Not for publication or presentation

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A G E N D A
CIBMTR WORKING COMMITTEE FOR REGIMEN-RELATED TOXICITY AND SUPPORTIVE CARE
Orlando, FL
Saturday February 22, 2020, 12:15 – 2:15 pm

Co-Chair:	**Shin Mineishi, MD, Penn State Hershey Medical Center, Hershey, PA;**
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Co-Chair:	**Edward Stadtmauer, MD, University of Pennsylvania Medical Center**
	Telephone: 215-662-7910; E-mail: Edward.stadtmauer@uphs.upenn.edu
Co-Chair:	**Bipin Savani, MD; Vanderbilt University Medical Center;**
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1. **Introduction**
   a. Minutes and Overview Plan from February 2019 TCT meeting (Attachment 1)
   b. Introduction of incoming Co-Chair:
   Mohamed Sorror, MD, MSc; Fred Hutchinson Cancer Research Center;
   Email: msorror@fredhutch.org; Phone: (206) 667-6298

2. **Accrual summary** (Attachment 2)

3. **Presentations, published or submitted papers**
   a. **RT13-02** Sabloff M, Chhabra S, Wang T, Fretham C, Kekre N, Abraham A, Adekola K, Auletta JJ, Barker C, Beitinjaneh AM, Bredeson C, Cahn J-Y, Diaz MA, Freytes C, Gale RP, Ganguly S, Gergis U, Guinan E, Hamilton B, Hashmi S, Hematti P, Hildebrandt G, Holmberg L, Hong S, Lazarus HM, Martino R, Muffly L, Nishihori T, Perales M-A, Yared J, Mineishi S, Stadtmauer EA, Pasquini MC, Loren AW. *Comparison of high doses of total body irradiation in myeloablative conditioning prior to hematopoietic cell transplantation*. ***Biology of Blood and Marrow Transplantation: Journal of the American Society for Blood and Marrow Transplantation.*** doi:10.1016/j.bbmt.2019.08.012. Epub 2019 Aug 29.
   b. **RT14-01** Parikh SH, Satwani P, Ahn KW, Sahr NA, Fretham C, Abraham AA, Agrawal V, Auletta JJ, Abdel-Azim H, Copelan E, Diaz M-A, Dvorak CC, Frangoul HA, Freytes CO, Gadalla SM, Gale RP, George B, Gergis U, Hashmi S, Hematti P, Hildebrandt GC, Keating AK, Lazarus HM, Myers K, Olsson RF, Prestidge T, Rotz S, Savani BN, Shereck E, Williams KM, Wirk B, Pasquini MC, Loren AW. *Survival trends in infants undergoing allogeneic hematopoietic cell transplant.* ***Journal of the American Medical Association Pediatrics.*** doi:10.1001/jamapediatrics.2019.0081. Epub 2019 Mar 18. PMC6503511.

c. **RT14-02** Epperla N, Li A, Logan B, Fretham C, Chhabra S, Aljurf M, Chee L, Copelan E, Freytes CO, Hematti P, Lazarus HM, Litzow M, Nishihori T, Olsson RF, Prestidge T, Saber W, Wirk B, Yared JA, Loren A, Pasquini M. *Incidence, Risk Factors for and Outcomes of Transplant-Associated Thrombotic Microangiopathy*. ***British Journal of Haematology***. **In press.**

d. **RT14-03** Zinter MS, Logan BR, Fretham C, Sapru A, Abraham A, Aljurf MD, Arnold SD, Artz A, Auletta JJ, Chhabra S, Copelan E, Duncan C, Gale RP, Guinan E, Hematti P, Keating AK, Marks DI, Savani BN, Olsson R, Ustun C, Williams KM, Pasquini MC, Dvorak CC. *Comprehensive prognostication in critically ill pediatric hematopoietic cell transplant patients: Results from merging the Center for International Blood and Marrow Transplant Research (CIBMTR) and Virtual Pediatric Systems (VPS) Registries.* ***Biology of Blood and Marrow Transplantation.*** doi:10.1016/j.bbmt.2019.09.027. Epub 2019 Sep 26.

e. **RT17-01a** Dias A, Farhadfar N, Wang T, Fretham C, Murthy H, Logan B, Mineishi S, Savani B, Stadtmauer E, Chhabra S, Wingard JR, Ganguly S, Pasquini MC. *Impact of Renal Dysfunction Measured By Estimated Glomerular Filtration Rate (eGFR) on Outcomes after Allogeneic Hematopoietic Cell Transplantation (HCT)*. ***Presented at ASH, December 2019.***

f. **RT17-01b** Farhadfar N, Murthy H, Wang T, Fretham C, Dias A, Logan B, Mineishi S, Savani B, Stadtmauer E, Chhabra S, Ganguly S, Wingard JR, Pasquini MC. *Development of the Renal Adjusted Hematopoietic Cell Transplant Comorbidity Index (RA-HCT-CI) Using Different Levels of Renal Dysfunction According to Estimated Glomerular Filtration Rate (eGFR).* ***Presented at TCT, February 2020.***

g. **RT18-04** Broglie L, Fretham C, Al-Seraihy, George B, Kurtzberg J, Loren A, MacMillan M, Martinez C, Davies SM, Pasquini M. *Pulmonary complications in pediatric and adolescent patients following allogeneic hematopoietic cell transplantation.* ***Biology of Blood and Marrow Transplantation: Journal of the American Society for Blood and Marrow Transplantation.*** doi:10.1016/j.bbmt.2019.06.004. Epub 2019 Jun 12.

4. Studies in progress (Attachment 3)

a. **RT17-01** Allogeneic hematopoietic stem cell transplant outcome of patients with end stage renal disease on dialysis (N Farhadfar/A Dias/JR Wingard/H Murthy/S Ganguly) **Manuscript preparation**

b. **RT18-01** A Modified Hematopoietic Cell Transplantation (HCT) Risk Assessment Tool for Pediatric and Young Adult Patients Undergoing Allogeneic Transplantation**.** (B Friend/L Broglie/ G Schiller/M Thakar/M Sorror) **Analysis**

c. **RT18-02** The effect of obesity on outcomes after alternative donor stem cell transplants (M Abou-Ismail/G Ravi/L Metheny/M de Lima) **Datafile preparation**

d. **RT18-03** An Analysis of Non-Infectious Pulmonary Toxicities in Total Body Irradiation versus Chemotherapy-Based Conditioning Regimens after Allogeneic Hematopoietic Cell Transplantation for Hematologic Malignancies (S Patel/B Hamilton/N Majhail/C Ustun) **Datafile preparation**

e. **RT19-01** Analysis of comorbidity-associated toxicity at a regimen-based level (R Shouval/ B Savani/ A Nagler) **Protocol development**

f. **RT19-02** Hemorrhagic cystitis as a complication of hematopoietic stem cell transplantation in the post-transplant cyclophosphamide graft-versus-host disease prophylaxis era compared to other allogeneic stem cell transplants (K Adekola/ N Ali/ O Frankfurt/ L Metheny/ J Moreira/ M de Lima) **Protocol development**

5. Proposals

Future/proposed studies

a. **PROP 1911-167** CMV Serotype and Graft Failure (M Pamukcuoglu/ M Arora) (Attachment 4)

b. **PROP 1911-181** Significance of a prior cancer diagnosis as exclusion criteria in clinical trials among patients with Hematological malignancies undergoing hematopoietic stem cell transplant (HSCT) (A Kansagra/ S Hashmi/ B Savani/ M Hamadani/ S Devine) (Attachment 5)
c. **PROP 1911-198** Outcomes and safety of hematopoietic stem cell transplants from HTLV positive donors and HTLV positive recipients (M Janakiram/ G Okov) (Attachment 6)
d. **PROP 1911-234** Patterns of Veno-Occlusive Disease in Patients with AML and ALL in the era of Monoclonal Antibodies and Antibody Drug Conjugates (L Gowda/ M Byrne/ P Kebriaei/ D Porter) (Attachment 7)
f. **PROP 1911-46** The PTCY-CI and PTCY-CDRI: prognostic tools for the use of post-transplant cyclophosphamide based GVHD prophylaxis regimens in allogeneic stem cell transplants for malignant conditions (R Shapiro/ R Romee/ A Bashey) (Attachment 8)
g. **PROP 1911-60** Toxicities of Older Adults Receiving Allogeneic Hematopoietic Cell Transplant Compared to Younger Patients (R Jayani/ H Muff) (Attachment 9)

Dropped proposed studies

a. **PROP 1907-01** Validation of an Allogeneic Pre-Transplant Prognostic Score for Common Hematological Diseases in a Large CIBMTR Cohort and Comparison with Conventional Prognostic Scores (S Cyriac/ F Michelis) *Dropped due to low scientific impact*
b. **PROP 1908-03** Complications Post-Transplant in the Unrelated Setting with Patients Who Received Post-Transplant Cyclophosphamide Versus Those Who Received "Conventional" Transplants (J Wagner) *Dropped due to overlap with study SC15-03*
c. **PROP 1911-05** Allogeneic Hematopoietic Stem Cell Transplant in Patients with Prior History of Solid Organ Transplant (M Abdul-Hay/ A Samer Al-Homsi/ T Spitzer) *Dropped due to overlap with study LE12-03*
d. **PROP 1911-10** Risk Prediction of Post-Transplant Lymphoproliferative Disorder in Patients Undergoing Allogeneic Hematopoietic Cell Transplant (N Bhatt/ A Sharma) *Dropped due to low scientific impact*
e. **PROP 1911-106** Hemorrhage as cause of death post-transplant; Analysis of Bleeding Timelines and Risk Factors (L Gowda) *Dropped due to feasibility*
f. **PROP 1911-113** Risk Factors and Outcomes of Thrombotic Microangiopathy after Allogeneic Hematopoietic Stem Cell Transplantation: A CIBMTR study (A Qasrawi/ R Munker/ G Hildebrandt) *Dropped due to overlap with study RT14-02*
g. **PROP 1911-119** Machine Learning Approach to Estimate Toxicity Related Mortality Following Allogeneic Hematopoietic Cell Transplantation (A Mussetti/ V Moreno/ A Sureda) *Dropped due to overlap with study RT19-01*
h. **PROP 1911-147** Identification of Risk Factors Associated with Mortality Among Teenage Patients Undergoing HLA matched Allogeneic Hematopoietic Stem Cell Transplantation in the Contemporary Era (2008-18) (L Davis/ P Satwani/ L Broglie) *Dropped due to overlap with study RT18-01*
i. **PROP 1911-193** Impact of Cytokine release syndrome on survival in patients receiving Haplo-identical transplants (I Varadarajan) *Dropped due to feasibility*
j. **PROP 1911-220** Identifying patterns of Check Point Inhibitor Use and its Toxicities to Plan on Preparations Needed in Allogeneic Stem Cell Transplant Setting (L Gowda/ B Oran/ A Zeidan/ M Arora) *Dropped due to feasibility, small sample and short follow-up*
k. **PROP 1911-54** Immune Reconstitution After Hematopoietic Stem Cell Transplantation In Children With Chronic Kidney Disease (B Stotter/ S Bhatt/ K Barton) *Dropped due to feasibility, small sample with low scientific impact*

l. **PROP 1911-69** Oral Complications of Hematopoietic Stem Cell Transplantation in Malignant and Non-Malignant Diseases: Evidence based review (P Prasad/ S Fournier) *Dropped due to feasibility*

m. **PROP 1911-99** Risk factors and impact of fludarabine-related neuro-toxicity in allogeneic hematopoietic cell transplantation (H Murthy/ N Farhadfar/ J Wingard) *Dropped due to feasibility*

o. **PROP 1911-12** Comparing reduced toxicity conditioning allogeneic hematopoietic cell transplantation in older and unfit patients: Flu/Mel140 vs. Flu/Bu (A Kanate/ M Hamadani) *Dropped due to overlap with studies LK16-01 and RT19-01*

p. **PROP 1911-163** Impact of anti-thymocyte globulin on the outcomes of patients undergoing T cell replete haploidentical hematopoietic cell transplantation with post-transplant cyclophosphamide (B Dholaria/ B Savani) *Dropped due to low sample size*

e. **PROP 1911-249** Very Early Death After Stem Cell Transplant: Risk factors and Causes of Death (R Cook/ R Maziarz) *Dropped due to low sample size*

6. Other business

Biorepository Accruals (Attachment 10)

MINUTES AND OVERVIEW PLAN
CIBMTR WORKING COMMITTEE FOR REGIMEN-RELATED TOXICITY AND SUPPORTIVE CARE
Houston, TX
Thursday, February 21, 2019, 12:15 – 2:15 pm

Co-Chair:	**Alison Loren, MD, MSCE, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA; Telephone: 215-615-3138; E-mail: alison.loren@uphs.upenn.edu**
Co-Chair:	**Shin Mineishi, MD, Penn State Hershey Medical Center, Hershey, PA; Telephone: 717-531-0003; E-mail: smineishi@pennstatehealth.psu.edu**
Co-Chair:	**Edward Stadtmauer, MD, University of Pennsylvania Medical Center Telephone: 215-662-7910; E-mail: Edward.stadtmauer@uphs.upenn.edu**
Scientific Director:	**Marcelo C. Pasquini, MD, MS, CIBMTR Statistical Center, Milwaukee, WI; Telephone: 414-805-0700; E-mail: mpasquini@mcw.edu**
Statistical Director:	**Brent Logan, PhD, CIBMTR Statistical Center, Milwaukee, WI; Telephone: 414-456-8849; E-mail: blogan@mcw.edu**
Statistician:	**Caitrin Fretham, MPH, CIBMTR Statistical Center/NMDP, Minneapolis, MN; Telephone: 763-406-4126; E-mail: cfretha3@nmdp.org**

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1. **Introduction**

   Dr. Stadtmauer announced the CIBMTR Regimen-Related Toxicity and Supportive Care Committee (RRTWC) meeting started at 12:15pm on Thursday, February 21, 2019. He introduced the RRTWC leadership, the incoming and outgoing chairs, the goals, areas of focus and limitations of the RRTWC. He then introduced Marcelo up to the podium to continue.

2. **Accrual summary** (Attachment 2)

   The accrual summary was not presented in order to provide more time for the discussion of RT studies that are ongoing, published in the last year, and of the potential proposed studies to be presented at the meeting.

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

   Marcelo gave a brief overview of the studies published and submitted within the past year. Many studies were moved forward and publish or submitted. He also stated there is a wide variety of journals we are submitting to instead of staying only to BBMT. He believes it is good we are expanding our horizons.

   a. **RT07-01b** Broglie L, Thakar M, Logan B, Artz A, Jacobsohn D, Bunin N, Burroughs L, Martinez C, Nelson A, Woolfrey A, Pasquini M, Sorror, M. *Evaluation of the Hematopoietic Cell Comorbidity Index (HCT-CI) in Recipients of Allogeneic Transplantation for Non-Malignant Diseases.* ***European Society for Blood and Marrow Transplantation Annual Meeting, Lisbon, Portugal, March 2018.***

   b. **RT07-01b** Thakar M, Broglie L, Logan B, Artz A, Bunin N, Burroughs LM, Fretham C, Jacobsohn DA, Loren AW, Kurtzberg J, Martinez CA, Mineishi S, Nelson AS, Woolfrey A, Pasquini MC, Sorror ML. *The Hematopoietic Cell Transplant Comorbidity Index predicts survival after*

allogeneic transplant for non-malignant diseases. ***Blood.*** doi:10.1182/blood-2018-09-876284. Epub 2018 Dec 13.

c. **RT09-04b/IB09-06** Wang J, Clay-Gilmour A, Karaesman E, Rizvi A, Zhu Q, Yan L, Preus L, Liu S, Stram D, Pooler L, Sheng X, Haiman C, Van Den Berg D, Webb A, Brock G, Spellman S, Pasquini M, McCarthy P, Allen J, Onel K, Hahn T, Sucheston-Campbell L. *Genome wide association analyses identify pleiotropic variants associated with Acute Myeloid Leukemia (AML) and Myelodysplastic Syndrome (MDS) susceptibility.* ***American Society of Hematology Annual Meeting, San Diego, CA, December 2018.***

d. **RT09-04b/IB09-06** Zhu Q, Yan L, Liu Q, Zhang C, Wei L, Hu Q, Preus L, Clay-Gilmour AI, Onel K, Stram DO, Pooler L, Sheng X, Haiman CA, Zhu X, Spellman SR, Pasquini M, McCarthy PL, Liu S, Hahn T, Sucheston-Campbell LE. *Exome chip analyses identify genes affecting mortality after HLA-matched unrelated-donor blood and marrow transplantation.* ***Blood. 2018 May 31; 131(22):2490-2499.*** doi:10.1182/blood-2017-11-817973. Epub 2018 Apr 2. PMC5981168.

