorders

Data requirements:
For conduction of this study, the following CIBMTR data will be collected and analyzed:
Patient specific data:

- Recipient age
- Recipient gender (male/ female)
- Disease indication for first HCT
- Disease status prior to first HCT (complete remission/ persistent disease)

Donor specific data:

- Donor age
- Donor gender (male/ female)

- HLA match (fully matched/ partially matched/ haploidentical)
- ABO compatibility (compatible/ major mismatch/ minor mismatch)

Transplant related data:
- Year of HCT
- Conditioning regimen
- Conditioning intensity (MA/ RIC)
- Anti-thymocyte globulin (yes/ no)
- Donor type (MSD/ MUD/ haploidentical/ umbilical cord blood)
- Graft source (peripheral blood/ bone marrow/ umbilical cord blood)
- Graft product (fresh/ cryopreserved)
- CD34+ cell dose
- CD3+ cell dose
- GVHD prophylaxis
- Primary graft failure (yes/ no)
- Acute GVHD (yes/ no)
- Chronic GVHD (yes/ no)
- Death from primary graft failure (yes/ no)

Salvage/ second transplant:
- Conditioning regimen
- Fludarabine (yes/ no)
- Anti-thymocyte globulin (yes/ no)
- Alemtuzumab (yes/ no)
- Rituximab (yes/ no)
- Donor type (MSD/ same MUD/ different MUD/ haploidentical/ umbilical cord blood)
- Graft source (peripheral blood/ bone marrow/ umbilical cord blood)
- Graft product (fresh/ cryopreserved)
- CD34+ cell dose
- CD3+ cell dose
- Neutrophil engraftment (yes/ no)
- Time to engraftment
- Failure to engraft (yes/ no)
- Third HCT (yes/ no)

Outcomes after salvage transplant:
- Follow up duration
- Relapse (yes/ no)
- Time to relapse
- Death (yes/ no)
- Time to death

Sample requirements:
No biological samples will be required to conduct this study.

Study design:
This study is a proposed retrospective CIBMTR study. Continuous variables will be described using medians and ranges. Categorical variables will be compared using Chi square or Fisher Exact test, while continuous variables using Mann Whitney U test. All *p* values will be two-tailed and significant at < 0.05. Time to event analysis would be determined using Kaplan-Meier method, and compared using log-rank tests. Cumulative incidence rates will be used when competing risks are present for calculation of probabilities of relapse/ non-relapse mortality and neutrophil engraftment rate.

Non-CIBMTR data source:
Not applicable for conduction of this study

Conflicts of interest:
No

References:
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Characteristics of patients who underwent second allogeneic HCT for hematologic malignancy who had graft failure and reported to CIBMTR between 2008-2018

Characteristic	First Allo Transplant	Subsequent Transplant
No. of patients	631	147
Time between transplant and graft failure – median	1 month	NE
Patient age – no. (%)		
Median (min-max)	57 (18-78)	52 (19-75)
18-29 yrs	63 (10)	20 (14)
30-39 yrs	65 (10)	19 (13)
40-49 yrs	82 (13)	28 (19)
50-59 yrs	165 (26)	36 (25)
60-69 yrs	208 (33)	37 (25)
≥70 yrs	48 (8)	7 (5)
Disease - no. (%)		
AML	290 (46)	63 (43)
ALL	92 (15)	21 (14)
MDS	249 (40)	63 (43)
Donor type - no. (%)		
HLA-identical sibling	66 (10)	15 (10)
HLA-matched other relative	10 (2)	3 (2)
HLA mismatched other relative	54 (9)	14 (10)
Haploidentical donor	69 (11)	28 (19)
HLA-Matched Unrelated Donor	155 (25)	18 (12)
HLA-Mismatched Unrelated Donor	68 (11)	38 (26)
UCB, 6/6	7 (1)	0
UCB, 5/6	49 (8)	3 (2)
UCB, LE4/6	84 (13)	18 (12)
UCB, degree of match Unknown	69 (11)	10 (7)
Year of transplant - no. (%)		
2008-2013	301 (48)	69 (47)
2014-2019	330 (52)	78 (53)
Follow-up - median (min-max)	36 (2-122)	48 (3-121)

Proposal: 1911-20

Title:
Outcomes after Double Unrelated Umbilical Cord Blood (dUCB) versus HLA-Mismatched Unrelated (MMUD) Transplants using Post-Transplantation Cytoxan for Patients with Hematologic Malignancies

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Research hypothesis:
Patients with hematologic malignancies who undergo allogeneic hematopoietic cell transplantation (allo-HCT) using mis-matched unrelated donor (MMUD) with post-transplant cyclophosphamide (PTCy) have similar overall survival to those with double umbilical cord (dUCB) transplantation.

Specific aims:
Primary objectives :

- The primary objective is to compare 1-year overall survival (OS) between patients who receive dUCB transplantation versus MMUD transplantation using PTCy.

Secondary objectives:

- Progression-free-survival (PFS) at 1 -year post-HCT
- Transplant-related mortality (TRM) at Day+100 and 1-year post-HCT
- Cumulative incidence of neutrophil and platelet recovery
- Cumulative incidences of acute GVHD (aGVHD) and chronic GVHD (cGVHD)
- Cumulative incidences of early (+100 days) viral reactivations and infections

Scientific impact:
Allogeneic hematopoietic cell transplantation (allo-HCT) is the only curative option for treatment of several malignant hematologic diseases. Only near 30% of the patients who require an allo-HCT will have a HLA-matched sibling donor. Despite more than 20 million adult volunteer donors in the National Marrow Donor Program, many patients, especially racial/ethnic minorities, will not have a matched unrelated donor. In the recent years, haploidentical transplantation has emerged as a suitable alternative option for patients without an HLA-matched donor with the advantage of providing a readily available source of stem cells for transplantation. Despite the widespread availability of haploidentical donors, there are still some patients who does not have a suitable donor. HLA- MMUDs or dUCB have been used as a donor source in these situations (1). The number of unrelated cord blood transplants (UCBT) are declining (2). The decline is partly due to the slow engraftment and delayed immune reconstitution of UCBT, which result in a significant risk of infection (3,4).
Historically, MMUD transplantation using conventional GVHD prophylaxis (Calcineurin inhibitor based) has been associated with increased risk of graft failure, NRM, and GVHD, in turn contributing to worse OS (5). In recent years, several strategies including MMUD transplantation using PTCY as a GVHD prophylaxis have been tested in an attempt to improve the unfavorable outcomes. Study by Mehta et al, comparing the efficacy of PTCy-based GVHD prophylaxis and conventional GVHD prophylaxis in 113 HLA-MMUD HCT recipients demonstrated that the use of PTCy as GVHD prophylaxis is safe and results in significantly lower risk of earlier occurrence of acute GVHD (6). In a non-randomized phase II clinical trial, Gaballa et al, investigated the safety and efficacy of GVHD prophylaxis with PTCy, tacrolimus, and MMF after a reduced-intensity conditioning regimen in patients with advanced hematologic malignancies who underwent HCT

from a haploidentical donor or a single antigen MMUD. Overall, both arms had comparable 2-year OS rates. The NRM rate was somewhat higher in the 9/10 MUD arm (34% vs 23%) due to a higher proportion of patients experiencing grade II and IV aGVHD (7). A recent study by Jorge et al, there was no significant difference in 100-day cumulative incidence of grades II to IV acute GVHD grades, NRM , PFS and OS at 2 years between MUD with conventional GVHD prophylaxis and MMUD with PTCY in 86 adults HCT recipients with advanced hematologic malignancies (8). Currently, a multi-center, single arm Phase II study to assess the safety and efficacy of MMUD bone marrow transplantation using PTCy completed accrual (results pending)

There is limited data available regarding whether an unrelated dUCB or HLA-MMUD should be selected as an alternative donor for patients without suitable related or MUD. Results of this study will enhance our understanding of trend in utilization of MMUD transplantation in more recent years and also add to the growing literature on alternative donor transplants.

Scientific justification:

Success in overcoming barriers of HLA-mismatching with the use of PTCy has led to increase in utilization of MMUD transplants. In a survey study evaluating future practice trends in the HCT field among the 315 HCT clinicians practicing in the United States, majority of participants predicted MMUD as the preferred donor source (over UCB) in an adult patient who lack available MRD, MUD and haploidentical donor in the near future (unpublished data). While this question (MMUD vs. dUCB) ideally should be answered in a prospective randomized study, this trial will not be funded or completed in a timely fashion. The results of this study will provide guidance in selecting an appropriate alternative donor.

Patient eligibility population:

Study population includes ages of 18 and 65 years with the diagnosis of a hematologic malignancy who underwent dUCB transplantation or HLA-MMUD using PTCy (bone marrow and peripheral blood graft source included)

- MMUD is described as a partially (4/8 – 7/8) HLA-MMUD defined by high resolution typing at HLA-A, -B, -C and –DRB1.
- Double umbilical cord: 4-6/6 HLA matched grafts with at least 2.0×10^7/kg total nucleated cell dose.