e. **RT14-01** Parikh S, Satwani P, Ahn KW, Sahr NA, Fretham C, Abraham A, Agrawal V, Auletta J, Abdel-Azim H, Copelan E, Diaz MA, Dvorak C, Frangoul H, Freytes C, Gadalla SM, Gale RP, George B, Gergis U, Hashmi S, Hematti P, Hildebrandt G, Keating A, Lazarus HM, Myers K, Olsson R, Prestidge T, Rotz S, Savani B, Shereck EB, Williams K, Wirk B, Pasquini MC. *Survival Trends in Infants Undergoing Allogeneic Hematopoietic Cell Transplantation.* ***Journal of the American Medical Association – Pediatrics. Submitted January 2019 – pending decision.***

f. **RT14-03** Zinter MS, Logan BR, Fretham C, Sapru A, Abraham A, Aljurf MD, Arnold SD, Artz A, Auletta JJ, Chhabra S, Copelan E, Duncan C, Gale RP, Guinan E, Hematti P, Keating AK, Marks DI, Savani BN, Olsson R, Ustun C, Williams KM, Pasquini MC, Dvorak CC. *Optimizing Mortality Prognositcation for Critically Ill Pediatric Allogeneic Hematopoietic Cell Transplant Patients: Results from a Center for International Blood and Marrow Transplant Research (CIBMTR) and Virtual Pediatric Systems (VPS) Database Merger.* ***Intensive Care Medicine. Submitted January 2019 – pending decision.***

g. **RT15-01** Harris AC, Boelens JJ, Ahn KW, Fei M, Abraham A, Artz A, Dvorak C, Frangoul H, Freytes C, Gale RP, Hong S, Lazarus HM, Loren A, Mineishi S, Nishihori T, O'Brien T, Williams K, Pasquini MC, Levine JE. *Comparison of pediatric allogeneic transplant outcomes using myeloablative busulfan with cyclophosphamide or fludarabine.* ***Blood Advances. 2018 Jun 12; 2(11):1198-1206.*** doi:10.1182/bloodadvances.2018016956. Epub 2018 May 29. PMC5998928.

h. **RT15-02** McCune JS, Wang T, Bo-Subait K, Mahmoud A, Beitinjaneh A, Bubalo J, Cahn J-Y, Cerny J, Chhabra S, Cumpston A, Dupuis LL, Lazarus HM, Marks DI, Maziarz RT, Norkin M, Prestidge T, Mineishi S, Pasquini MC, Martin PJ. *Association of antiepileptic medications with outcomes after allogeneic hematopoietic cell transplantation with busulfan/cyclophosphamide conditioning.* ***Biology of Blood and Marrow Transplantation. Submitted November 2018 – pending decision.***

i. **RT16-01** Brunstein CG, Pasquini MC, Kim S, Fei M, Adekola K, Ahmed I, Aljurf M, Agrawal V, Auletta JJ, Battiwalla M, Bejanyan N, Bubalo J, Cerny J, Chee L, Ciurea S, Freytes C, Gadalla SM, Gale RP, Ganguly S, Hashmi SK, Hematti P, Hildebrandt G, Holmberg L, Lahoud OB, Landau H, Lazarus HM, de Lima M, Mathews V, Maziarz R, Nishihori T, Norkin M, Olsson R, Reshef R, Rotz S, Savani B, Schouten HC, Seo S, Wirk BM, Yared J, Mineishi S, Rogosheske J, Perales M-A. *The effect of conditioning regimen dose reduction in obese patients undergoing autologous hematopoietic cell transplantation.* ***Biology of Blood and Marrow Transplantation.*** doi:10.1016/j.bbmt.2018.11.005. Epub 2018 Nov 10.

4. Studies in progress (Attachment 3)

Marcelo presented the studies in progress. A few studies from many years back are being prioritized to finish this year. The rest of the studies are fairly new and are on schedule with their

current goals. The goal is to make sure studies stay on two-year timeline from here on out, with the goal to have a study presented at ASH, TCT, or another relevant meeting within one year of their inception.

Marcelo also brought up the issue of authorship and discussed that it is very important for writing committee members to contribute to these studies, but many participate and we only include authors who provide the utmost thought and work towards the protocol, analysis interpretation and manuscript.

a. **RT13-02** Safety of high-dose total body irradiation followed by an allogeneic hematopoietic cell transplant for hematologic malignancies (M Sabloff) **Manuscript preparation**
b. **RT14-01** Trends and risk factors for infant mortality following allogeneic hematopoietic cell transplant: Case-Control study (P Satwani/S Parikh) **Submitted**
c. **RT14-02** Endothelial injury complications after allogeneic hematopoietic cell transplantation (N Epperla/A Li) **Manuscript preparation**
d. **RT14-03** Multicenter cohort identification of transplant-related risk-factors for infection, organ failure, and mortality among pediatric hematopoietic stem cell transplant patients requiring intensive care unit admission (C Dvorak/M Zinter/A Sapru) **Submitted**
e. **RT15-02** Association of anti-epileptic medication with outcomes after conditioning with targeted busulfan followed by cyclophosphamide before allogeneic hematopoietic cell transplantation (PJ Martin/JS McCune) **Submitted**
f. **RT17-01** Allogeneic hematopoietic stem cell transplant outcome of patients with end stage renal disease on dialysis (N Farhadfar/JR Wingard/H Murthy/S Ganguly) **Data file preparation**
g. **RT18-01** A Modified Hematopoietic Cell Transplantation (HCT) Risk Assessment Tool for Pediatric and Young Adult Patients Undergoing Allogeneic Transplantation**.** (B Friend/L Broglie/G Schiller/M Thakar/M Sorror) **Protocol development**
h. **RT18-02** The effect of obesity on outcomes after alternative donor stem cell transplants (M Abou-Ismail/G Ravi/L Metheny/M de Lima) **Protocol development**
i. **RT18-03** An Analysis of Non-Infectious Pulmonary Toxicities in Total Body Irradiation versus Chemotherapy-Based Conditioning Regimens after Allogeneic Hematopoietic Cell Transplantation for Hematologic Malignancies (S Patel/B Hamilton/N Majhail/C Ustun) **Protocol development**
j. **RT18-04** Pulmonary Complications in Pediatric Patients after Allogeneic Hematopoietic Cell Transplantation (L Broglie) **Manuscript preparation**

5. Proposals

Future/proposed studies

Marcelo provided the information on the proposals for the year. There were 11 total proposals for the RRTWC. Four were combined into two, and three were dropped due to feasibility or overlap with current studies, which left six proposals to be presented at the meeting. The proposal themes were trends in NRM, toxicity, comorbidities, and conditioning regimens.

Marcelo reminded the audience about the importance of voting and voting highest on those that would impact a clinician's ability to treat patients.

a. **PROP 1811-45** Risk factor analysis for early vs intermediate vs late non-relapse mortality (M Battiwalla) (Attachment 4)

Dr. Loren introduced Dr. Battiwalla. The hypothesis is that risk factors differentially impact early (<1 year) versus intermediate (1-3 years) versus late (>3 years) non-relapse mortality (NRM) following alloHCT. The study aims to 1) evaluate the different clinical risk factors that

predict early (<1 year) versus intermediate (1-3 years) versus delayed (>3 years) non-relapse mortality; and 2) understand which phase of NRM (early versus intermediate versus late) has most improved over recent years.

During the discussion, one attendee brought up why the study will restrict only to hematologic malignancies and why not to open up to other malignancies and also non-malignant diseases. Dr. Battiwalla responded that he is willing to expand the population. Another attendee mentioned looking at NRM at 30 days or less as this is a quality marker and has other implications. Dr. Battiwalla responded that he agrees and is interested in finding the right cutoff for time. Another attendee asked how we plan to account for the increasing number of patients with high numbers of comorbidities being transplanted and this effect on relapse and NRM. Dr. Battiwalla responded that he wants to consider HCT-CI as a variable in the model to account for this. Dr. Mineishi asked Dr. Battiwalla what he wants to do with this data if he has already found the factors associated with the three levels of NRM. Dr. Battiwalla said many are validated risk factors, but would like to explore this with larger data and exploring this outcome with a more time-dependent approach.

b. **PROP 1811-124** Second allogeneic hematopoietic cell transplantation for primary graft failure: effect of conditioning regimen, graft source and GVHD prophylaxis on outcome (S Prem/R Kumar/M Mahapatra) (Attachment 5)

Dr. Mineishi introduced Dr. Prem up to the podium. Dr. Prem introduced the study and stated the hypothesis is that the success of the second alloHCT for primary graft failure is influenced by conditioning regimen, GVHD prophylaxis, graft source, cell dose, disease, and other patient and transplant related factors. The study aims are to 1) study the effect of conditioning regimen on outcome of second hematopoietic cell transplantation (HCT) for primary graft failure; and 2) assess impact of GVHD prophylaxis regimen, primary disease, and stem cell source in outcomes after second HCT for primary graft failure.

During the discussion, one attendee asked if it is possible to clarify if the graft failure was caused by becoming aplastic or no autologous recovery. Dr. Prem mentioned that although this data would be helpful that it may not be available. Another attendee asked if we have data on time from graft failure to second transplant, as this would be important to consider. He also mentioned that GVHD prophylaxis and conditioning should be considered. Marcelo responded describing the way that graft failure is captured on CIBMTR forms and that we do not capture dates for this as some may never engraft and therefore we cannot capture a date. Dr. Mineishi asked if we should consider the chimerism data for this. Dr. Prem mentioned that for primary graft failure this will not be as applicable or needed for this study. Dr. Stadtmauer mentioned that the median age is showing a very young population and there is likely bimodal ages here with one younger group and one older group. If accepted, it should be considered. He is also interested in knowing the graft failure rate for this population. Dr. Prem mentioned it was 6.7% in the previous study, although that cohort was only myeloablative regimens.

c. **1811-160** Exploring Ensemble Machine Learning Methods to Better Predict Veno-Occlusive Disease Following Allogeneic Hematopoietic Stem Cell Transplantation (D Shyr/C Lee/ S Brewer) (Attachment 6)

Dr. Stadtmauer introduced Dr. Shyr to the stage for the presentation. The study hypothesizes that machine learning methods can be used to make robust predictions of VOD in patients receiving alloHCT prior to the clinical diagnosis of VOD. The proposed study aims to determine if ensemble machine (decision tree ensembles) learning methods to predict VOD is feasible.

During the discussion, Dr. Stadtmauer asked for clarification if machine learning is an algorithm and if we would need funding to utilize a method for this. Dr. Shyr clarified that no funding is needed and these methods are readily available in statistical programs as statistical packages that are open to the public. He also said this study is more of a data and statistical methods experiment. Another attendee asked if there is plan to validate this updated risk assessment for VOD. Dr. Shyr explained that he plans to validate by partitioning the original dataset into training and validations cohorts. Another attendee asked Dr. Shyr what a clinician could do with this type of analysis and how that would change practice. Marcelo followed up with Dr. Artz's question and asked how this study is different from the previous VOD risk score study. Dr. Shyr mentioned that he does not want to replace the old VOD risk score but rather improve upon the previous version. Another attendee mentioned his concern that the event rate is very low to generate a robust model with so few events and also asked if it is possible to sample patients overtime and collect data prospectively instead of retrospectively as VOD is ever changing. Dr. Shyr mentioned that this analysis has already been done so we can only build upon what we have already done and also agreed that we would have more information if we collected prospectively but is limited to the data that is provided.

d. **PROP 1811-189** Analysis of Comorbidity associated Toxicity at a Regimen based Level (R Shouval/B Savani/A Nagler) (Attachment 7)

Dr. Loren introduced Dr. Shouval to the stage to present. The study hypothesizes that the hazard of comorbidities is exerted in a regimen-specific manner. The aims of this study are to 1) evaluate the non-relapse mortality (NRM) hazard (primary outcome) associated with pre-transplantation comorbidities in predefined conditioning regimens; and 2) evaluate NRM hazard associated with pre-transplantation comorbidities in conditioning intensity categories (non-myeloablative, reduced intensity conditioning, myeloablative conditioning) and 3) explore toxicities associated with specific conditioning regimen stratified by preexisting comorbidities.

During the discussion, one attendee mentioned that they think it would be best to only include years 2008 and beyond due to comorbidity data only being available on forms starting in 2008. He also mentioned that it might be important to look at NRM at different time points such as occurring before or after 1-year post transplant. Dr. Shouval mentioned that he does not want to look at HCT-CI but rather separate comorbidities because HCT-CI has already been assessed with conditioning regimen in previous validation study. Dr. Shouval also responded that he is more interested in the later effects of NRM rather than immediate NRM events related to these risk factors. Marcelo mentioned that there is some overlap with this proposal and a current study. He said we would need to restrict to age 40 and older as well. Dr. Mineishi asked about what he plans to do with the population that receives post-transplant cyclophosphamide. Dr. Shouval said he would be willing to remove these patients and haplos if needed.

e. **PROP 1811-35/1811-167** Outcomes of Patients with Inflammatory Bowel Disease After Hematopoietic Cell Transplantation (D Faleck/K Boughan/M Scordo/MA Perales/L Cohen) (Attachment 8)

Dr. Mineishi introduced Dr. Boughan to the podium to present the next proposal. The study hypothesizes that outcomes after alloHCT and autoHCT will be similar among patients with IBD as compared to matched controls. The aims of the study are to 1) compare overall outcomes

including adverse events, incidence of graft-versus-host disease (GVHD), non-relapse mortality (NRM), relapse, progression-free (PFS) and overall survival (OS) between patients with and without IBD undergoing HCT; and 2) Determine the impact of HCT on IBD activity and outcomes, including clinical and endoscopic response and the need for immunosuppressive therapy, hospitalization, and surgery post-HCT.

During the discussion, Dr. Stadtmauer if this would be considered a non-inferiority analysis and if this population would be feasible for this. Dr. Logan responded that there is large enough sample size that we can do a non-inferiority analysis here. Dr. Pasquini clarified that on the forms, we capture history of IBD in the comorbidities section but not current or active IBD at transplant. He also mentioned that we have no follow-up data on IBD outcomes post-transplant. Dr. Mineishi asked about if the Dr. Boughan anticipated any confusion regarding gut GVHD and if this would be related to active IBD at transplant. Dr. Pasquini mentioned that we could take a sample of the IBD cases and ask centers for more data on this data to see if patients with active IBD have higher probability of gut GVHD. Dr. Loren mentioned that we could also due a case-control type method where we only sample from centers with highest IBD reporting. Dr. Stadtmauer asked how often patients with active IBD are transplant and Dr. Boughan responded that it happens often enough to be interested in exploring.

f. **PROP 1811-85/1811-159** Hemorrhagic Cystitis as a Complication of Hematopoietic Stem Cell Transplantation in the Post-Transplant Cyclophosphamide Graft-Versus-Host Disease Prophylaxis Era compared to other Allogeneic Stem Cell Transplants (K Adekola/N Ali/O Frankfurt/L Metheny/J Moreira/M de Lima) (Attachment 9)

Dr. Stadtmauer introduced Dr. Ali to the podium to present. This study hypothesizes that the inclusion of post-CY as GVHD prophylaxis for patients getting haplo-HCT as well as non-haplo-SCT results in an increase in HC/ BK nephropathy. The study's primary aim is to determine the incidence of HC and BK nephropathy in patients who received post-Cy as part of GVHD prophylaxis regimen versus those who did not.

During the discussion, Dr. Stadtmauer asked if the plan is to look at HC and BK as a combined endpoint or separately. Dr. Pasquini said that BK nephropathy is not easily collected and is not necessarily collected as a part of hemorrhagic cystitis (HC) questions. We could look at incidence of HC and covariates associated with development and see if BK virus is a factor that contributes to the model. We also do not collected severity or grading for HC. One attendee commented that BK nephropathy is not relevant anymore and does not recommend analyzing these variables. He also recommended looking at engraftment kinetics as part of the model and as outcomes. Dr. Ali agreed with the attendee regarding engraftment.

Dropped proposed studies

a. **PROP 1811-21** Thrombopoietic agents in SCT and effect on outcomes (S Farhan/N Janakiraman/E Peres/J Emole) *Dropped due to feasibility of supplemental data collection.*
b. **PROP 1811-129** Transplant associated thrombotic microangiopathy (TA-TMA): Outcomes and late toxicities (M Schoettler/C Duncan) *Dropped due to overlap with current RRTWC study RT14-02.*
c. **PROP 1811-161** Metabolic health: Effect of donor and recipient BMI on post-transplant outcomes (N Chandhok/L Gowda/A Zeidan/R Perry/T Prebet) *Dropped due to overlap with current RRTWC study RT18-02.*

6. Other business

Dr. Stadtmauer adjourned the meeting and thanked all for attending. He reminded everyone the important of voting and asked all to consider thoughtful responses during voting.

Dr. Pasquini also mentioned that the pre-TED's next revision was just finished and there are some edits to both the comorbidities and regimen sections that will be impactful to our future studies and recommends everyone to review these for future meetings.

Biorepository Accruals (Attachment 10)

Study Proposal Acceptance:

Prior to meeting the CIMBTR Advisory Committee released recommendations for each committee with the numbers of proposals allowed to proceed as accepted CIBMTR WC studies. The RRTWC was recommended to accept no more than three studies, given the number of studies in progress and the statistical hours allocated to the committee. The RRTWC leadership has decided they will accept two studies: RT19-01 (proposal #1811-189) and RT19-02 (proposal #1811-85/1811-159). These were accepted based on voting scores, scientific impact in the TCT community and feasibility.

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 6/30/2019	Hours allocated 7/1/2019-6/30/2020	Total Hours allocated
RT13-02: Safety of high-dose TBI followed by alloHCT for hematologic malignancies.	Manuscript preparation	Submission to BBMT by March 2019	20	20	20	5	**25**
RT14-01: Trends and risk factors for infant mortality following allogeneic hematopoietic cell transplant: a case-control study.	Submitted	Published by July 2019	0	0	0	0	**0**
RT14-02: Endothelial injury complications after alloHCT.	Manuscript preparation	Submission to BBMT by April 2019	70	70	70	5	**75**
RT14-03: Multicenter cohort identification of transplant-related risk factors for infection, organ failure, and mortality among pediatric alloHCT patients requiring PICU admission.	Submitted	Published by July 2019	10	10	10	5	**15**
RT15-02: Association of anti-epileptic medication with outcomes after conditioning with targeted busulfan	Submitted	Published by July 2019	10	10	10	5	**15**

followed by cyclophosphamide before alloHCT.							
RT17-01: AlloHCT outcome of patients with end stage renal disease on dialysis.	Data file preparation	Analysis by March 2019	160	30	90	70	**160**
RT18-01: A modified HCT risk assessment tool for pediatric and young adult patients undergoing alloHCT.	Protocol development	Data file preparation by March 2019.	250	20	50	180	**230**
RT18-02: The effect of obesity on outcomes after alternative donor stem cell transplants.	Protocol development	Data file preparation by July 2019.	310	100	60	180	**240**
RT18-03: An analysis of non-infectious pulmonary toxicities in regards to conditioning regimens, graft source and early vs. delayed engraftment.	Protocol development	Data file preparation by July 2019.	310	100	60	180	**240**
RT19-01: Analysis of comorbidity-associated toxicity at a regimen based level.	Protocol pending	Data file preparation by July 2020	330	0	100	230	**330**
RT19-02: Hemorrhagic cystitis as a complication of HCT in the Pt-Cy GVHD prophylaxis era compared to other alloHCTs.	Protocol pending	Data file preparation by July 2020	330	0	100	230	**330**

Oversight Assignments for Working Committee Leadership (March 2019)

Shin Mineishi	**RT13-02**: Safety of high-dose TBI followed by alloHCT for hematologic malignancies.
	RT18-03: An analysis of non-infectious pulmonary toxicities in regards to conditioning regimens, graft source and early vs. delayed engraftment.
Edward Stadtmauer	**RT14-02:** Endothelial injury complications after alloHCT.
	RT18-02: The effect of obesity on outcomes after alternative donor stem cell transplants.
Bipin Savani	**RT19-01: A**nalysis of comorbidity-associated toxicity at a regimen based level.
	RT19-02: Hemorrhagic cystitis as a complication of HCT in the Pt-Cy GVHD prophylaxis era compared to other alloHCTs.
Marcelo Pasquini	**RT17-01:** AlloHCT outcome of patients with end stage renal disease on dialysis.
	RT18-01: A modified HCT risk assessment tool for pediatric and young adult patients undergoing alloHCT.

Accrual Summary for the Regimen-Related Toxicity and Supportive Care Working Committee

Characteristics of recipients of autologous transplant reported to the CIBMTR between 2000 and 2019 in research retrieval

Characteristic	N (%)
Number of patients	25502
Number of centers	356
Age, median (range), years	56 (0-83)
Sex	
Male	15061 (59)
Female	10441 (41)
Disease	
AML	770 (3)
ALL	70 (<1)
Other leukemia	43 (<1)
CML	13 (<1)
MDS/MPN	41 (<1)
Non-Hodgkin lymphoma	6438 (25)
Hodgkin lymphoma	2270 (9)
PCD/MM	13795 (54)
Other Malignancies	1894 (7)
SAA	5 (<1)
Inherited abnormalities of erythrocyte differentiation or function	5 (<1)
SCID and other immune system disorders	41 (<1)
Inherited disorders of metabolism	2 (<1)
Histiocytic disorders	2 (<1)
Autoimmune Diseases	103 (<1)
Other	10 (<1)
HCT-CI	
0	5376 (21)
1	2089 (8)
2	2293 (9)
3+	5526 (22)
Not Reported	166 (1)
NA, pre-TED not completed before 2008	10052 (43)
IPn or ARDS/IPS	
No	23329 (92)
Yes	1169 (5)
Not Reported	1004 (4)
Bronchiolitis obliterans	
No	24287 (95)
Yes	154 (1)

Characteristic	N (%)
Not Reported	1061 (4)
Pulmonary hemorrhage	
No	23770 (93)
Yes	140 (1)
Not Reported	1592 (6)
Cryptogenic organizing pneumonia	
No	23200 (91)
Yes	43 (<1)
Not Reported	2259 (9)
VOD/SOS	
No	24314 (95)
Yes	182 (1)
Not Reported	1006 (4)
TMA	
No	24268 (95)
Yes	193 (1)
Not Reported	1041 (4)
Renal failure severe enough to warrant dialysis	
No	23182 (91)
Yes	1235 (5)
Not Reported	1085 (4)
Year of transplant	
2000-2003	4562 (18)
2004-2007	5801 (23)
2008-2011	4602 (18)
2012-2015	5009 (20)
2016-2019	5528 (22)

Characteristics of recipients of allogeneic transplant reported to the CIBMTR between 2000 and 2019 in research retrieval

Characteristic	N (%)
Number of patients	66464
Number of centers	431
Age, median (range), years	42 (0-88)
Sex	
Male	39143 (59)
Female	27321 (41)
Disease	
AML	20260 (31)
ALL	9389 (14)
Other leukemia	1761 (3)
CML	4068 (6)
MDS/MPN	11576 (17)
Non-Hodgkin lymphoma	5542 (8)
Hodgkin lymphoma	1259 (2)
PCD/MM	1496 (2)
Other Malignancies	377 (1)
SAA	3542 (5)
Inherited abnormalities of erythrocyte differentiation or function	3194 (5)
SCID and other immune system disorders	2142 (3)
Inherited abnormalities of platelets	90 (<1)
Inherited disorders of metabolism	1027 (2)
Histiocytic disorders	612 (1)
Autoimmune Diseases	44 (<1)
Other	85 (<1)
HCT-CI	
0	13479 (20)
1	4738 (7)
2	4017 (6)
3+	12643 (19)
Not Reported	840 (1)
NA, pre-TED not completed before 2008	30747 (46)
IPn or ARDS/IPS	
No	56248 (85)
Yes	8482 (13)
Not Reported	1734 (3)
Bronchiolitis obliterans	
No	62231 (94)
Yes	1898 (3)

Characteristic	N (%)
Not Reported	2335 (4)
Pulmonary hemorrhage	
No	54946 (83)
Yes	1534 (2)
Not Reported	9984 (15)
Cryptogenic organizing pneumonia	
No	53120 (80)
Yes	338 (1)
Not Reported	13006 (20)
VOD/SOS	
No	60429 (91)
Yes	3490 (5)
Not Reported	2545 (4)
TMA	
No	61528 (93)
Yes	2087 (3)
Not Reported	2849 (4)
Renal failure severe enough to warrant dialysis	
No	57244 (86)
Yes	6285 (10)
Not Reported	2935 (4)
Hemorrhagic cystitis	
No	58415 (88)
Yes	3837 (6)
Not Reported	4212 (6)
Year of transplant	
2000-2003	14556 (22)
2004-2007	16549 (25)
2008-2011	11693 (18)
2012-2015	12660 (19)
2016-2019	11006 (17)

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CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH

TO: Regimen-Related Toxicity and Supportive Care Working Committee Members

FROM: Marcelo C. Pasquini, MD, MS and Saurabh Chhabra, MD, MS; Scientific Directors for the Regimen-Related Toxicity and Supportive Care Working Committee

RE: Studies in Progress Summary

RT17-01: Allogeneic hematopoietic stem cell transplant outcome of patients with end stage renal disease on dialysis (N Farhadfar/JR Wingard/H Murthy) The primary objectives of this study are to: 1) evaluate the impact of renal function measured by estimated glomerular filtration rate (eGFR) on allo-HCT transplant outcomes; 2) describe the characteristics and outcomes of patients on renal replacement therapy at the time of allo-HCT; and 3) explore the utilization of degrees of renal dysfunction based on eGFR to optimize the HCT-Comorbidity Index (HCT-CI). The results will be presented at the 2020 TCT Meetings in Feb 2020 in Orlando, FL. The study is in manuscript preparation with the goal to move to submit by April 2020.

RT18-01: A Modified Hematopoietic Cell Transplantation (HCT) Risk Assessment Tool for Pediatric and Young Adult Patients Undergoing Allogeneic Transplantation (L Broglie/B Friend/G Schiller/M Thakar/M Sorror) The study aims to: 1) describe the frequency of the HCT-CI defining comorbidities and other health related biomarkers in pediatric and young adult patients and analyze the effect of each on overall survival (for non-malignant diseases) and non-relapse mortality (for malignant diseases) in pediatric and young adult patients; 2) create a broader risk score for pediatric and young adult patients using only weighted pre-HCT comorbidities and biomarkers that are shown to affect outcomes; 3) compare the new risk score to the standard HCT-CI in each population. The study results were presented at the 61st Annual ASH Meeting in Dec 2019 in Orlando, FL. The study is in analysis with the goal to move to submit manuscript by May 2020.

RT18-02: The effect of obesity on outcomes after alternative donor stem cell transplants (M Yazan Abou-Ismail/G Ravi/L Metheny/M de Lima) The study aims to: 1) investigate the difference in non-relapse mortality risk related and overall survival to obesity (as measured by BMI, weight, and body surface area) between patients who underwent MUD or MRD transplants, haploidentical transplants, and umbilical cord transplants; 2) determine impact of BMI, weight, and body surface area on NRM, OS, RFS, engraftment rates, aGVHD and cGVHD rates after alternative stem cell transplant. The study is currently in data file preparation with goal to move to manuscript preparation by July 2020.

RT18-03: An analysis of non-infectious pulmonary toxicities in regards to conditioning regimens, graft source and early vs. delayed engraftment (S Patel/B Hamilton/N Majhail/C Ustun) The study aims to 1) assess the incidence and risk factors of non-infectious pulmonary toxicities over time, specifically investigating conditioning regimen and intensity, and graft source; 2) evaluate the impact non-infectious pulmonary toxicity on non-relapse mortality (NRM) and overall survival (OS); 3) assess the presence of concurrent infection(s) with BOS, COP, DAH, or IPS and how this influences NRM or OS. The study is in data file preparation with the goal to move to manuscript preparation by May 2020.

RT 19-01: Analysis of comorbidity-associated toxicity at a regimen-based level (R Shouval/ B Savani/ A Nagler). The study aims to 1) evaluate the comorbidity-specific risk of non-relapse mortality and overall mortality within patients receiving pre-defined conditioning regimens, and 2) within patients stratified by conditioning intensity groups (myeloablative, reduced-intensity, and non-myeloablative, and 3) explore toxicities associated with specific conditioning regimen stratified by preexisting comorbidities. The protocol has been finalized, and the goal to move to analysis by July 2020.

RT 19-02: Hemorrhagic cystitis (HC) as a complication of hematopoietic cell transplantation with post-transplant cyclophosphamide (PTCy)-based graft-versus-host disease prophylaxis compared to other allogeneic transplants (K Adekola/ N Ali/ O Frankfurt/ L Metheny/ J Moreira/ M de Lima). The study aims to determine the incidence and severity of HC in patients who received PTCy as part of GVHD prophylaxis, 2) to describe disease characteristics and pre-transplant regimens in patients that developed HC after receiving PTCy-based GVHD prophylaxis and 3) to evaluate survival outcomes in PTCy patients with HC. The study is in protocol development with the goal to move to data file preparation by July 2020.

Proposal: 1911-167

Title:
CMV Serotype and Graft Failure: Is pre-transplant recipient / donor Cytomegalovirus (CMV) serotype one of the factors that affect primary graft failure and secondary graft failure?

Merve Pamukcuoglu, MD, drmpamuk@gmail.com, University of Minnesota; City Hospital of Ankara
Mukta Arora, Professor, arora005@umn.edu, University of Minnesota

Hypothesis:
Graft failure may occur from dominant recipient CMV positive active NK/T cells as opposed to donor CMV positive NK / T cells.

Specific aims:
To determine impact of pre-transplant recipient/ donor CMV serotype on graft failure that considered as 4 groups:

- 1-Recipient/donor CMV serotype are positive-positive,
- Recipient / donor CMV serotype are positive -negative
- Recipient / donor CMV serotype are negative-positive
- Recipient / donor CMV serotypes are negative-negative

Scientific justification:
Graft failure is one of the serious complications of hematopoietic stem cell transplantation (HSCT). Graft failure has been defined as either primary graft failure or secondary graft failure: primary graft failure was defined as no hematopoietic reconstitution of donor origin on day +45, secondary graft failure was defined as patients who had loss of donor cells after a transient engraftment and returned to transfusion dependency[2]. Cytomegalovirus virus infection is major cause of morbidity and mortality after HSCT and solid organ transplantation (SOT)[3,4]. In additional, some of the studies were showed that CMV infection and reactivation had close relationship with acute and chronic allograft rejection after SOT and graft failure after HSCT[5,6,7]. However; there is no coincidental study about relationship between pre-transplant recipient/ donor CMV serotype with primary or secondary graft failure after HSCT.
There was a bidirectional relationship between CMV disease and acute rejection at SOT[8]. For instance; CMV can cause acute rejection via immunomodulation and upregulation of alloantigen, conversely acute rejection can cause transactivation of CMV[8]. Cytomegalovirus reactivation had two major effect. These are: CMV disease direct effect and cellular indirect effect (immunologic phenomena)[9]. Natural killer (NK) cell and $CD8^+$ T cells, $CD4^+$ T cells, some of cytokines and major histocompatibility complex (MHC) have roles on immunologic phenomena[10].
Similar to the immune pathologic mechanism of SOT; CMV positive active T and NK cells may be in a competition with recipient CMV positive active T and NK cells after HSCT, if recipient/ donor CMV serotype are positive-positive. There is some clinical research that was showing CMV reactivation after HSCT might have a beneficial affect protecting from disease relapse, especially in Acute Myeloid Leukemia[11,12,13]. This beneficial effect depends on donor CMV positive NK and T cells[14]. Contrary; recipient CMV positive NK and T cells may cause graft failure via blocking the engraftment[15].

Patient eligibility population:
Inclusion criteria:

The study will include all patients in the CIBMTR database who have undergone a myeloablative peripheral blood stem cell transplant for AML, ALL, CML or MDS between 2008-2017.

Exclusion criteria:
Ex vivo or in- vivo T cell depletion.

Data requirements:
Study population:
All patients who underwent a myeloablative peripheral hematopoietic stem cell transplantation with HLA identical related donor or 8/8 unrelated donor (URD) for Acute Myeloid Leukemia, Acute Lymphocytic Leukemia, Myelodysplastic Syndrome, Chronic Myeloid Leukemia or Lymphoma.

Primary outcome:
Primary graft failure or secondary graft failure

Secondary outcome:
Description of treatment for graft failure (donor lymphocyte infusion (DLI), $CD34^{+}$ boost cell, second hematopoetic stem cell transplantation)

Recipient variables:
Age, sex, presence of co-morbidities and Karnofsky performance status at time of transplant (≥ 90% vs <90%).

Disease variables:
Disease status at transplant

Transplant variables:
Donor type (identical sibling, unrelated), CMV status of recipient/donor type, GVHD prophylaxis, conditioning regimen.

Study design:
This study is a retrospective comparison of groups of recipient/donor CMV serotype with primary graft failure and secondary graft failure. Treatment options at primary graft failure and secondary graft failure will be reviewed and will descriptive to each other with median survival.

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Characteristics of patients who underwent allo HCT for AML, ALL, MDS, CML, or Lymphoma with peripheral blood reported to the CIBMTR 2008-2018

Characteristic	N (%)
No. of patients	9592
No. of centers	204
Patient age - no. (%)	
Median (min-max)	57 (1 -82)
≤17 years	93 (1)
18-29 years	706 (7)
30-39 years	826 (9)
40-49 years	1400 (15)
50-59 years	2671 (28)
60-69 years	3194 (33)
≥70 years	702 (7)
Sex - no. (%)	
Male	5747 (60)
Female	3845 (40)
HCT-CI - no. (%)	
0	2468 (26)
1	1281 (13)
2	1358 (14)
3+	4348 (45)
Missing	137 (1)
Karnofsky performance score - no. (%)	
90-100	5485 (57)
< 90	3968 (41)
Missing	139 (1)
Disease - no. (%)	
AML	3384 (35)
ALL	987 (10)
Other leukemia	399 (4)
CML	298 (3)
MDS	3477 (36)
Other acute leukemia	68 (1)
Non-Hodgkin lymphoma	812 (9)
Hodgkin lymphoma	167 (2)
Donor type - no. (%)	
HLA-identical sibling	4663 (49)
HLA-matched other relative	234 (2)
HLA-Matched Unrelated Donor	4695 (49)
Donor/recipient CMV serostatus - no. (%)	
+/+	3173 (33)
+/-	1053 (11)
-/+	2605 (27)
-/-	2433 (25)
Missing	328 (3)
Conditioning regimen intensity – no. (%)	

Characteristic	N (%)
MAC	4753 (50)
RIC/NMA	4384 (46)
Missing	455 (5)
GVHD prophylaxis - no. (%)	
No GVHD prophylaxis	86 (1)
Post-CY + other(s)	468 (5)
Post-CY alone	4 (<1)
TAC + MMF ± other(s) (except post-CY)	1376 (14)
TAC + MTX ± other(s) (except MMF, post-CY)	5023 (52)
TAC + other(s) (except MMF, MTX, post-CY)	881 (9)
TAC alone	115 (1)
CSA + MMF ± other(s) (except post-CY)	577 (6)
CSA + MTX ± other(s) (except MMF, post-CY)	716 (8)
CSA + other(s) (except MMF, MTX, post-CY)	23 (<1)
CSA alone	32 (<1)
Other(s)	75 (1)
Missing	216 (2)
Region	
US	8961 (93)
Canada	52 (1)
Europe*	126 (1)
Asia	160 (2)
Australia/New Zealand	148 (2)
Mideast/Africa	66 (1)
Central/South America	81 (1)
Year of transplant - no. (%)	
2008-2011	3114 (33)
2012-2015	3774 (39)
2016-2018	2704 (28)
Follow-up - median (min-max)	49 (1-131)

*Due to the GDPR some cases may be removed.