Data requirements:

<u>Disease related:</u>

- Primary disease
- Remission status at HCT
- Refined disease risk index (DRI)

<u>Patient related:</u>

- Age
- Gender
- Race
- Ethnicity
- CMV status
- ABO status
- HCT-CI
- Performance status: KPS 90-100 vs <90

Donor related:
- Age
- CMV status
- ABO status

Transplant related:
- Conditioning type: MA vs. RIC/NMA
- Source of stem cell: Bone marrow versus peripheral blood vs cord
- GvHD prophylaxis
- ATG vs No ATG
- Year of transplant

Sample requirements:
Not applicable

Study design:
Comparison between groups used χ^2 testing for categorical variables and *t* tests for continuous variables. Probabilities of TRM and relapse will be generated using cumulative incidence estimates to accommodate competing risks. The incidences of acute GVHD and chronic GVHD will be calculated using the cumulative incidence function, with death, relapse, or disease progression as competing risks. Probabilities of overall OS and PFS will be calculated using the Kaplan-Meier estimator.

Non-CIBMTR data source:
Not applicable

Conflicts of interest:
No

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Characteristics of patients who underwent first allo HCT for malignant disease and reported to CIBMTR 2016-2018

Characteristic	mMUD	dUCB, 6/6	dUCB, 5/6	dUCB, LE 4/6
No. of patients	72	15	110	205
Patient age - no. (%)				
Median (min-max)	60 (22-76)	55 (28-73)	55 (20-72)	40 (19-74)
18-29 yrs	1 (1)	2 (13)	17 (16)	35 (17)
30-39 yrs	5 (7)	0	16 (15)	41 (20)
40-49 yrs	11 (15)	3 (20)	17 (16)	38 (18)
50-59 yrs	20 (28)	7 (47)	21 (19)	50 (24)
60-69 yrs	29 (40)	2 (13)	35 (32)	38 (18)
≥70 yrs	6 (8)	1 (7)	4 (4)	3 (2)
Disease - no. (%)				
AML	23 (32)	5 (33)	53 (48)	112 (55)
ALL	10 (14)	3 (20)	18 (16)	48 (23)
Other leukemia	1 (1.4)	0	1 (1)	1 (1)
CML	3 (4.2)	0	0	5 (2)
MDS	31 (43.1)	4 (27)	21 (19)	21 (10)
Other acute leukemia	1 (1.4)	0	0	2 (1)
Non-Hodgkin lymphoma	2 (2.8)	3 (20)	14 (13)	15 (7)
Hodgkin lymphoma	1 (1.4)	0	3 (3)	1 (1)
Conditioning regimen intensity - no. (%)				
MAC	24 (33.3)	8 (53)	48 (44)	113 (55)
RIC/NMA	48 (66.7)	7 (47)	62 (56)	92 (45)
GVHD Prophylaxis - no. (%)				
PT-Cy +CNI+ MMF	72	0	0	0
CNI + MMF	0	15	110	205
Graft Source - no. (%)				
Bone marrow	18 (25)	0	0	0
Peripheral blood	54 (75)	0	0	0
Umbilical cord blood	0	15	110	205
Year of transplant - no. (%)				
2016	12 (17)	7 (47)	47 (43)	85 (41)
2017	25 (35)	5 (33)	44 (40)	57 (28)
2018	35 (49)	3 (20)	19 (17)	63 (31)
Follow-up - median (min-max)	12 (3-39)	24 (3-37)	24 (3-37)	23 (3-39)

Proposal: 1911-39

Title:
Reduced Intensity (RIC) Conditioning and Transplantation of Double Unrelated Umbilical Cord Blood (dUCB) *versus* HLA-Haploidentical Related Bone Marrow (BM) for Patients with Acute Leukemias: Comparison of Survival Outcomes from a Randomized Clinical Trial with Outcomes from a Contemporaneous Cohort from the CIBMTR Registry.

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Research hypothesis:
Overall survival (OS) at 2 yr is significantly higher for haploidentical transplants

Specific aims:
Primary endpoint:
To compare OS at 2 yr post-transplant for patients with acute leukemias in CR

- Multivariate analysis to include: age, gender, race/ethnicity, Karnofsky Score, HCT-CI, HLA matching score for UCB units, TNC at infusion, CR status, center

Secondary endpoints:
To compare hematopoietic recovery, graft failure, acute and chronic GvHD, relapse, non-relapse mortality (NRM) and progression-free survival (PFS)

Scientific impact:
Comparison of findings from a randomized study to a contemporaneous patient population matched to conditioning regimen and GvHD prophylaxis derived from the CIBMTR registry database will estimate the generalizability of results from the randomized study.