Proposal: 1911-181

Title:
Significance of a prior cancer diagnosis as exclusion criteria in clinical trials among patients with Hematological malignancies undergoing hematopoietic stem cell transplant (HSCT)

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Research hypothesis:
History of prior cancer is a widespread exclusion criterion in cancer trials. We previously demonstrated that 80% of NCI-sponsored and 80% of industry-sponsored lung cancer trials exclude patients with a prior cancer.[1] We suspect this exclusion is commonly applied in other cancer trials, although no hard data exist. Prior cancer is especially common among older patients and those with certain cancer types. Among patients >65 years, 15.1% overall have prior cancer; of the three most common hematological cancer types, prevalence of prior cancer ranges from 17.4% in Multiple Myeloma, 18.7% in Lymphoma, 20% in Lymphocytic leukemia and as high as 24.9% in Myeloid leukemia [2]
Examining this exclusion criterion is critically important today because the number of US cancer survivors is large and rapidly growing. Over the past 30 years, the survivor population has increased four-fold to 15.5 million and is expected to reach 26.1 million by 2040 [3] The growing numbers of survivors of prior cancers is driven by the aging population and improvements in cancer detection and treatment. Almost half of all survivors now live 10 years beyond initial diagnosis.[4] To our knowledge, arbitrarily excluding cancer survivors from trials is not evidence-based and the NCI has indicated that arbitrary exclusion of these patients may violate the *Americans with Disability Act* (ADA). Exclusion presumably arises from assumptions that higher mortality of patients with prior cancer could hinder study conduct and bias trial outcomes. However, few data exist to support this assumption of higher mortality. In fact, our prior work demonstrated that lung cancer patients with a prior cancer have similar or lower mortality risk, compared to those without prior cancer.[5-7]
We have received a R01 grant in August 2018 to study in depth the exclusion criteria in clinical trials for various malignancies including lung cancer, GI cancer and lymphoma. We reviewed 40 CTN clinical trial protocols to identify exclusion criterias, and identified that 79% of the cancer clinical trials have prior malignancy as exclusion.(as shown in table below) The exclusion criteria included anywere from early stage breast/prostate cancer to non-melanomatous skin lesions. In patients undergoing HSCT, prior malignancy is considered a high risk factor and taken into consideration before deciding candidacy for stem cell transplant. However it is unclear that including these prior malignancy as exclusion criteria leads to any difference in outcomes of patients in clinical trials, and may even potentially lead to poor accrual in study. This study will help us understand outcomes of patients with prior cancer who underwent transplant on clinical trial vs on standard of care, and if we identify no difference in outcomes between two groups, this will provide important data to improve future clinical trial exclusion criterias.

Characteristics of Bone Marrow Transplant trials included in the analysis

Characteristics	**No. (%)**
Total Trials	40 (100%)
Phase of study*	
Phase I	1 (3%)
Phase II	19 (47.5%)
Phase III	19 (47.5%)
Type of Transplant	
Allogeneic	30 (75%)
Autologous	10 (25%)
Primary endpoint	
Overall survival	10 (25%)
Progression free survival	10 (25%)
Others/Biomakers/GVHD	20 (50%)
Prior cancer Exclusion	
Yes	26 (79%)
No	7 (21%)
Time frame of prior cancer exclusion#	
Active cancer	1 (2.5%)
Within 1-2 years	0 (0%)
Within 2-3 years	2 (5%)
Within 5 years	18 (45%)
Within 10 years	0 (0%)
Any prior cancer	2 (5%)
Type of exceptions to prior cancer treatment#	
In situ Cervical cancer	17 (42%)
Non-melanoma skin cancer	20 (50%)
Early stage breast cancer	40 (100%)
Early stage prostate cancer	40 (100%)
DCIS or LCIS	2 (5%)
Other *in situ* cancer	3 (7.5%)

* - studies with both Phase I and Phase II component were counted as Phase II

- Studies with multiple reasons for exclusion

DCIS: Ductal Carcinoma in Situ, LCIS: Lobular Carcinoma in Situ

Association between trial characteristics and prior exclusion criteria

Characteristics	Prior cancer exclusion	No prior cancer exclusion	P*
Year of activation			
2004-2009	5 (50%)	5 (50%)	0.81
2010-2012	5 (45%)	6 (55%)	
2013-2015	5 (63%)	3 (37%)	
2016-2018	7 (64%)	4 (36%)	
Study phase			
I	1 (100%)	0 (0%)	0.14
II	8 (42%)	11 (52%)	
III	13 (68%)	6 (32%)	
Transplant			
Allogeneic	14 (47%)	16 (53%)	0.08
Autologous	8 (80%)	2 (20%)	
Protocol type			
Active	9 (64%)	5 (36%)	0.5
Terminated	13 (50%)	13 (50%)	
Study End point			
Overall survival	7 (70%)	3 (30%)	0.46
Progression free survival	11 (78%)	3 (22%)	0.08
Non survival endpoints	7 (35%)	13 (65%)	0.02

Specific aims:

- Evaluate the overall and progression free survival between patients on clinical trial and standard of care.
- Evaluate the risk of secondary non-hematological malignancies in between two groups.

Scientific impact:

History of prior cancer is a widespread exclusion criterion in cancer trials, and upto 79% of the BMT-CTN clinical trials have prior malignancy as exclusion. This study can have significant impact, if we do not identify significant differences in outcomes despite having stringent exclusion criteria on clinical trials, especially prior malignancy, this will help us have an improved study design for future clinical trials.

Patient eligibility population:

- Patients enrolled on BMT-CTN 0901 Clinical trial
- Matched cohort from CIBMTR database for patients treated on standard of care. (Match for age, disease, type of transplant and time of transplant).

Data requirements:

Patient-related:

- Age: person years at risk: continues variable
- Age: age at HCT: continuous variable
- Gender: male or female
- Karnovsky performance status at the time of transplant

- Race of the patient: nominal variable

Primary disease-related:

- Primary disease for which chemo/radiation therapy was given
- Cytogenetics or FISH information of primary disease: normal or abnormal
- Prior treatment with anthracycline: yes/no
- Prior treatment with alkylating agents
- Radiation prior to transplant: yes/no
- Infections prior to HCT
- Number of lines of prior therapy
- Primary immunodeficiency: yes/no
- Genetic or familial disease: yes/no

Transplant-related:

- Blood group compatibility: major, minor or bidirectional
- Donor sex: male vs. female
- Donor type: Related/Unrelated
- Matching: degree of HLA match: Donor/Recipient
- Recipient and donor CMV status: +ve/-ve
- Conditioning therapy type: Myeloablative/Reduced-intensity
- T cell depleted graft: yes/no
- TBI dose ≤800 cGy: yes/no
- EBV status
- GVHD prophylaxis used
- Acute GVHD: yes/no
- Time of aGVHD diagnosis:
- Acute GVHD grade: continuous
- Chronic GVHD: yes/no
- Time of cGVHD diagnosis:
- Chronic GVHD grade (NIH grade, or extensive/limited classification): continuous
- Post-transplant infections
- Post-transplant lymph proliferative disorder: yes/no
- Karnofsky performance status at 1 year, 2 years and 5 years.
- Cord blood bank: Continent i.e. North America, South America, Europe, Australia, Asia
- Transplant related mortality at 1 year, 2 years, and 5 years

Secondary cancer related:

- Secondary cancer defined by a tissue diagnosis: yes/no
- Cancer relapse: yes/no
- Type of secondary cancer: nominal
- Time of secondary cancer development
- Prognosis after second cancer diagnosis

Sample requirements:
None

Study design:
Comparative analysis

Conflicts of interest:
NO to all.

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Characteristics of patients who underwent allo HCT for AML or MDS reported to the CIBMTR June 2, 2011- April 18, 2014.

Characteristic	non-CTN 0901 cases	CTN 0901 cases
No. of patients	1000	263
No. of centers	126	32
Patient age – no. (%)		
Median (min-max)	57 (19-66)	55 (22-66)
Sex – no. (%)		
Male	580 (58)	143 (51)
Female	420 (42)	129 (49)
HCT-CI score – no. (%)		
0	266 (27)	86 (33)
1-2	350 (35)	97 (37)
≥3	384 (38)	86 (33)
Disease - no. (%)		
AML	528 (53)	218 (80)
MDS	472 (47)	54 (20)
Was there a history of malignancy? - no. (%)		
No	302 (30)	185 (70)
Yes	115 (12)	30 (11)
AML	6 (5)	0
Other Leukemia/ALL	11 (10)	3 (10)
Hodgkin Disease	2 (2)	0
Lymphoma	12 (10)	0
Melanoma	3 (3)	2 (7)
MDS/MPN	13 (11)	0
Breast cancer	24 (21)	5 (17)
GI malignancy	3 (3)	1 (3)
Genitourinary malignancy	11 (10)	2 (7)
Lung cancer	2 (2)	0
Oropharyngeal cancer	3 (3)	0
Sarcoma	3 (3)	2 (7)
Thyroid	3 (3)	0
Other malignancy	7 (6)	7 (23)
Unknown malignancy	12 (10)	8 (27)
Missing	583 (58)	48 (18)

Characteristic	non-CTN 0901 cases	CTN 0901 cases
Interval prior malignancy to transplant (years)- median (min-max)*	4 (1-34)	5 (1-20)
Donor type - no. (%)		
Related		
Matched	356 (36)	115 (44)
Mismatched	0	7 (3)
Unrelated		
Matched	535 (54)	124 (47)
Mismatched	109 (10)	26 (10)
Graft Source- no. (%)		
Bone marrow	141 (14)	22 (9)
Peripheral blood	859 (86)	250 (91)
Conditioning regimen intensity - no. (%)		
MAC	652 (65)	131 (50)
RIC	348 (35)	132 (50)
Conditioning regimen - no. (%)		
TBI/Cy	126 (13)	8 (3)
Bu/Cy	212 (21)	40 (15)
Flu/Bu	501 (50)	176 (67)
Flu/Mel	161 (16)	21 (8)
GVHD prophylaxis - no. (%)		
No GVHD prophylaxis	5 (1)	0
Ex-vivo T-cell depletion	2 (<1)	0
CD34 selection	3 (<1)	0
Post-CY + other(s)	14 (1)	0
TAC + MMF	110 (11)	13 (5)
TAC + MTX	617 (62)	222 (84)
TAC + other(s)	85 (9)	22 (8)
TAC alone	22 (2)	0
CSA + MMF	41 (4)	1 (<1)
CSA + MTX	74 (7)	6 (2)
CSA + other(s)	4 (<1)	0
CSA alone	9 (1)	0
Other(s)	12 (1)	8 (3)
Missing	2 (<1)	0
ATG Used		

Characteristic	non-CTN 0901 cases	CTN 0901 cases
Yes	323 (32)	40 (15)
No	675 (68)	232 (88)
Missing	2 (<1)	0
Region		
US	935 (94)	263
Canada	4 (<1)	0
Europe**	15 (2)	0
Asia	23 (2)	0
Australia/New Zealand	10 (1)	0
Mideast/Africa	4 (<1)	0
Central/South America	9 (1)	0
Year of transplant - no. (%)		
2008-2011	121 (12)	26 (10)
2012-2015	879 (88)	241 (90)
Follow-up - median (min-max)	62 (3-101)	68 (5-97)

*Malignancies of non-CTN cohort with interval greater than 3 years (n=65, 57%) and 5 years (n=43, 37%); CTN 0901 cases with interval greater than 3 years (n=11, 37%) and 5 years (n=8, 27%).
**Due to the GDPR some cases may be removed.

Proposal: 1911-198

Title:
Outcomes and safety of hematopoietic stem cell transplants from HTLV positive donors and HTLV positive recipients

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Scientific justification:
Human T-lymphotropic virus (HTLV) is a human retrovirus and to date, four types of HTLVs (HTLV-1, HTLV-2, HTLV-3, and HTLV-4) have been identified. It was initially isolated in 1980 from a patient with peripheral T cell lymphoma.[1,2] Few years later another retrovirus was isolated in Japan, from a patient with adult T-cell leukemia (ATL), and hence was named ATL virus (ATLV).[3] It was found that HTLV-1 and ATLV are the same viruses in 1984. The linkage between ATL and HTLV-1 was also found around the same period.[2] Later in Japan, it was discovered that HTLV-1 can induce a condition, which results in lower limbs proximal muscle weakness, hyperreflexia and unstable gait, named HTLV-1-associated myelopathy (HAM) or tropical spastic paraparesis (TSP).[4] HTLV-1 can also cause inflammatory processes like alveolitis, uveitis, arthritis, dermatitis and cystitis.[5,6,7] HTLV-2 can cause processes similar to HAM. However, it was not shown to be associated with T cell hematologic malignancy.
HTLV-1 is endemic in Japnn, Caribbean region, several parts of South America, West Africa, Asia, and Oceania. Approximately 10-20 million people in the world are infected with HTLV-1, but only 5% of infected individuals will develop HTLV-associated disease. [8] HTLV-I is transmitted by breast feeding, blood transfusion, needles, and sexual intercourse. Vertical transmission also occurs.
The risk of conversion to T-cell leukemia/lymphoma is usually low and is estimated around 4-5%. The hematologic malignancy usually arises after a prolonged latent period of several years.[9] However shorter latent period was reported in immunocompromised patients.[10]
Hematopoietic stem cell transplant (HSCT) has become one of the main modalities to manage patients with incurable hematologic conditions. Transmission of the infection from donor to recipient remains a major risk associated with transplantation. Hence donors undergoing HSCT are routinely checked for multiple infectious agents, including, but not limited to HIV, HTLV-1 and HTLV-2, West Nile virus, CMV, hepatitis, syphilis. The review of CIBMTR retired forms (2004, Infectious disease markers) has confirmed that all donors were routinely checked for HTLV 1/2 types.
Studies describing the outcomes after confirmed HTLV-1 donor transplants are limited to case reviews or case series and are majorly done in solid organ transplant patients.[2] From 1989 to 2000, 10 cases of HTLV-1 associated ATL and 2 cases of HAM were reported after cadaveric kidney transplant, however donor HTLV-1 status was not checked and reported for each single case. [11] There is also a case report about reverse virus transmission from recipient cells to donor cells, which subsequently resulted in progressive expansion of donor T cells, infected with HTLV-1, and development of HTLV-1 associated disease in patient, who received transplant from HTLV-1 negative donor.[12]
Hence we propose a retrospective review using CBMTR database and evaluate outcomes in cohort of patients, receiving HSCT from HTLV-1 positive donors compared to patients, who received their transplant from HLTV-1 negative donors.

Scientific impact:
As discussed above, the study will describe characteristics and clinical outcomes in patients after HSCT from HTLV-1 positive donors. Currently individuals undergoing transplant are routinely informed about HTLV-1 status of the donor. However, current limited data restricts the further detailed discussion

regarding results and outcomes after transplant from HTLV-1 positive donor with the patients undergoing HSCT. In the absence of extensive evidence and small number of post-transplantation cases of HTLV-induced disease, mostly described in the literature as a case studies after solid organ transplantation, a scientific approach is needed to advise whether HSCT from positive donors is safe and comparable to one from HTLV-1 negative donor. However, the disease relapse risk and mortality of patients wait-listed for the transplant, support the use of infected donors, if no other options are available. Prognostic models for outcomes, related progression free survival (PFS) and non-relapse mortality (NRM) will be informative for counselling patients and designing future studies.

Research hypotheses:

- The outcomes in patients, who received HSCT from HTLV-1 positive donors are expected to be similar compared to patients with HSCT from HTLV-1 negative donors.
- The rate of secondary malignancies (including HTLV-related lymphoma/leukemia) is expected to be similar in patients who received the HSCT from HTLV-1 positive donors compared to patients with negative HTLV-1 donors.
- The rate of secondary malignancies (including HTLV-related lymphoma/leukemia) is expected to be similar in HTLV-1 positive recipients for both autologous and allogeneic transplants
- The PFS and NRM are expected to be similar in both cohorts.

Objectives:

- To identify whether the HTLV-1 positivity status of the donor will affect the course and results of HSCT in recipients.
- To assess HTLV-1 status of recipients since virus transmission from recipient to donor cells was reported. 12
- To study the incidence of HTLV-1-related conditions (HAM, T-cell leukemia/lymphoma)

Primary endpoints:

- Progression free survival (PFS). Survival without relapse, progression or death, which are considered events. Those, who meet following criteria, are censored at last contact.
- Non-relapse mortality (NRM). NRM is defined as a death not related to relapse or disease progression.
- Development of secondary malignancy including Adult T cell leukemia Lymphoma

Secondary endpoints:

- Overall survival (OS). Duration of survival until death from any cause, which is considered an event. Patients will be censored at last contact.

Study population:

Inclusion criteria:

- Patients, who are HTLV-1 positive and underwent autologous HSCT
- Patients who underwent allogeneic HSCT from HTLV-1 positive donors
- HTLV-1 negative recipient after HSCT from HTLV-1 negative donor (as a control group)

Exclusion criteria:

- HSCT performed outside specified time range

Variables to be collected:

Patient related:

- Age, continuous by decade
- Gender: male versus female
- Race: Caucasian vs American Indian vs. Asian vs. African American vs. Hispanic vs. Native Hawaiian/Pacific Islander
- Karnofsky performance score: <90 vs. >90

Disease and transplant related:

- Donor HTLV-1 status: positive vs. negative
- Recipient HTLV-1 status: positive or negative:
- Donor HTLV-2 status: positive vs. negative
- Recipient HTLV-2 status: positive or negative
- Type of disease: Acute leukemias vs. CML/CLL vs Lymphoma vs Other
- Transplant type: Allogeneic vs. autologous
- Type of conditioning regimen: Myeloablative with TBI vs. Myeloablative without TBI vs. Reduced intensity/Non-myeloablative
- Graft type: Peripheral blood vs. bone marrow vs. umbilical cord blood
- Donor type: Related vs. unrelated
- Acute Graft-versus-Host disease: Yes or No
- Chronic GVHD: Yes or No
- Systemic immunosuppression therapy (IST): Yes or No

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Characteristics of patients who underwent allo HCT who were tested for HTLV pre-transplant 2008-2018

Characteristic	Negative	Positive	Unknown
No. of patients	26839	217	4863
No. of centers	259	89	224
Patient age - no. (%)			
Median (min-max)	49 (<1-88)	44 (<1 -74)	39 (<1-79)
0-17	5756 (21)	70 (32)	1512 (31)
18-29 yrs	2593 (10)	12 (6)	581 (12)
30-39 yrs	2173 (8)	11 (5)	404 (8)
40-49 yrs	3189 (12)	34 (16)	524 (11)
50-59 yrs	5419 (20)	41 (19)	813 (17)
60-69 yrs	6371 (24)	39 (18)	845 (17)
≥70 yrs	1338 (5)	10 (5)	184 (4)
Sex - no. (%)			
Male	15766 (59)	117 (54)	2922 (60)
Female	11073 (41)	100 (46)	1941 (40)
HCT-CI - no. (%)			
0	9122 (34)	87 (40)	2456 (51)
1	3696 (14)	25 (12)	605 (12)
2	3243 (12)	25 (12)	398 (8)
3+	10255 (38)	75 (35)	1170 (24)
Missing	523 (2)	5 (2)	234 (5)
Karnofsky performance score - no. (%)			
90-100	16802 (63)	140 (65)	3531 (73)
< 90	9447 (35)	74 (34)	1234 (25)
Missing	590 (2)	3 (1)	98 (2)
Race - no. (%)			
Caucasian	20810 (78)	145 (67)	2959 (61)
African-American	2778 (10)	41 (19)	260 (5)
Asian	1319 (5)	6 (3)	805 (17)
Pacific islander	130 (1)	3 (1)	39 (1)
Native American	211 (1)	0	26 (1)
More than one race	329 (1)	5 (2)	23 (1)
Missing	1262 (5)	17 (8)	751 (15)
Disease - no. (%)			
AML	8804 (33)	40 (18)	1235 (25)
ALL	3331 (12)	27 (12)	613 (13)
Other leukemia	716 (3)	16 (7)	120 (3)
CML	735 (3)	3 (1)	111 (2)
MDS	6514 (24)	39 (18)	959 (20)
Other acute leukemia	256 (1)	2 (1)	51 (1)
Non-Hodgkin lymphoma	1732 (7)	36 (17)	289 (6)
Hodgkin lymphoma	424 (2)	0	107 (2)
Plasma cell disorder, multiple myeloma	295 (1)	3 (1)	67 (1)
Other Malignancies	13 (<1)	0	8 (<1)
Severe aplastic anemia	1285 (5)	4 (2)	327 (7)

Characteristic	Negative	Positive	Unknown
Inherited abnormality erythrocyte differentiation function	1231 (5)	6 (3)	448 (9)
SCID & other immune system disorders	771 (3)	32 (15)	394 (8)
Inherited abnormality of platelets	33 (<1)	0	4 (<1)
Inherited disorder of metabolism	415 (2)	0	59 (1)
Histiocytic disorders	233 (1)	8 (4)	64 (1)
Autoimmune diseases	17 (<1)	0	3 (<1)
Other, specify	34 (<1)	1 (1)	4 (<1)
Donor type - no. (%)			
HLA-identical sibling	6484 (24)	49 (23)	1423 (29)
HLA-matched other relative	398 (2)	2 (1)	34 (1)
HLA 1-antigen mismatched relative	127 (1)	0	20 (<1)
Haploidentical donor	2021 (8)	14 (7)	288 (6)
Mismatched relative, degree of mismatch unknown	754 (3)	17 (8)	650 (13)
Related CB	255 (1)	2 (1)	13 (<1)
HLA-Matched Unrelated Donor	9224 (34)	68 (31)	1251 (26)
HLA-Mismatched Unrelated Donor	2198 (8)	15 (7)	335 (7)
Unrelated Donor, HLA-match unknown	165 (1)	2 (1)	135 (3)
Unrelated single CB, 6/6	301 (1)	2 (1)	52 (1)
Unrelated single CB, 5/6	774 (3)	5 (2)	83 (2)
Unrelated single CB, ≤4/6	408 (2)	3 (1)	46 (1)
Unrelated single CB, degree of match Unknown	1821 (7)	18 (8)	319 (7)
Unrelated double CB, 6/6	93 (<1)	0	9 (<1)
Unrelated double CB, 5/6	629 (2)	4 (2)	67 (1)
Unrelated double CB, ≤4/6	1063 (4)	12 (6)	101 (2)
Unrelated double CB, degree of match Unknown	8 (<1)	1 (1)	1 (<1)
Missing	116 (<1)	3 (1)	36 (1)
Donor HTLV Serostatus - no. (%)			
Negative	12292 (46)	97 (45)	1704 (35)
Positive	42 (<1)	5 (2)	5 (<1)
Unknown	14505 (54)	115 (53)	3154 (65)
Conditioning regimen intensity - no. (%)			
MAC	14419 (54)	109 (50)	1905 (39)
RIC	7516 (28)	62 (29)	1162 (24)
NMA	4160 (16)	35 (16)	852 (18)
Missing	744 (3)	11 (5)	944 (19)
GVHD prophylaxis - no. (%)			
No GVHD prophylaxis	388 (1)	4 (2)	239 (5)
Ex-vivo T-cell depletion	263 (1)	3 (1)	143 (3)
CD34 selection	756 (3)	7 (3)	69 (1)
Post-CY + other(s)	2749 (10)	17 (8)	677 (14)
Post-CY alone	75 (<1)	0	10 (<1)
TAC + MMF ± other(s) (except post-CY)	4323 (16)	37 (17)	424 (9)

Characteristic	Negative	Positive	Unknown
TAC + MTX ± other(s) (except MMF, post-CY)	9071 (34)	63 (29)	900 (19)
TAC + other(s) (except MMF, MTX, post-CY)	1278 (5)	10 (5)	270 (6)
TAC alone	574 (2)	6 (3)	32 (1)
CSA + MMF ± other(s) (except post-CY)	3692 (14)	35 (16)	423 (9)
CSA + MTX ± other(s) (except MMF, post-CY)	2087 (8)	16 (7)	904 (19)
CSA + other(s) (except MMF, MTX, post-CY)	690 (3)	8 (4)	123 (3)
CSA alone	296 (1)	2 (1)	162 (3)
Other(s)	350 (1)	3 (1)	73 (2)
Missing	247 (1)	6 (3)	414 (9)
Graft source - no. (%)			
Bone marrow	5870 (22)	51 (24)	1250 (26)
Peripheral blood	15616 (58)	119 (55)	2921 (60)
Umbilical cord blood	5353 (20)	47 (22)	692 (14)
Region			
US	24491 (91)	199 (92)	2641 (54)
Canada	388 (2)	1 (<1)	42 (1)
Europe*	313 (1)	1 (<1)	587 (12)
Asia	43 (<1)	3 (1)	1099 (23)
Australia/New Zealand	551 (2)	0	239 (5)
Mideast/Africa	535 (2)	9 (4)	177 (4)
Central/South America	518 (2)	4 (2)	78 (2)
Year of transplant - no. (%)			
2008-2011	8786 (33)	89 (41)	1292 (27)
2012-2015	9996 (37)	73 (34)	1812 (37)
2016-2018	8057 (30)	55 (25)	1759 (36)
Follow-up - median (min-max)	48 (1-136)	60 (3 -122)	36 (1-130)

*Due to the GDPR some cases may be removed.

Characteristics of patients who underwent auto HCT who were tested for HTLV pre-transplant 2008-2018

Characteristic	Negative	Positive	Unknown
No. of patients	12270	71	1236
No. of centers	199	45	158
Patient age - no. (%)			
Median (min-max)	58 (<1-82)	55 (2 -74)	55 (<1-83)
0-17	680 (6)	2 (3)	96 (8)
18-29 yrs	544 (4)	0	103 (8)
30-39 yrs	666 (5)	7 (10)	109 (9)
40-49 yrs	1572 (13)	13 (18)	173 (14)
50-59 yrs	3530 (29)	26 (37)	332 (27)
60-69 yrs	4334 (35)	21 (30)	353 (29)
≥70 yrs	944 (8)	2 (3)	69 (6)

Characteristic	Negative	Positive	Unknown
Missing	0	0	1 (<1)
Sex - no. (%)			
Male	7070 (58)	33 (47)	731 (59)
Female	5200 (42)	38 (54)	505 (41)
HCT-CI - no. (%)			
0	4036 (33)	24 (34)	520 (42)
1	1694 (14)	7 (10)	154 (13)
2	1871 (15)	7 (10)	190 (15)
3+	4584 (37)	33 (47)	358 (29)
Missing	85 (1)	0	14 (1)
Karnofsky performance score - no. (%)			
90-100	6835 (56)	42 (59)	783 (63)
< 90	5077 (41)	29 (41)	418 (34)
Missing	358 (3)	0	35 (3)
Race - no. (%)			
Caucasian	8390 (68)	33 (47)	820 (66)
African-American	2821 (23)	34 (48)	158 (13)
Asian	474 (4)	3 (4)	159 (13)
Pacific islander	26 (<1)	0	2 (<1)
Native American	104 (1)	0	12 (1)
More than one race	84 (1)	1 (1)	9 (1)
Missing	371 (3)	0	76 (6)
Disease - no. (%)			
AML	149 (1)	5 (7)	8 (1)
ALL	14 (<1)	0	2 (<1)
Other leukemia	12 (<1)	0	1 (<1)
MDS	1 (<1)	0	2 (<1)
Other acute leukemia	2 (<1)	0	0
Non-Hodgkin lymphoma	2852 (23)	20 (28)	270 (22)
Hodgkin lymphoma	869 (7)	4 (6)	218 (18)
Plasma cell disorder, multiple myeloma	7525 (61)	40 (56)	641 (52)
Other Malignancies	796 (7)	2 (3)	51 (4)
Breast cancer	2 (<1)	0	0
Severe aplastic anemia	1 (<1)	0	0
Inherited abnormality erythrocyte diff-function	1 (<1)	0	0
SCID & other immune system disorders	5 (<1)	0	35 (3)
Inherited disorder of metabolism	2 (<1)	0	1 (<1)
Histiocytic disorders	2 (<1)	0	0
Autoimmune diseases	33 (<1)	0	5 (<1)
Other, specify	4 (<1)	0	2 (<1)
Conditioning regimen group- no. (%)			
TBI/Cy	98 (1)	0	2 (<1)
TBI/Cy/VP	130 (1)	0	0
TBI/VP	5 (<1)	0	0
TBI/Mel	17 (<1)	0	3 (<1)
TBI/Flu	48 (<1)	0	0

Characteristic	Negative	Positive	Unknown
TBI/other(s)	8 (<1)	0	1 (<1)
Bu/Cy/Mel	1 (<1)	0	0
Bu/Cy	463 (4)	5 (7)	14 (1)
Bu/Mel	223 (2)	1 (1)	33 (3)
Flu/Bu	6 (<1)	0	0
Flu/Mel	6 (<1)	0	1 (<1)
Cy/Flu	2 (<1)	0	3 (<1)
Cy alone	17 (<1)	0	2 (<1)
CBV	262 (2)	2 (3)	30 (2)
BEAM	2381 (19)	13 (18)	115 (9)
BEAM like	145 (1)	4 (6)	19 (2)
Mel alone	7295 (60)	40 (56)	439 (36)
Mel/ other(s)	315 (3)	0	16 (1)
Carb/Etop	265 (2)	1 (1)	10 (1)
Carb/other(s)	139 (1)	2 (3)	8 (1)
TLI	1 (<1)	0	0
Other(s)	383 (3)	3 (4)	49 (4)
Missing	60 (1)	0	491 (40)
Graft Source - no. (%)			
Bone marrow	37 (<1)	0	33 (3)
Peripheral blood	12229 (100)	71	1201 (97)
Umbilical cord blood	4 (<1)	0	2 (<1)
Region			
US	11846 (97)	65 (92)	924 (75)
Canada	220 (2)	2 (1)	22 (2)
Europe*	5 (<1)	0	53 (4)
Asia	3 (<1)	0	123 (10)
Australia/New Zealand	31 (<1)	0	4 (<1)
Mideast/Africa	4 (<1)	2 (3)	23 (2)
Central/South America	161 (1)	3 (4)	87 (7)
Year of transplant - no. (%)			
2008-2011	3840 (31)	17 (24)	175 (14)
2012-2015	4009 (33)	22 (31)	485 (39)
2016-2018	4421 (36)	32 (45)	576 (47)
Follow-up - median (min-max)	47 (<1-138)	33 (4 -110)	31 (<1-129)

*Due to the GDPR some cases may be removed.

Proposal: 1911-234

Title:
Patterns of Veno-Occlusive Disease in Patients with AML and ALL in the era of Monoclonal Antibodies and Antibody Drug Conjugates

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Hypothesis:
We hypothesize that with the advent of drugs like Gemtuzumab ozagamicin (GO), and Inotuzumab ozagamicin (Ino), incidence of veno-occlusive disease (VOD) post allogeneic stem cell transplant (ASCT) for patients with AML and ALL in real world population is substantially higher with significant mortality/morbidity compared to published literature in small volume prospective studies.

Aim:
To examine the burden of VOD in patients treated with pre or post-transplant GO or Ino in managing patients with acute myeloid leukemia (AML) or acute lymphoblastic leukemia (ALL) and identifying prophylaxis and treatment strategies used in modern era.

- Frequency of VOD
- Timing- patterns of VOD
- Mortality associated with VOD
- Risk factors for VOD with INo/GO use
- Predictors of survival in those who had VOD post INo/GO
- Length of stay for those with VOD
- Prophylaxis and treatment used fr VOD mitigation

Rationale:
As a post remission strategy ASCT has promising data for patients with AML and ALL(1). It is long known events upstream of transplant like the quality/depth of response, pre-transplant comorbidities, infections and a host of other factors including pharmacologic agents influence post-transplant survival. In recent times many novel drugs have been approved to treat AML and ALL. Based on pivotal INO-VATE and Blina trials the likelihood of patients with relapsed/refractory (R/R) ALL attaining remission and then subsequently undergoing transplant is higher compared to conventional chemotherapy era(2). In innovate trial (n-326) adult patients who underwent ASCT after attaining remission achieved durable remissions and the use of ASCT was identified as a positive predictor of survival. About 14% of patients experienced VOD in INO arm compared to 2.1% in conventional chemo arm(2). Data from compassionate INO use in pediatric population reported only patients that had INO followed by ASCT developed VOD, wherein the rates were as high as 52% (3). Similarly use of Blina in R/R setting (n-97) followed by ASCT is associated with survival benefit compared to standard of care followed by ASCT. ASCT compared to no-ASCT was associated with 55% reduction in risk of death (Jabbour et al BBMT abstract 2018, Vol 24 issue- 3). Multiple patients receiving Blinatumomab had abnormal LFT's, however the rates of VOD in this population is not well known. Finally, GO has seen re-birth after initial trials a decade ago showed high rates of VOD. In the ALFA-0701 trial the risk of VOD was 4.4% and slightly higher around 9% in post-marketing studies. Currently it is offered as upfront agent in combination with

chemotherapy for subtypes of leukemia and in R/R cases. Knowing GO can affect hepatic vascular endothelium integrity, rates of VOD in patients exposed to GO and proceeding to ASCT in modern era is not well known. A few have raised a potential interaction between alkylators (PTCY) and increased VOD risk with INo/GO, which needs further validation(4). Given the clinical and economic burden of VOD, it is important for the transplant community to design proactive remedial strategies to mitigate this adverse event. Phase-3 approval trials despite showing some concerns for VOD, likely underrepresent VOD burden based on the fact a select few were able to get to transplant. Hence, to identify the real-world problem CIBMTR database offers unparalleled resource. A prior CIBMTR analysis helped developed VOD risk calculator(5), unfortunately this does not include GO or INo patients. Hence, we believe it is timely to visit this landscape with increasing use of monoclonal antibodies and antibody drug conjugates.