Scientific justification:
A randomized phase III trial of RIC and transplantation of dUCB *versus* HLA-haploidentical related bone marrow (haplo-BM) for patients with hematologic malignancies (BMT CTN 1101; NCT01597778) was recently completed and a manuscript is in preparation (co-chairs of BMT CTN 1101 are the PI's of this proposed CIBMTR study). The trial enrolled 368 patients and 342 patients received the assigned transplants. Analysis by intent-to-treat or by assigned arm showed no significant difference between graft sources in progression-free survival at 2 yr (P=0.409), the primary endpoint of the study. Secondary endpoints included hematopoietic recovery, acute and chronic GvHD, relapse, NRM and OS. At 2 yr post-transplant, patients who received haplo-BM had significantly lower NRM (11% vs. 19%, P=0.03) and significantly higher OS (59% vs. 47%, P=0.023). For the other secondary endpoints, there was no significant differences between the two arms.
It is important to determine if findings from a randomized study are comparable to findings from a registry study of a matched patient population.

Patient eligibility population:

- Patients $\geq$ 18 and $\leq$ 70 years of age who were transplanted between 6/19/2012 and 6/30/2018 and NOT enrolled on BMT CTN 1101.

- Karnofsky Score ≥70%
- Patients with a diagnosis of acute lymphoid or myeloid leukemia in CR1 or CR2
    - Acute Lymphoblastic Leukemia (ALL) in first complete remission (CR1) that is NOT considered favorable-risk as defined by the presence of at least one of the following:
        - Adverse cytogenetics such as t(9;22), t(1;19), t(4;11), other MLL rearrangements,
        - White blood cell counts of greater than 30,000/mcL (B-ALL) or greater than 100,000/mcL (T-ALL) at diagnosis,
        - Recipient age older than 30 years at diagnosis,
        - Time to CR greater than 4 weeks
    - Acute Myelogeneous Leukemia (AML) in first complete remission (CR1) that is NOT considered as favorable-risk.
        - Favorable risk is defined as having one of the following:
            - t(8,21) without cKIT mutation
            - inv(16) without CKIT mutation or t(16;16)
            - Normal karyotype with mutated NPM1 and not FLT3-ITD
            - Normal karyotype with double mutated CEBPA
            - APL in first molecular remission at end of consolidation
    - Acute Leukemias in 2nd CR
    - Biphenotypic/Undifferentiated/Prolymphocytic Leukemias in first or second CR
- For dUCB transplants: two partially HLA-matched UCB units, each with a minimum of 1.5 x 107/kg pre-cryopreserved total nucleated cell dose (for non-red blood cell depleted units, the minimum cryopreserved total nucleated cell dose of each unit must be at least 2.0 x 107/kg)
- For haplo transplants: HLA-mismatched (≥2 HLA-A, -B, -C, -DRB1 loci) related donor BM.
- RIC:
    - The preparative regimen for dUCB transplantation will consist of: fludarabine 200 mg/m2 over 5d, cyclophosphamide 50 mg/kg IV x 1d, total body irradiation (TBI) either 200 cGy or 300 cGy
    - The preparative regimen for haplo-BM or haplo-PBSC transplantation will consist of: fludarabine 150 mg/m2 over 5d, cyclophosphamide (Cy) 14.5 mg/kg IV x 2d, TBI 200 cGy x 1 (Hopkins Regimen)
- GVHD prophylaxis:
    - Regimen for dUCB transplantation will consist of cyclosporine or tacrolimus and mycophenolate mofetil (MMF) until Day 35.
    - The GVHD prophylaxis regimen for haplo-BM transplantation will consist of Cy 50 mg/kg IV on 3, 4 (PTCy), tacrolimus or cyclosporine (starting on D5), MMF until Day 35

Data requirements:
Per CIBMTR forms

Sample requirements:
None

Study design:
Point-wise comparisons of endpoints at 2 yr and Cox proportional hazards regression model. Protocol design may be limited by the number of haplo-BM transplants reported to the CIBMTR exclusive of BMT CTN 1101 transplants. Since 2012, there has been a marked increase in haplo transplants compared to UCB transplants but this increase has been primarily in haplo transplants using PBSC as the graft source.

Feasibility of this proposal will depend on the number of non-1101 haplo-BM transplants available for analysis. Otherwise, an alternative study would be to compare dUCB transplants to haplo-PBSC transplants using the same eligibility criteria and endpoints as proposed above.

Data source:
CIBMTR Research Database. Comparative data from BMT CTN database.