Significance:
Ability to regain remission in R/R ALL with novel drugs is a welcome change. Similarly GO reduces relapse risk in AML, both upfront and in R/R setting. While many of these new antibodies are now tested to move ASCT to CR2 or beyond, it is critically important we first characterize patterns of VOD with these drug use that could direct future clinical trial, need for CAR-T in this setting and the timing of ASCT. Results from this study will also help propel appropriate VOD and antifungal prophylactic studies to mitigate VOD and direct other preventive and interventional measures that is needed for this select population.

Inclusion:
Patients with a diagnosis of ALL or AML undergoing first ASCT and receiving peri-transplant INO, Blina or GO

Data requirements:
CIBMTR report forms will be used for data analysis. Supplemental data if made available will also be used. Study Period will be from 2010 till 2019 (assuming most VOD events are proximal to date of transplant).
Patient Related: Age at transplant, sex, Karnofsky performance scale, HCTCI, race, Donor-Recipient ABO and CMV status, relation between donor and patient (for haplo).
Disease Related: Time from date of diagnosis to ASCT, induction and salvage therapy peri- transplant, best response to induction therapy (complete remission- CR, Partial Remission- PR or Stable Disease-SD), and disease status pre-transplant (MRD if available). Duration from last GO, INA or Blina to ASCT. Number of cycles of INA or blina or GO prior to VOD.
VOD information: Time to VOD post-transplant, Max Grade of VOD
Graft Related: Bone marrow vs peripheral blood vs others.
Donor relation to patient: Degree and loci of HLA mismatch
Transplant Information: Pre-transplant therapy, conditioning regimen (chemotherapy vs radiotherapy, intensity of regimen- MAC vs RIC, use of alkylator or thiotepa), GVHD Prophylaxis, year of transplant, maintenance post-alloSCT therapy (Y/N). Use of Azole prophylaxis (Y/N), Use of VOD prophylaxis with actigal or defibriotide (Y/N). Treatment with Defibriotide (Y/n)
Study Design:
This will be a retrospective CIBMTR study reviewing the impact of peri-transplant Ino/Blina or GO on VOD risk post-transplant. The analysis will be restricted to time frame Jan 2010 to Dec 2019. Descriptive statistics will be reported as median for continuous variables and percent of total for categorical values. We plan to identify the burden of VOD, Timing, risk factors, incidence of organ failure, grading (Baltimore or Seattle), preventive and treatment strategies in clinical practice. Patient, treatment and disease related variables will be summarized using $\chi 2$ or Fisher exact test for categorical variables and

the Mann-Whitney test for continuous variables. Cumulative incidence for VOD, relapse, infections, NRM, aGVHD, cGVHD will be calculated using fine and gray competing risk regression models. Kaplan-Meier product limit estimates will be used to calculate the probabilities of OS and PFS. If available NIH cGVHD criteria will be reported. If sample size is permissive MVA models will be built to determine predictors of survival and non-relapse mortality for patients that developed VOD. The potential interactions between main effect and all significant risk factors will be tested. Again if numbers are permissive we propose building a risk score akin to prior CIBMTR work(5). We would also like to evaluate if the incidence of VOD has changed since the recent introduction of GO/Ino compared to historical data and the relationship between alkylators (PTCY etc.) with GO/INo VOD risk.

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Characteristics of patients who underwent allo HCT for AML or ALL with monoclonal antibodies pre-HCT 2008-2019

Characteristic	N (%)
No. of patients	664
No. of centers	142
Patient age	
Median (min-max)	33 (<1-75)
0-18	236 (36)
18-29 yrs	81 (12)
30-39 yrs	70 (11)
40-49 yrs	88 (13)
50-59 yrs	84 (13)
60-69 yrs	88 (13)
≥70 yrs	17 (3)
Sex - no. (%)	
Male	348 (52)
Female	316 (48)
HCT-CI - no. (%)	
0	277 (42)
1	106 (16)
2	66 (10)
3+	210 (32)
Missing	5 (1)
Karnofsky performance score - no. (%)	
90-100	446 (67)
< 90	205 (31)
Missing	13 (2)
Race - no. (%)	
Caucasian	512 (77)
African-American	50 (8)
Asian	43 (7)
Pacific islander	6 (1)
Native American	3 (1)
More than one race	22 (3)
Missing	28 (4)
Disease - no. (%)	
AML	459 (69)
ALL	205 (31)
Donor type - no. (%)	
HLA-identical sibling, BM or PB	127 (19)
HLA-matched other relative, BM or PB	1 (<1)
HLA 1-antigen mismatched other relative	5 (1)
Haploidentical donor	37 (6)
Other mismatched relative, degree of mismatch unknown	45 (7)
Related CB	1 (<1)
HLA-Matched Unrelated Donor	196 (30)
HLA-Mismatched Unrelated Donor	49 (7)
Unrelated Donor, HLA-match unknown	15 (2)

Characteristic	N (%)
Unrelated single CB, 6/6	5 (1)
Unrelated single CB, 5/6	22 (3)
Unrelated single CB, LE4/6	15 (2)
Unrelated single CB, degree of match Unknown	103 (16)
Unrelated double CB, 6/6	2 (<1)
Unrelated double CB, 5/6	14 (2)
Unrelated double CB, LE 4/6	23 (4)
Unrelated double CB, degree of match Unknown	1 (<1)
Missing	3 (1)
Monoclonal Antibody*	
Inotuzumab	63 (10)
Blinatumomab	86 (13)
Mylotarg	459 (69)
Blinatumomab and Inotuzumab	56 (8)
Conditioning regimen intensity - no. (%)	
MAC	478 (72)
RIC	95 (14)
NMA	68 (10)
Missing	23 (4)
GVHD prophylaxis - no. (%)	
No GVHD prophylaxis	6 (1)
Ex-vivo T-cell depletion	18 (3)
CD34 selection	11 (2)
Post-CY + other(s)	92 (14)
Post-CY alone	3 (1)
TAC + MMF ± other(s) (except post-CY)	108 (16)
TAC + MTX ± other(s) (except MMF, post-CY)	170 (26)
TAC + other(s) (except MMF, MTX, post-CY)	20 (3)
TAC alone	19 (3)
CSA + MMF ± other(s) (except post-CY)	117 (18)
CSA + MTX ± other(s) (except MMF, post-CY)	57 (9)
CSA + other(s) (except MMF, MTX, post-CY)	20 (3)
CSA alone	10 (2)
Other(s)	3 (1)
Missing	10 (2)
Graft source - no. (%)	
Bone marrow	168 (25)
Peripheral blood	310 (47)
Umbilical cord blood	186 (28)
Region	
US	606 (91)
Canada	10 (2)
Europe**	23 (3)
Asia	0
Australia/New Zealand	20 (3)
Mideast/Africa	1 (<1)

Characteristic	N (%)
Central/South America	4 (1)
Year of transplant - no. (%)	
2008-2011	371 (56)
2012-2015	33 (5)
2016-2019	260 (39)
Follow-up - median (min-max)	66 (2-128)

*n=23 cases with monoclonal antibodies post-transplant

**Due to the GDPR some cases may be removed.

Table 2. Characteristics of VOD/SOS cases

	VOD/SOS N (%)		
Monoclonal Agent(s)	**No**	**Yes**	**Total**
Inotuzumab	51 (82)	11 (18)	62
Blinatumomab	81 (98)	2 (2)	83
Mylotarg	402 (88)	54 (12)	456
Blinatumomab and Inotuzumab	41 (76)	13 (24)	54
Totals	575 (88)	80 (12)	655

Footnote: Table displays counts and row proportions not incidence.

Proposal: 1911-46

Title:
The PTCY-CI and PTCY-CDRI: prognostic tools for the use of post-transplant cyclophosphamide based GVHD prophylaxis regimens in allogeneic stem cell transplants for malignant conditions

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Research hypothesis:
- A PTCY-CI risk score incorporating elements of the HCT-CI along with additional patient and disease characteristics can be developed and used to predict which patients may safely receive PTCY for GVHD prophylaxis. The primary outcome is 2-year non-relapse mortality.
- A PTCY-CDRI risk score can be developed incorporating elements of the PTCY-CI and DRI risk scores along with additional patient and disease characteristics that can be predictive of overall survival in all patients receiving an allogeneic stem cell transplant with PTCY-based GVHD prophylaxis. The primary outcome is 2-year overall survival.

Specific aims:
Aim 1: Validate the HCT-CI and DRI risk scores and their components in all allogeneic stem cell transplants using a PTCY-based GVHD prophylaxis regimen.
a. Validate the HCT-CI risk score and its components in all 8/8 HLA-matched allotransplant receiving a PTCY-based GVHD prophylaxis regimen. The primary outcome is 2-year NRM.
b. Independently validate the HCT-CI risk score and its components in HLA-mismatched allogeneic stem cell transplants using a PTCY-based GVHD prophylaxis regimen. The primary outcome is 2-year NRM.
c. Validate the DRI and its components in all allogeneic stem cell transplants using a PTCY-based GVHD prophylaxis regimen. The primary outcome is 2-year overall survival.

Aim 2: Develop a novel PTCY-CI risk score incorporating the components of the HCT-CI that are most predictive of the safety of PTCY in both HLA-matched and HLA-mismatched transplants. The outcome correlated to the score is 2-year NRM.

Aim 3: Develop a novel PTCY-CDRI risk score that may be applied prior to transplantation based on elements of the PTCY-CI and DRI that are most predictive of 2-year OS.

Scientific impact:
None of the current transplant prognostic risk scores have been validated in the setting of post-transplant cyclophosphamide (PTCY)-based GVHD prophylaxis regimens. The determination of prognostic risk scores predictive of transplant outcomes in patients receiving PTCY will have great impact as PTCY-based regimens are becoming used more frequently in both HLA-mismatched and HLA-matched transplants.

Scientific justification:
Since its introduction, post-transplant cyclophosphamide (PTCY) has substantially expanded the scope of allogeneic stem cell transplantation [1, 2]. By promoting the expansion of Tregs and reducing the quantity of alloreactive proliferating T-cells, PTCY has made it possible for transplantation from HLA-

mismatched donors [1]. With current practice, haploidentical transplantation is achieving comparable outcomes to HLA-matched transplantation for malignant hematological disorders [3]. Furthermore, PTCY has served as a platform regimen for the use of adoptive cell therapy with NK cells in the setting of post-transplant relapse [4].

The use of PTCY is not limited to HLA mismatched transplantation. In the first reported trial of PTCY as GVHD prophylaxis for matched unrelated donor transplants, bone marrow was used as the donor graft source. The cumulative incidences of grades III-IV acute GVHD was around 10% for both matched related and unrelated donor transplants [5]. However, the outcomes with a peripheral blood stem cell (PBSC) graft were considerably different. In a small prospective phase 2 trial of PTCY as a single agent GVHD prophylaxis in HLA-matched PBSC transplants using reduced intensity conditioning (RIC), severe acute GVHD was seen in 4 out of 5 patients prompting early closure of the trial [6]. Similar findings were noted in another phase II prospective trial of PTCY as the sole GVHD prophylaxis regimen for RIC transplants using Fludarabine-Busulfan conditioning in matched sibling donor (MSD) and matched unrelated donor (MUD) transplants [7]. These prospective trial results prompted the need to combine additional immunosuppressive therapy (IST) to PTCY when using PBSC grafts.

In a recent retrospective registry study from the EBMT, GVHD prevention strategies using PTCY were compared to PTCY in addition to other immunosuppressive agents for HLA-matched transplants in AML and ALL [2]. There was no significant difference in incidence of grade II-IV acute GVHD between any of the PTCY-based regimens, although the incidence of extensive cGVHD was significantly higher with PTCY alone compared to PTCY with additional immunosuppression. There was no difference in the rate of leukemia relapse between any of the PTCY-based regimens, although on multivariable analysis the use of PTCY with 2 additional IST regimens was associated with a reduced non-relapse mortality (NRM). Similarly, the use of PTCY with two additional IST was associated with a superior overall survival (OS) [2]. Concurrently, a recent randomized phase 2 trial has shown that PTCY-based GVHD prophylaxis yielded favorable results compared to tacrolimus/methotrexate in reduced intensity transplants [8]. Given the anticipated increased use of PTCY-based regimens in transplant, it becomes important to validate existing comorbidity and transplant efficacy assessments in the PTCY-setting.

<u>HCT-CI score in the age of PTCY</u>

The HCT-CI comorbidity score was originally developed in the HLA-matched transplant setting [11]. The individual components of the score along with their relative weights were based on a discovery and validation cohort of patients who received a variety of GVHD prophylaxis regimens, none of which included PTCY. It has been assumed but not proven that the HCT-CI is applicable to patients receiving PTCY, but there are specific considerations with this regimen that must be taken into account. High dose cyclophosphamide has toxicity, including cardiotoxicity and hemorrhagic cystitis. In the original study by Luznik et al, significant toxicities included grade IV transaminitis in around 10% of patients, reversible VOD in 7%, hemorrhagic cystitis, pericardial effusions and multiorgan failure [5]. Furthermore, there has been an association between the use of PTCY and an increased risk of cGVHD, particularly in those patients receiving PBSC grafts [2]. Given these comorbidities are not typical of other GVHD prophylaxis regimens, there may be patients for whom post-transplant cyclophosphamide may represent a higher risk option. This becomes all the more relevant as studies are undertaken to combine additional IST with PTCY for GVHD prophylaxis, potentially resulting in a further increased risk of complications that could increase NRM [8]. Validation of the HCT-CI and potential improvement of the score to better predict NRM in patients who receive PTCY is required.

<u>DRI score in the age of PTCY</u>

The disease risk index (DRI) was developed in order to facilitate the design of clinical trials by risk-stratifying patients with respect to their overall survival post-transplant. The score takes into account

characteristics of the disease as well as its stage at the time of transplant, and has been validated to be predictive of post-transplant overall survival independently of the HCT-CI. While the DRI was developed in the context of HLA-matched and mismatched transplants, none of the patients in the discovery or validation sets received PTCY [9,10]. This implies that for a significant and growing proportion of the transplanted population, the DRI may not have the same predictive capacity as it did for the discovery and validation cohorts in which it was developed. Validation of the DRI in the setting of allotransplant using PTCY is therefore required.

Patient eligibility population:

Inclusion

- Age >= 18
- Malignant indication for allo-transplantation (MDS, AML, ALL, any lymphoma including also CLL/SLL, multiple myeloma)
- GVHD prophylaxis with a PTCY-based regimen (including PTCY alone or in combination with additional agents such as MMF, Tacrolimus, etc)
- First transplant done during the period of 2008 – 2019

Exclusion

- Prior allogeneic stem cell transplant
- Ex-vivo T-cell depletion
- In vivo depletion with anti-thymocyte globulin (ATG) or alemtuzumab (Campath) containing conditioning regimens
- Non-malignant indication for allo-transplantation

Data requirements:

- Age at transplant
- Karnofsky Performance Score (>90 vs <90 and continuous)
- Patient gender
- Ethnicity
- Type of induction/consolidation chemotherapy (3+7, Vyxeos, GO, HyperCVAD, Dana-Farber protocol with or without peg-asparaginase, azacitidine, venetoclax, etc.)
- Use of pre-transplant targeted agents such as FLT3 inhibitors, IDH1/2 inhibitors, or otherwise
- HCT post- first induction vs in primary induction failure versus relapse
- Number of prior relapses
- Duration of remission if relapsed
- Time from diagnosis to HCT: 0-6 versus 6-12 versus >12 months and continuous
- Refined Disease Risk Index [9,10], including the individual components as well as additional information as outlined below:
    - AML subtype
        - Including ELN 2017 risk category
        - Prior exposure to Gemtuzumab-ozogamicin and dose
    - ALL type (T cells vs. B cells and Ph+ chromosome positivity status)
    - MDS IPSS-R score at the time of transplantation
    - CML phase
        - Including the type of TKI(s) used
    - Myeloproliferative neoplasm
        - Including the type of therapy (ruxolitinib, interferon, hydroxyurea, etc.)