Conflicts of interest
None

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Characteristics of patients who underwent first allo HCT with RIC and reported to CIBMTR 6/19/2012-6/30/2018

	CTN1101		Non-CTN1101		
Characteristic	**BM**	**dUCB**	**BM**	**PB**	**dUCB**
No. of patients	157	185	319	409	147
No. of centers	29	31	40	73	38
Karnofsky score prior to HCT - no. (%)					
90-100%	101 (64)	115 (62)	227 (71)	211 (52)	97 (66)
< 90%	53 (34)	66 (36)	91 (29)	198 (48)	50 (34)
Not reported	3 (2)	4 (2)	0	0	0
Disease					
Acute myelogenous leukemia	91 (58)	97 (52)	167 (53)	264 (65)	96 (65)
Acute lymphoblastic leukemia	25 (16)	30 (16)	75 (24)	60 (15)	30 (20)
Other acute leukemia	4 (3)	3 (2)	0	0	0
Non-Hodgkin lymphoma	28 (18)	43 (23)	56 (18)	62 (15)	17 (12)
Hodgkin lymphoma	9 (6)	12 (7)	20 (6)	23 (6)	4 (3)
Year of transplant - no. (%)					
2012	3 (2)	2 (1)	19 (6)	3 (1)	15 (10)
2013	25 (16)	29 (16)	43 (14)	11 (3)	38 (26)
2014	31 (20)	31 (17)	40 (13)	32 (8)	37 (25)
2015	36 (23)	40 (22)	56 (18)	64 (16)	23 (16)
2016	28 (18)	41 (22)	66 (21)	100 (24)	17 (12)
2017	26 (17)	33 (18)	52 (16)	117 (29)	15 (10)
2018	8 (5)	9 (5)	42 (13)	82 (20)	2 (1)
Follow-up - median (25^{th}, 75^{th} percentile)	36 (14-48)	37 (24-48)	36 (13-42)	24 (12-36)	49 (24-60)

Proposal: 1911-19/1911-210

Title:
Impact of Cell Dose on Haploidentical Stem Cell Transplantation Outcome

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Research hypothesis:
Cell dose of the graft predicts haploidentical transplant outcomes

Specific aims:
- To investigate the impact of bone marrow and peripheral blood graft cell dose on haploidentical hematopoietic stem cell transplant (HSCT) outcomes.
- To identify the optimal cell dose of bone marrow graft and peripheral stem cell graft for haploidentical HSCT.

Scientific justification:
Over the past decade, allogeneic hematopoietic stem cell transplant (HSCT) has been used to treat numerous malignant and nonmalignant hematologic diseases. An adequate stem cell dose is recognized as one of the most important donor factors influencing the outcome of HSCT. Numerous studies have demonstrated that infusion of larger numbers of bone marrow cells improve survival after HSCT [1-5]. In a retrospective study of 572 patients with acute myeloid leukemia (AML) who underwent MRD allogeneic transplant using bone marrow grafts[1], a nucleated cell dose above the mean (2.6 x 10^8 TNC/kg recipient body weight) was associated with lower non-relapse mortality, disease relapse and improved disease-free survival, neutrophil, and platelet engraftment. There was no relationship seen between the dose of TNC and the risk of acute GVHD. Patients who received >3.8 x 10^8 TNC/kg were shown to have 30% increase in disease-free survival compared to patients who received < 1.6x10^8 TNC/kg. A subsequent study evaluated the effect of TNC dose on graft function and transplant outcomes in 905 allogeneic bone marrow graft recipients (753 MRD, 30 MMUD, 135 MUD) [2]. A higher TNC doses was associated with faster engraftment, lower TRM and better OS. The effect of cell dose was more pronounced in patients older than 30 years, with advanced disease, and with alternative donors. In a more recent study of 372 adults with hematologic malignancies who underwent reduced intensity haplo-BMT with PTCy at Johns Hopkins between 2002 and 2012, higher nucleated cell graft dose was associated with improved OS and PFS and decreased risk of grades III to IV aGVHD[7]. Currently, a TNC dose of 3 x 10^8/kg or higher in bone marrow grafts is generally accepted as an optimal for transplant outcomes, although more recent data has begun to question its significance.
Recently, haploidentical hematopoietic stem cell transplantation has been increasingly used for treatment of hematologic malignancies, primarily due to development of post-transplant cyclophosphamide as an effective strategy for GVHD prophylaxis[6]. The optimal bone marrow cell dose for T-cell replete haploidentical transplant is not known. Given the continued growth of haploidentical stem cell transplantation in adults over the past decade, we sought to determine whether there is a correlation between cell dose of the graft and clinical outcome in haploidentical HSCT.