        - Size of the spleen at transplant
    - Lymphoma characteristics (as long as it is the indication for transplant)
        - Age at diagnosis
        - Primary or transformed from prior indolent lymphoma
        - Any relevant FISH
        - If DLBCL, then is it dual expressor or double hit
        - CNS involvement
        - HIV associated disease
        - Prior chemoimmunotherapy given
        - Prior radiation given
        - Prior autologous stem cell transplant given?
            - If so, what was the conditioning regimen?
    - Myeloma characteristics (as long as it is the indication for transplant)
        - Age at diagnosis
        - Any relevant cytogenetics/karyotype
        - Prior treatment, including chemotherapy, antibody-based therapy, or immunomodulatory therapy
        - Prior autologous stem cell transplant given?
            - If so, then include the conditioning regimen
    - Previous treatment with immunotherapy (antibody-based like Rituximab, Blinatumomab, Inotuzumab, CAR-T, etc)
    - Cytogenetics and relevant molecular mutation profile (FLT3 mutation, NPM1, IDH1/2, etc)
    - Median blast percentage on pre-transplant bone marrow
- Sorror HCT-CI Co-morbidity Index [11]
    - All individual components of the HCT-CI (arrhythmia, cardiovascular comorbidity including the pre-transplant ejection fraction, inflammatory bowel disease, diabetes, cerebrovascular disease, psychiatric disturbance, hepatic comorbidity, obesity, infection, rheumatologic comorbidity, peptic ulcer, renal comorbidity, pulmonary comorbidity, prior solid tumor, heart valve disease)
- Previous history of MI, CVA or PAD
    - Pre-transplant ejection fraction on ECHO must be included as a continuous variable
- If prior history of cancer that is not the indication for transplant, type and date of chemotherapy and/or radiation given
    - Includes any prior hematological malignancies that are not the indication for transplant

<u>Transplant characteristics (for the most recent transplant)</u>

- Graft type: peripheral versus marrow
- Extent of Donor-recipient HLA match
- CMV status of host and donor
- TBI-based conditioning
    - Myeloablative dose vs non-myeloablative dose
- Conditioning regimen (non-radiation) intensity
    - Non-myeloablative vs myeloablative
        - If non-myeloablative, then reduced intensity (RIC) vs non-RIC
- Use of pre-transplant Cyclophosphamide as conditioning
    - If so, the total planned pre-transplant cyclophosphamide dose
- GVHD prophylaxis in addition to PTCY

- Host and donor ABO type
- Donor age
- Donor gender
- Presence or absence of donor-specific antibodies

Outcomes
- 2-year non-relapse mortality (primary outcome for PTCY-CI)
- 2-year overall survival (primary outcome for PTCY-CDRI)

Secondary outcomes for both PTCY-CI and PTCY-CDRI risk scores
- Acute GvHD, including cumulative incidence of grades all grades and grade 3-4 acute GVHD
- Chronic GvHD, including cumulative incidence of all grades and moderate/severe chronic GvHD
- GFRS (GvHD-free/relapse-free survival)
- 2-year event-free survival (survival without relapse)
- Relapse rates
- Incidence of graft failure
- Median time to neutrophil and platelet recovery
- Incidence of any reported fungal infection

Sample requirements:
No biological samples required.

Study design:
This is a retrospective analysis of the CIBMTR database of patients receiving PTCY for GVHD prophylaxis in the setting of 8/8 HLA-matched and mismatched allogeneic stem cell transplants. The first step is to validate the HCT-CI score in the setting of 8/8 HLA-matched allotransplant patients, and to determine which components of the score are most predictive of 2-year NRM (***Specific Aim 1a***). Concurrently the HCT-CI is to be validated in the setting of HLA-mismatched allotransplant patients, and to determine on multivariable analysis which components of the score are most predictive of 2-year NRM (***Specific Aim 1b***).
Using the results of Specific Aims 1a & 1b (selecting the components with the greatest predictive value for 2-year NRM in the setting of PTCY), a novel PTCY-CI score is to be developed in all allotransplant patients receiving a PTCY-based GVHD prophylaxis regimen that is to be predictive of 2-year NRM (***Specific Aim 2***). To develop the PTCY-CI score, two thirds of patients may be assigned to the training set. A cox proportional hazards model applied to the training set may be used to derive hazard ratios for 2-year NRM with respect to each comorbid condition in the PTCY-CI score. Death due to relapse will serve as a competing risk. The hazard ratios will then be used to calculate the PTCY-CI score. Model validation will be done in the remaining one-third of patients. The PTCY-CI score will be compared to the HCT-CI in terms of its ability to predict 2-yr NRM for patients receiving PTCY as part of their GVHD prophylaxis. The c-statistic will be computed for NRM on time to event over the first 2 years. For NRM, patients will be censored at the time of disease relapse.
Concurrently, a retrospective analysis of the CIBMTR database of patients receiving PTCY for GVHD prophylaxis is to be used to validate the DRI (***Specific Aim 1c***). Using the results of Specific Aims 1c & 2 as well as additional disease-related data (***Data requirements***), a novel PTCY-CDRI score is to be developed in all allotransplant patients receiving a PTCY-based GVHD prophylaxis regimen that is predictive of 2-year OS (***Specific Aim 3***). To develop the PTCY-CDRI score, two thirds of patients may be assigned to the training set. A cox proportional hazards model applied to the training set may be used to derive hazard

ratios for 2-year OS with respect to each element in the PTCY-CI, DRI score, and other data points. The hazard ratios will then be used to calculate the PTCY-CDRI score. Model validation will be done in the remaining one-third of patients. The PTCY-CDRI score will be compared to the DRI score in terms of its ability to predict 2-yr OS for patients receiving PTCY as part of their GVHD prophylaxis. The c-statistic will be computed for 2-year OS based on time to event over the first 2 years.
A secondary outcome for the PTCY-CDRI score will be GVHD-free and relapse-free survival (GFRS). GRFS events will be defined at 1- and 2- years after HCT as the first occurrence of grade III–IV acute GvHD, extensive or systemic chronic GvHD requiring therapy, relapse, or death. Additional secondary outcomes include 2-year event-free survival, rate of relapse, incidence of graft failure, and incidence of a number of viral and fungal infections as outlined in the data requirements section.

Non-CIBMTR data source:
No non-CIBMTR data source required.

Conflicts of interest:
No

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Characteristics of patients who underwent allo HCT for any malignant disease with PTCY reported to the CIBMTR 2008-2018

Characteristic	N (%)
No. of patients	8353
No. of centers	224
Patient Age	
Median (min-max)	55 (18-82)
18-29	1043 (13)
30-39	939 (11)
40-49	1279 (15)
50-59	2050 (25)
60-69	2479 (30)
70+	563 (7)
Sex - no. (%)	
Male	4938 (59)
Female	3415 (41)
HCT-CI - no. (%)	
0	2267 (27)
1	1226 (15)
2	1228 (15)
3+	3608 (43)
Missing	24 (<1)
Karnofsky performance score - no. (%)	
90-100	4921 (59)
< 90	3205 (38)
Missing	227 (3)
Disease - no. (%)	
AML	3438 (41)
ALL	1196 (14)
Other leukemia	239 (3)
CML	319 (4)
MDS	1589 (19)
Other acute leukemia	114 (1)
Non-Hodgkin lymphoma	943 (11)
Hodgkin lymphoma	332 (4)
Plasma cell disorder/Multiple Myeloma	166 (2)
Other Malignancies	17 (<1)
Refined disease risk index - no. (%)	
Low	506 (6)
Intermediate	4111 (49)
High	1209 (15)

Characteristic	N (%)
Very high	210 (3)
Missing cytogenetics, disease status, or disease risk	1731 (21)
N/A - no DRI for patient characteristics	586 (7)
Donor type - no. (%)	
HLA-identical sibling	1073 (13)
HLA-matched relative	201 (2)
HLA 1-antigen mismatched relative	125 (2)
Haploidentical donor	3974 (48)
Mismatched relative, degree of mismatch unknown	1142 (14)
HLA-Matched Unrelated Donor	1127 (14)
HLA-Mismatched Unrelated Donor	554 (7)
Unrelated Donor, HLA-match unknown	156 (2)
Conditioning regimen intensity - no. (%)	
MAC	2510 (30)
RIC/NMA	3585 (43)
Missing	2258 (27)
GVHD prophylaxis - no. (%)	
Post-CY + other(s)	7804 (93)
Post-CY alone	549 (7)
Graft source - no. (%)	
Bone marrow	2976 (36)
Peripheral blood	5377 (64)
Region	
US	7208 (86)
Canada	68 (1)
Europe*	535 (6)
Asia	133 (2)
Australia/New Zealand	141 (2)
Mideast/Africa	20 (<1)
Central/South America	248 (3)
Year of transplant - no. (%)	
2008-2011	734 (9)
2012-2015	2337 (28)
2016-2018	5282 (63)
Follow-up - median (min-max)	24 (0-124)

*Due to the GDPR some cases may be removed.

Proposal: 1911-60

Title:
Toxicities of Older Adults Receiving Allogeneic Hematopoietic Cell Transplant Compared to Younger Patients

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Research hypothesis:
Older adult recipients of allogeneic hematopoietic cell transplant (HCT) experience toxicities at a greater rate than younger HCT recipients.

Specific aims:
Primary aims:
To understand toxicities experienced by older adults (age ≥60) compared to younger adults (age18-59) receiving HCT.

- To evaluate frequency of organ toxicity in the acute period after HCT (≤100 days after HCT) in older adult recipients (age ≥60) compared to younger adult recipients (age 18-59).
- To evaluate frequency of late effects of HCT (100 days to 365 days after HCT) in older adult recipients (age ≥60) compared to younger adult recipients (age 18-59).

Secondary aims:

- To evaluate the impact of pre-existing comorbid conditions on organ toxicity and late effects of HCT in older HCT recipients (age ≥60) compared to younger HCT recipients (age 18-59).
- To evaluate the impact of organ toxicities experienced during the acute period after HCT (≤100 days after HCT) on disease-related and transplant-related survival in older HCT recipients (age ≥60) compared to younger HCT recipients (age 18-59).
- To explore differences in acute and chronic GVHD rate and severity between older HCT recipients (age ≥60) compared to younger HCT recipients (age 18-59).

Scientific impact:
Understanding the unique toxicities of older adults compared to younger adults receiving HCT will inform future studies to explore novel and early interventions to mitigate the short-term and long-term toxicities unique to older adults.

Scientific justification:
Allogeneic HCT offers the best chance of cure for many hematologic malignancies but comes with risk of significant morbidity and mortality. The most common indications for HCT are hematologic malignancies which occur primarily in older adults.[1,2] Despite age being a historic limitation to HCT, an increasing number of older adults are receiving this intensive therapy.[1] With the aging population and the association between cancer and aging, this number is expected to continue rising.[3]
The removal of age restrictions has been enabled by improvements in transplant technology and supportive care. Survival of older adults receiving HCT continues to improve.[4,5] Despite the growing evidence of utility of HCT in older adults, there is limited information on toxicities in this vulnerable population. Reduced-intensity or nonmyeloablative conditioning (RIC/NMA) regimens, which have contributed to increase use of allogeneic HCT in older adults, are associated with improved survival and

lower rate of severe or life-threatening toxicity compared to traditional myeloablative conditioning (MAC) regimens in patients of all ages.[6] Despite this, over two-thirds of older adults experience severe toxicity with these less intensive regimens.[7] Although no differences are seen in rates of severe organ toxicity among adults age ≥60, there is a **gap in knowledge** on how this compares to younger HCT recipients.[8] Improved safety with haploidentical HCT utilizing post-transplant cyclophosphamide has contributed to an increasing number of older adults receiving this intensive therapy due to expanded donor options.[9,10] Although there are concerns for increased toxicity with this approach, there is limited information on the toxicities older adults experience.

Although long-term complications of HCT are well studied in younger patients, there is limited information in older adults.[11] There is a suggestion of potential increased long-term effects in older adults. In autologous HCT, a CIBMTR study found worse overall survival of older adult recipients compared to younger adults despite no difference in disease-related survival by age.[12] A higher rate of death due to vascular or unknown causes was noted in older adults, although the primary cause of death for all age groups was relapsed disease. Despite the improvements in treatment-related mortality of older adults receiving allogeneic HCT, the overall survival of this vulnerable population remains lower than that of younger patients.[4,5]

Older adult HCT recipients have historically had an increased risk of chronic GVHD,[13] but more recent studies have shown no difference in either acute or chronic GVHD among older adults (≥60)[7] or compared to younger adults (age 55-64 vs ≥65).[14] A CIBMTR study showed older HCT recipients (>50) have a lower likelihood of achieving an immunosuppression-free and GVHD-free state after HCT.[15] Understanding GVHD in older adults is important as GVHD, particularly chronic GVHD, and its treatment, such as steroids, are known to affect physical function in this population. [16] Chronic GVHD is also known to impact health-related quality of life,[17] although older age appears to have a protective effect.[16]

This study will investigate toxicities, including GVHD, experienced by older adult recipients of HCT compared to younger adults. Understanding toxicities and GVHD risk will inform future studies on measures to decrease toxicity and inform decision making of GVHD preventative regimens.

Patient eligibility population:

Patients who received an allogeneic HCT from 01/01/2008 to 12/31/2017 reported to the CIBMTR will be included if they are age ≥18 years at time of HCT and received an allogeneic HCT. Patients will be excluded if they are age <18 at time of HCT or received an autologous HCT.

Data requirements:

The following baseline patient variables will be captured from form 2400: age at HCT (18-59; ≥60), gender, ABO type, Karnofsky Performance Status (KPS; <70%; 80-100%), Hematopoietic Cell Transplant-Comorbidity Index (HCT-CI; <3; ≥3); arrhythmia, cardiovascular disease, inflammatory bowel disease, diabetes mellitus, cerebrovascular disease, psychiatric disturbance, hepatic disease, obesity, active infection, rheumatologic disorder, peptic ulcer disease, renal disease, pulmonary disease, heart valve disease, prior solid malignancy (excluding non-melanoma skin).

The following baseline disease-related variables will be collected with form 2402 (after January 2017, form 2400 prior to January 2017): disease, date of initial diagnosis, disease status at HCT.

The following transplant-related variables will be captured from form 2400: type (matched related, matched unrelated, haploidentical, cord blood); year of HCT, conditioning regimen, conditioning regimen intensity, donor age, donor gender, donor ABO type, source of stem cells, GVHD prophylaxis regimen. Donor age will be captured from form 2100 prior to October 2013.

The following survival and disease related outcomes will be captured on form 2450 at Day 100, Day 180, and Day 365: disease response, disease relapse, death, cause of death.

The following post-HCT variables will be captured from form 2450: day of neutrophil recover, day of platelet recover, acute GVHD maximum organ stage, chronic GVHD maximum severity.

Post-HCT Toxicity*	**Description**
KPS	<70% vs 80-100%
Engraftment syndrome[ʃ]	Identified with capillary leak syndrome, fever, rash, and pulmonary edema
Infection	Viral, bacterial, or fungal
Pulmonary toxicity	Including but not limited to: interstitial pneumonitis, acute respiratory distress syndrome, idiopathic pulmonary syndrome, bronchiolitis obliterans, cryptogenic organization pneumonia, bronchiolitis obliterans organizing pneumonia, diffuse alveolar hemorrhage, endotracheal tube or mechanical ventilation requirement.
Liver toxicity	Including veno-occlusive disease/sinusoidal obstruction syndrome or cirrhosis.
Renal toxicity	Such as acute renal failure, chronic kidney disease, renal failure.
Cardiac toxicity	Including but not limited to arrhythmia, congestive heart failure, coronary artery disease, myocardial infarction, hypertension.
Vascular toxicity	Such as deep venous thrombosis or pulmonary embolism.
Neurologic toxicity	Including but not limited to: CNS hemorrhage, encephalopathy, neuropathy, seizures, stroke.
Endocrine toxicity	Such as diabetes mellitus, hyperglycemia, hypothyroidism.
Genitourinary toxicity	Including hemorrhagic cystitis.
Musculoskeletal toxicity	Including but not limited to: vascular necrosis, osteonecrosis of the jaw, osteoporosis, osteoporotic fracture.
Psychiatric toxicity	Such as depression, anxiety, post-traumatic stress disorder.
Ocular toxicities	Such as cataracts.
Other toxicities	Including hyperlipidemia, mucositis, and secondary malignancies.

*****Captured at Day 100, Day 180, Day 365 unless otherwise noted
[ʃ]Captured at Day 100 only

Primary outcomes:

- Frequency of organ toxicity in the acute period after HCT (≤100 days after HCT) in older adults recipients (age ≥60) compared to younger adult recipients (age 18-59).
- Frequency of late effects of HCT (100 days to 365 days after HCT) in older adults recipients (age ≥60) compared to younger adult recipients (age 18-59).

Secondary outcomes:

- Association of pre-existing comorbid conditions with organ toxicities and late effects of HCT in older HCT recipients and younger HCT recipients.
- Association of organ toxicities during the acute period after HCT (≤100 days after HCT) with disease-related and transplant-related survival in older HCT recipients and younger HCT recipients.
- Severity of acute and chronic GVHD of older HCT recipients and younger HCT recipients.

Sample requirements:
Not applicable.