Scientific impact:
Several studies have identified CD34+ and MNC cell dose as a critical factor affecting stem cell transplantation outcome. Most of these studies primarily focused on MRD and MUD peripheral blood or

bone marrow grafts. In the absence of a suitable HLA matched sibling donor, haploidentical donors are increasingly considered due to donor availability and a relatively lower treatment related mortality [8]. The effect of donor graft cell dose (CD34+, TNC) on clinical outcomes in haploidentical HSCT has not been well characterized. This study will be the first to identify the optimal bone marrow and peripheral stem graft cell dose for haploidentical HSCT.

Patient eligibility population:
Patients aged 18 years or older who have undergone first haploidentical transplant for hematologic malignancies from 2010 – 2019
Patients who received manipulated grafts, such as ex-vivo T cell depletion or CD34+ selection, will be excluded.
Haploidentical transplants without post-transplant cyclophosphamide for GVHD prophylaxis will be excluded

Outcomes:
Primary outcome:
- To investigate the impact of graft cell dose (TNC and CD34+) on overall survival (OS).

Secondary outcomes:
- Incidence of grade II-IV and grade III-IV acute and chronic GVHD
- Cumulative incidence of Non-relapse mortality (NRM)
- Relapse/progression-free survival (PFS)
- Time to engraftment: Defined as time between day of transplantation and recovery of neutrophils and platelets.
- GVHD free/relapse free survival (GFRS)
- Primary graft failure (failure to achieve ANC>500/mm^3 for three days or donor chimerism < 5% (If information available)

Variables:
Main effect:
Bone marrow graft Cell dose (CD34+ and TNC dose) and Peripheral stem cell graft (CD34+) – continues variable or patient can be divided into 4 quartiles

Patient-related:
- Age at transplant: continuous & by age group: decades
- Gender: male vs. female
- Karnofsky performance status at transplant: ≥ 90 vs. < 90 vs. missing
- HCT comorbidity index at transplant: 0 vs 1-2 vs ≥ 3 vs. missing
- Race/ethnicity: Caucasian vs. others vs. missing
- Recipient BMI (normal vs overweight vs obese)

Disease-related:
- Disease type
- Remission status at HCT: CR vs PR vs. resistant vs. untreated/unknown
- Disease risk index

Transplant-related:

- Conditioning regimen: MAC vs. NMA
- TBI dose in conditioning regimen (none vs. ≤450 cGy vs. >450 cGy)
- GVHD prophylaxis: Post- transplant Cy +/- calcineurin inhibitor
- Donor-recipient sex match: male-male vs. male-female vs. female-male vs. female-female vs. missing
- Donor-recipient CMV status: -/+ vs. others vs. missing
- Year of transplant: continuous
- Donor-recipient blood group ABO match (Matched, minor mismatch, major mismatched, not reported)
- Donor specific anti-HLA antibody (if available)
- Degree of match (Number of mismatches)

Statistical analysis:

This study aims at assessing the impact of TNC cell dose on outcome of haploidentical HSCT. Categorical variables were compared using the X^2 test. The probability of OS is calculated using the Kaplan-Meier estimator. The probabilities of neutrophil and platelet recovery, acute and chronic GVHD, non-relapse mortality and relapse were calculated using the cumulative incidence method. To study the association between clinical outcomes and TNC cell dose, Cox regression models is used for acute and chronic GVHD, NRM, relapse and OS. Results are expressed as hazard ratio (HR) together with the 95% confidence interval (CI).

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Title:
Optimal Stem Cell Dosing for Peripheral Blood Stem Cell Transplantation with Post-Transplant Cyclophosphamide

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Research hypothesis:
We hypothesize that infused CD34+ cell dose is an important predictor of post-transplant outcomes in the setting of allogeneic peripheral blood (PB) haploidentical donor hematopoietic cell transplant (Haplo-HCT) with post-transplant cyclophosphamide (PTCy).

Specific aims:
- Determine the impact of infused CD34+ cell dose on transplant outcomes following PB Haplo-HCT w/PTCy.
- Determine the impact of infused total nucleated cell (TNC) dose on transplant outcomes following PB Haplo-HCT w/PTCy.
- Determine the impact of infused CD3+ cell dose on transplant outcomes following PB Haplo-HCT w/PTCy.

Scientific impact:
Allogeneic PB Haplo-HCT w/PTCy is an increasingly utilized platform to expand the donor pool for patients requiring transplant. Though this platform was initially developed with bone marrow grafts, peripheral blood stem cell grafts are commonly substituted for potential improvements in engraftment and relapse due to the putative graft-versus-leukemia effect.[1]Prior studies have suggested that infused cell dose influences outcomes of bone marrow Haplo-HCT w/PTCy.[2] Thus, it is likely that infused cell dose may also impact outcomes following peripheral blood stem cell transplants (PBSCT) with PTCy. As cell dose is a modifiable variable, identifying the optimal cell dose would result in a feasible strategy to improve outcomes for patients receiving PB Haplo-HCT w/PTCy.

Scientific justification:
The administration of high doses of post-transplant cyclophosphamide (PTCy) has proven to be a potent intervention to control donor/recipient alloreactivity and allow for safe HCT even when using HLA disparate donors.[3] Multiple studies have shown that HLA haploidentical (haplo) HCT with PTCy results in low rates of graft-versus-host disease (GVHD), nonrelapse mortality (NRM), and comparable survival compared to outcomes with matched donor transplants.[3-7] However, rates of relapse may be higher with this HCT platform, particularly in the setting of diseases at high risk for relapse such as myeloid neoplasms.[7]
Optimization of the graft source is one strategy to potentially improve the efficacy of HCT with PTCy. McCurdy, et al. demonstrated that administration of higher total nucleated cell dose with bone marrow Haplo-HCT w/PTCy yields decreased relapse rates and improved progression- free survival (PFS) and overall survival (OS), without increased GVHD.[2] However, this study did not address the use of PB stem cell grafts with PTCy. A subsequent CIBMTR analysis demonstrated that using PB vs. bone marrow for Haplo-HCT w/PTCy may reduce relapse rates and improve PFS in high risk diseases, though does result in higher rates of GVHD.[1]

In light of these results, many institutions prefer PB as the graft source for Haplo-HCT w/PTCy. Published trials have set varying caps on infused doses, though no study has compared outcomes based on cell dose to identify the optimal dose cap.[8,9] Single institution data being presented at the 61st American Society of Hematology Annual Meeting suggests that patients who received <5 x 10^6 CD34+ cells/kg experienced inferior OS (HR=3.2, 95% CI 1.4-7.6, p=0.01) and NRM (HR=4.1, 95% CI 1.2-14.5, p=0.03).[10] Larger studies are warranted to confirm this finding.
Existing data suggests that infused cell dose per recipient weight is likely to impact outcomes of PB Haplo-HCT w/PTCy. Thus, we propose using CIBMTR data to identify the optimal infused CD34+ cell dose per recipient body mass to help improve survival outcomes in patients receiving Haplo-HCT w/PTCy.

Patient eligibility population:

- Adult patients (age ≥ 18) who received allogeneic related donor haploidentical (at least 2 antigen level HLA mismatch) T-cell replete PBSCT with PTCy for hematologic malignancy between 2000 and 2018 and reported to CIBMTR
- Patients who received T-dell depletion (either *ex vivo* or *in vivo*) will be excluded
- Graft type would be only PB

Data requirements:

Patient related variables:

- Age: continuous, divided by decade
- Gender: male vs. female
- Ethnicity: Caucasian vs. African American vs. Asian/Pacific Islander vs. Hispanic vs. Others vs. missing
- Race: Hispanic or Latino vs. Non-Hispanic or non-Latino vs. non-resident of the U.S.
- Functional status (KPS): < 90 vs. 90-100
- Hematopoietic cell transplant comorbidity index (HCT-CI)11: 0 vs. 1-2 vs. ?3

Disease related variables:

- BMT Disease Risk Index (DRI)12
- Disease status at time of HCT: CR, CRi, PR, SD, or PD for relevant diseases
- Lines of therapy prior to HCT (continuous)

BMT related variables:

- Conditioning regimen
- Conditioning intensity (myeloablative vs. reduced intensity/nonmyeloablative)
- Donor age: continuous divided by decade
- Donor gender: male vs. female
- Donor relationship: sibling, parent, grandparent, grandchildren, cousin, vs. others
- Graft cell dose (TNC, CD34+ cells, and CD3+ cells) per recipient body weight
- Donor/Recipient cytomegalovirus matching
- Donor/recipient ABO compatibility
- GVHD prophylactic regimen (including duration)
    - PTCY only vs. PTCY-TAC -based vs. PTCY-others
- Post-BMT maintenance therapy (if any)

Outcomes:

Overall survival (OS): Time from allogeneic HCT to death from any cause. Patients will be censored at the

time of last follow up.

Non-relapse mortality (NRM): Death due to any cause in the first 28 days or death due to conditions other than disease relapse or progression beyond 28 days. Events will be summarized by the cumulative incidence estimate with relapse as a competing risk.
Progression-free survival (PFS): Time from allogeneic HCT to death or relapse. Patients will be censored at the time of last follow up.
Relapse/progression: Development of relapse/progression as defined by the CIBMTR. The event will be summarized by the cumulative incidence estimate. NRM will be a competing risk for this outcome.
Acute GVHD: Time to development of grade II-IV acute GVHD using the Glucksberg grading system. The event will be summarized by the cumulative incidence estimate, where death and relapse without grade II-IV acute GVHD will be treated as a competing risk.
Chronic GVHD: Time to the development of limited or extensive chronic GVHD. The event will be summarized by the cumulative incidence estimate, where death without chronic GVHD will be treated as the competing risk. Patients will be censored at second transplant or date of last follow-up. This will have both univariate and multivariate analyses.
Acute and chronic GVHD, relapse-free survival (GRFS): Survival without acute grade III- IV GVHD plus chronic GVHD plus disease relapse or progression or death
Chronic GVHD, relapse-free survival (CRFS): Survival without development of chronic GVHD plus disease relapse or progression or death
Graft failure: Primary and secondary graft failure are considered as one outcome. Primary graft failure is defined as failure to achieve absolute neutrophil count (ANC) of 0.5 x 10^9/L or donor chimerism <5% in any compartment (T-cell chimerism ≤5%, unsorted blood or marrow chimerism). Secondary graft failure is defined as initial engraftment followed by graft loss evidenced by sustained drop in neutrophil recovery to less than 0.5 x 10^9/L or loss of donor chimerism to <5% in any compartment. Time to graft failure is the interval between date of chimerism/date of ANC decline/date of second infusion and date of transplant; patients who are engrafted (full donor or mixed) are censored at 12 months.

Cause of death: causes of death will be presented in a table

Cytokine release syndrome (non-infectious fevers)

Sample requirements:
N/A

Study design:
This is a retrospective data review of all patients who have undergone allogeneic haploidentical PBSCT with PTCy within the CIBMTR database. The main effect comparison will be infused CD34+ cell dose <5 x 10^6 CD34+ cells/kg versus ≥5 x 10^6 CD34+ cells/kg, though alternate cut points may be explored. Outcomes will also be compared based on the total nucleated cell dose and the CD3+ cell dose. Patient-, disease- and transplant- related factors will be compared among different CD34 cell dose groups using the Chi-square test for categorical variables and the Kruskal Wallis test for continuous variables. The primary endpoint is OS. Other endpoints of interest will include PFS, relapse rates, NRM, GVHD, and engraftment, which would all be calculated from the time of HCT. Survival endpoints will be calculated using the Kaplan-Meier method. Cumulative Incidences (CuI) of other endpoints including GVHD, relapse rates, and NRM will be determined. Univariate will be pursued to determine variables associated with outcomes. Cox proportional hazards regression will be used to compare the different CD34 cell dose group. The variables to be considered in the multivariate models are listed above. The assumption of proportional hazards for each factor in the Cox model will be tested using

time- dependent covariates. The proportionality assumptions will be further tested. A backward stepwise model selection approach will be used to identify all significant risk factors. Each step of model building will contain the main effect for CD34 cell dose. Factors which are significant at a 5% level will be kept in the final model. The potential interactions between main effect and all significant risk factors will be tested. Adjusted probabilities of PFS and OS, and adjusted cumulative incidence curves for competing risks endpoints will be generated from the final regression models stratified on disease type and weighted averages of covariate values using the pooled sample proportion as the weight function.

Non-CIBMTR data source:
None

Conflicts of interest:
None

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Characteristics of patients who underwent first haploidentical HCT with peripheral blood and post-transplant cyclophosphamide for lymphoma/leukemia and reported to CIBMTR. 2014-2018

Characteristic	N (%)
No. of patients	742
Patient age - no. (%)	
Median (min-max)	58 (18-78)
18-29 yrs	91 (12)
30-39 yrs	68 (9)
40-49 yrs	95 (13)
50-59 yrs	184 (25)
60-69 yrs	232 (31)
≥70 yrs	72 (10)
Disease - no. (%)	
AML	336 (45)
ALL	117 (16)
MDS	220 (30)
Non-Hodgkin lymphoma	62 (8)
Hodgkin lymphoma	7 (1)
Conditioning regimen intensity - no. (%)	
MAC	324 (44)
RIC/NMA	418 (56)
Year of transplant - no. (%)	
2013	26 (4)
2014	66 (9)
2015	107 (14)
2016	144 (19)
2017	177 (24)
2018	222 (30)
CD34 infused cells x 10^8/ weight - median (25^{th},75^{th} quartiles)*	5 (4, 7)
CD34 infused cells x 10^8/ ideal weight - median (25^{th},75^{th} quartiles)	6 (5, 8)
Follow-up - median (min-max)	24 (3-74)

*Missing for n=205 (not included in the table).
**CD3 information available for n=589 cases.