Study design:
Patients who received HCT from 01/01/2008 to 12/31/2017 will be identified in the CIBMTR. Organ toxicities, late effects, and acute and chronic GVHD will be analyzed, stratified by age at HCT (18-59 vs ≥60) and conditioning regimen intensity (RIC/NMA vs MAC). Frequency of organ toxicities will be compared at each follow up time point: Day 100, Day 180, Day 365. Maximum stage acute GVHD and maximum severity of chronic GVHD will be analyzed and stratified by age group and transplant type. Baseline comorbidities will be evaluated for correlation with post-HCT organ toxicity, late effects, and acute and chronic GVHD. Patients will be stratified by age and conditioning regimen.
For Specific Aim 1, our outcomes will be the presence or absence of organ toxicity ≤100 days after HCT and the frequency of late effects of HCT >100 days to 365 days after HCT. We will compare baseline patient-related variables, disease-related variables, and transplant-related variables stratified by age (18-59 vs ≥ 60) using Student's T-test or Wilcoxon Rank-Sum test for continuous factors according to their distribution or using Chi-square tests for categorical variables. We will then conduct univariate analyses of early and late outcomes stratified by age and conditioning regimen (RIC/NMA vs MAC) using a similar analytic strategy. Based on sample sizes we will also conduct univariate analyses stratified based on additional possible confounding variables (disease type, GVHD preventative regimen, conditioning regimen). We will then construct logistic (dichotomous outcomes: organ toxicity) and linear (continuous outcomes: day of recovery) adjusting for confounders identified from univariate analysis and a priori confounders (HCT-CI, sex, KPS). Age will be evaluated as the independent variable and models will be constructed with age as both a continuous and categorical variable. The optimal selection of covariates in multiple regression analysis depends not only upon their numerical performance in the model, with or without appropriate transformations or a study of interactions, but also upon their biological or a priori importance to the study.
We will ascertain for confounding initially through stratified analyses, stratified by the potential confounding variable. We will compare crude odds ratios to stratum-specific odds ratios using the Cochran-Mantel-Haenszel chi square tests. We will also assess for confounders using a multivariable regression approach. For our multivariable analysis, covariates for inclusion within the model will be selected from those that are associated with both age and outcome risk in the univariate analysis. Any variable which has an appreciably affects on other variables (defined as a change in the variable coefficient by 10% or more) will be included within the model as a confounder. We will test whether the association between the exposure and outcome at different levels of the interaction variable are statistically different by using the chi-square test for homogeneity. We will also assess for effect modification within our multivariable analyses. We will create product terms between our exposure variable and interaction variable and include these two-way interaction terms within our multivariable models. We will investigate for interaction in variables based on logistic regression residuals or standardized residuals for linear regression.

Non-CIBMTR data source: Not applicable.

Conflicts of interest:
None

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Characteristics of patients who underwent allo HCT for 2008-2018

Characteristic	<60 years old	60+ years old
No. of patients	15794	8787
No. of centers	260	179
Patient age		
Median (min-max)	46 (18-60)	66 (60-88)
18-29	3186 (20)	0
30-39	2588 (16)	0
40-49	3747 (24)	0
50-59	6273 (40)	0
60-69	0	7255 (83)
≥70	0	1532 (17)
Sex		
Male	8866 (56)	5573 (63)
Female	6928 (44)	3214 (37)
HCT-CI - no. (%)		
0	5017 (32)	1743 (20)
1	2278 (14)	1107 (13)
2	2151 (14)	1173 (13)
3+	5904 (37)	4641 (53)
Missing	444 (3)	123 (1)
Karnofsky performance score - no. (%)		
90-100	9935 (63)	4591 (52)
< 90	5559 (35)	4035 (46)
Missing	300 (2)	161 (2)
Race - no. (%)		
Caucasian	11848 (75)	7795 (89)
African-American	1625 (10)	424 (5)
Asian	1192 (8)	295 (3)
Pacific islander	88 (1)	22 (<1)
Native American	105 (1)	30 (<1)
More than one race	120 (1)	22 (<1)
Missing	816 (5)	199 (2)
Disease - no. (%)		
AML	5988 (38)	2807 (32)
ALL	2347 (15)	323 (4)
Other leukemia	522 (3)	327 (4)
CML	699 (4)	73 (1)
MDS	2693 (17)	4450 (51)
Other acute leukemia	175 (1)	36 (<1)
Non-Hodgkin lymphoma	1364 (9)	577 (7)
Hodgkin lymphoma	476 (3)	22 (<1)
Plasma cell disorder, multiple myeloma	284 (2)	79 (1)
Other Malignancies	8 (<1)	4 (<1)
Severe aplastic anemia	818 (5)	84 (1)
Inherited abnormality erythrocyte differentiation function	284 (2)	3 (<1)
SCID & other immune system disorders	78 (1)	0

Characteristic	<60 years old	60+ years old
Inherited abnormality of platelets	1 (<1)	0
Inherited disorder of metabolism	9 (<1)	0
Histiocytic disorders	26 (<1)	2 (<1)
Autoimmune diseases	9 (<1)	0
Other, specify	13 (<1)	0
Donor type - no. (%)		
HLA-identical sibling	4432 (28)	1940 (22)
HLA-matched other relative	191 (1)	149 (2)
HLA 1-antigen mismatched other relative	76 (1)	46 (1)
Haploidentical donor	1171 (7)	821 (9)
Other mismatched relative, degree of mismatch unknown	672 (4)	192 (2)
Related CB	107 (1)	85 (1)
HLA-Matched Unrelated Donor	5238 (33)	4075 (46)
HLA-Mismatched Unrelated Donor	1398 (9)	665 (8)
Unrelated Donor, HLA-match unknown	152 (1)	83 (1)
Unrelated single CB, 6/6	27 (<1)	10 (<1)
Unrelated single CB, 5/6	100 (1)	41 (1)
Unrelated single CB, LE4/6	138 (1)	60 (1)
Unrelated single CB, degree of match Unknown	700 (4)	134 (2)
Unrelated double CB, 6/6	54 (<1)	29 (<1)
Unrelated double CB, 5/6	414 (3)	183 (2)
Unrelated double CB, LE 4/6	814 (5)	249 (3)
Unrelated double CB, degree of match Unknown	5 (<1)	1 (<1)
Missing	105 (1)	24 (<1)
Graft source - no. (%)		
Bone marrow	2868 (18)	1007 (12)
Peripheral blood	10563 (67)	6990 (80)
Umbilical cord blood	2363 (15)	790 (9)
Conditioning regimen intensity - no. (%)		
MAC	9488 (60)	1937 (22)
RIC	3325 (21)	4622 (53)
NMA	2350 (15)	1829 (21)
Missing	631 (4)	399 (5)
GVHD prophylaxis - no. (%)		
No GVHD prophylaxis	214 (1)	115 (1)
Ex-vivo T-cell depletion	133 (1)	65 (1)
CD34 selection	390 (3)	209 (2)
Post-CY + other(s)	1808 (11)	1225 (14)
Post-CY alone	68 (<1)	16 (<1)
TAC + MMF ± other(s) (except post-CY)	2409 (15)	1570 (18)
TAC + MTX ± other(s) (except MMF, post-CY)	5794 (37)	3240 (37)
TAC + other(s) (except MMF, MTX, post-CY)	841 (5)	531 (6)
TAC alone	320 (2)	229 (3)
CSA + MMF ± other(s) (except post-CY)	1580 (10)	885 (10)
CSA + MTX ± other(s) (except MMF, post-CY)	1439 (9)	259 (3)
CSA + other(s) (except MMF, MTX, post-CY)	109 (1)	35 (<1)

Characteristic	<60 years old	60+ years old
CSA alone	182 (1)	54 (1)
Other(s)	188 (1)	151 (2)
Missing	319 (2)	203 (2)
Region		
US	13703 (87)	8370 (95)
Canada	134 (1)	34 (<1)
Europe*	513 (3)	229 (3)
Asia	589 (4)	35 (<1)
Australia/New Zealand	327 (2)	73 (1)
Mideast/Africa	182 (1)	16 (<1)
Central/South America	346 (2)	30 (<1)
Year of transplant - no. (%)		
2008-2011	6043 (38)	1661 (19)
2012-2015	5494 (35)	3707 (42)
2016-2018	4257 (27)	3419 (39)
Follow-up - median (min-max)	49 (1-131)	40 (2-126)

*Due to the GDPR some cases may be removed.

Biorepository accruals

Unrelated Donor HCT Research Sample Inventory

Summary for first alloHCT in CRF and TED with biospecimens available through the CIBMTR Repository

Stratified by availability of paired samples, recipient only samples and donor only samples*

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Number of patients	39798	12259	7464
Source of data			
CRF	22542 (57)	6191 (51)	4354 (58)
TED	17256 (43)	6068 (49)	3110 (42)
Number of centers	251	224	338
Disease at transplant			
AML	13566 (34)	4431 (36)	2418 (32)
ALL	5866 (15)	1674 (14)	1232 (17)
Other leukemia	1340 (3)	349 (3)	235 (3)
CML	3283 (8)	894 (7)	747 (10)
MDS	65	2328 (19)	1031 (14)
	74 (17)		
Other acute leukemia	408 (1)	138 (1)	80 (1)
NHL	3703 (9)	1012 (8)	606 (8)
Hodgkins Lymphoma	823 (2)	179 (1)	128 (2)
Plasma Cell Disorders, MM	793 (2)	235 (2)	128 (2)
Other malignancies	55 (<1)	13 (<1)	17 (<1)
Breast cancer	7 (<1)	3 (<1)	1 (<1)
SAA	1267 (3)	358 (3)	304 (4)
Inherited abnormalities erythrocyte diff fxn	697 (2)	222 (2)	136 (2)
SCIDs	694 (2)	223 (2)	204 (3)
Inherited abnormalities of platelets	38 (<1)	11 (<1)	10 (<1)
Inherited disorders of metabolism	270 (1)	72 (1)	84 (1)
Histiocytic disorders	354 (1)	93 (1)	78 (1)
Autoimmune disorders	16 (<1)	9 (<1)	5 (<1)
Other	44 (<1)	15 (<1)	20 (<1)
AML Disease status at transplant			
CR1	6997 (52)	2391 (54)	1108 (46)
CR2	2700 (20)	841 (19)	499 (21)
CR3+	259 (2)	73 (2)	53 (2)
Advanced or active disease	3459 (26)	1085 (24)	707 (29)
Missing	147 (1)	41 (1)	47 (2)
ALL Disease status at transplant			
CR1	2842 (48)	871 (52)	516 (42)
CR2	1699 (29)	456 (27)	358 (29)
CR3+	482 (8)	127 (8)	118 (10)
Advanced or active disease	798 (14)	206 (12)	206 (17)
Missing	45 (1)	14 (1)	33 (3)
MDS Disease status at transplant			
Early	1299 (20)	383 (17)	236 (23)
Advanced	4769 (73)	1811 (78)	644 (63)
Missing	465 (7)	121 (5)	140 (14)
NHL Disease status at transplant			

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
CR1	483 (13)	173 (17)	69 (11)
CR2	684 (19)	177 (18)	101 (17)
CR3+	316 (9)	86 (9)	51 (8)
PR	431 (12)	108 (11)	78 (13)
Advanced	1711 (47)	451 (45)	294 (49)
Missing	46 (1)	8 (1)	10 (2)
Recipient age at transplant			
0-9 years	3515 (9)	937 (8)	943 (13)
10-19 years	3639 (9)	969 (8)	867 (12)
20-29 years	4192 (11)	1199 (10)	907 (12)
30-39 years	4637 (12)	1282 (10)	950 (13)
40-49 years	6197 (16)	1806 (15)	1185 (16)
50-59 years	8253 (21)	2481 (20)	1335 (18)
60-69 years	7889 (20)	2914 (24)	1114 (15)
70+ years	1476 (4)	671 (5)	163 (2)
Median (Range)	47 (0-84)	50 (0-79)	41 (0-79)
Recipient race/ethnicity			
Caucasian, non-Hispanic	33122 (86)	10232 (86)	5529 (85)
African-American, non-Hispanic	1831 (5)	516 (4)	319 (5)
Asian, non-Hispanic	883 (2)	399 (3)	267 (4)
Pacific islander, non-Hispanic	53 (<1)	19 (<1)	16 (<1)
Native American, non-Hispanic	147 (<1)	54 (<1)	26 (<1)
Hispanic	2375 (6)	631 (5)	339 (5)
Other	44 (<1)	26 (<1)	21 (<1)
Unknown	1343 (N/A)	382 (N/A)	947 (N/A)
Recipient sex			
Male	23241 (58)	7205 (59)	4411 (59)
Female	16557 (42)	5054 (41)	3053 (41)
Karnofsky score			
10-80	13300 (33)	4420 (36)	2281 (31)
90-100	24957 (63)	7241 (59)	4624 (62)
Missing	1541 (4)	598 (5)	559 (7)
HLA-A B DRB1 groups - low resolution			
<=3/6	22 (<1)	32 (<1)	1 (<1)
4/6	216 (1)	83 (1)	35 (1)
5/6	5551 (14)	1458 (14)	1056 (15)
6/6	33446 (85)	9188 (85)	5845 (84)
Unknown	563 (N/A)	1498 (N/A)	527 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	845 (2)	81 (1)	32 (1)
6/8	1667 (4)	115 (1)	125 (3)
7/8	7742 (20)	1454 (18)	1030 (22)
8/8	28076 (73)	6626 (80)	3395 (74)
Unknown	1468 (N/A)	3983 (N/A)	2882 (N/A)
HLA-DPB1 Match			
Double allele mismatch	9305 (30)	759 (24)	381 (28)
Single allele mismatch	16827 (54)	1585 (51)	711 (52)
Full allele matched	5008 (16)	779 (25)	273 (20)
Unknown	8658 (N/A)	9136 (N/A)	6099 (N/A)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
High resolution release score			
No	11077 (28)	12118 (99)	7291 (98)
Yes	28721 (72)	141 (1)	173 (2)
KIR typing available			
No	26106 (66)	12174 (99)	7425 (99)
Yes	13692 (34)	85 (1)	39 (1)
Graft type			
Marrow	14829 (37)	4153 (34)	3357 (45)
PBSC	24923 (63)	7973 (65)	4081 (55)
BM+PBSC	11 (<1)	6 (<1)	2 (<1)
PBSC+UCB	19 (<1)	117 (1)	2 (<1)
Others	16 (<1)	10 (<1)	22 (<1)
Conditioning regimen			
Myeloablative	25417 (64)	7348 (60)	4974 (67)
RIC/Nonmyeloablative	14204 (36)	4868 (40)	2389 (32)
TBD	177 (<1)	43 (<1)	101 (1)
Donor age at donation			
To Be Determined/NA	235 (1)	1392 (11)	77 (1)
0-9 years	6 (<1)	29 (<1)	1 (<1)
10-19 years	1105 (3)	397 (3)	157 (2)
20-29 years	17569 (44)	5031 (41)	2819 (38)
30-39 years	11434 (29)	3099 (25)	2318 (31)
40-49 years	7230 (18)	1763 (14)	1581 (21)
50+ years	2219 (6)	548 (4)	511 (7)
Median (Range)	31 (0-69)	30 (0-109)	33 (7-67)
Donor/Recipient CMV serostatus			
+/+	9790 (25)	3362 (28)	1809 (25)
+/-	4731 (12)	1591 (13)	939 (13)
-/+	13067 (33)	3680 (31)	2305 (32)
-/-	11653 (30)	3208 (27)	2043 (29)
CB - recipient +	1 (<1)	11 (<1)	0
CB - recipient -	1 (<1)	4 (<1)	0
CB - recipient CMV unknown	0	1 (<1)	0
Unknown	555 (N/A)	402 (N/A)	368 (N/A)
GvHD Prophylaxis			
Ex vivo T-cell depletion	1114 (3)	288 (2)	309 (4)
CD34 selection	723 (2)	313 (3)	127 (2)
Post-CY + other(s)	1071 (3)	643 (5)	171 (2)
Post-CY alone	72 (<1)	31 (<1)	19 (<1)
Tacrolimus + MMF +- others	4732 (12)	1276 (10)	619 (8)
Tacrolimus + MTX +- others (except MMF)	17262 (43)	5492 (45)	2083 (28)
Tacrolimus + others (except MTX, MMF)	2077 (5)	794 (6)	297 (4)
Tacrolimus alone	962 (2)	327 (3)	120 (2)
CSA + MMF +- others (except Tacrolimus)	2654 (7)	637 (5)	613 (8)
CSA + MTX +- others (except Tacrolimus, MMF)	6541 (16)	1701 (14)	2276 (30)
CSA + others (except Tacrolimus, MTX, MMF)	996 (3)	303 (2)	286 (4)
CSA alone	466 (1)	115 (1)	293 (4)
Other GVHD prophylaxis	702 (2)	218 (2)	123 (2)
Missing	426 (1)	121 (1)	128 (2)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Donor/Recipient sex match			
Male-Male	16408 (41)	4862 (40)	2936 (40)
Male-Female	10010 (25)	2981 (25)	1703 (23)
Female-Male	6681 (17)	2171 (18)	1421 (19)
Female-Female	6450 (16)	1941 (16)	1307 (18)
CB - recipient M	10 (<1)	68 (1)	0
CB - recipient F	12 (<1)	57 (<1)	2 (<1)
Unknown	227 (N/A)	179 (N/A)	95 (N/A)
Year of transplant			
1986-1990	349 (1)	45 (<1)	85 (1)
1991-1995	1795 (5)	448 (4)	619 (8)
1996-2000	3149 (8)	1111 (9)	902 (12)
2001-2005	5001 (13)	988 (8)	1437 (19)
2006-2010	9204 (23)	1853 (15)	1418 (19)
2011-2015	12925 (32)	3555 (29)	1805 (24)
2016-2019	7375 (19)	4259 (35)	1198 (16)
Follow-up among survivors, Months			
N Eval	17027	5940	3016
Median (Range)	60 (0-365)	36 (0-336)	49 (1-350)

Unrelated Cord Blood Transplant Research Sample Inventory

Summary for first alloHCT in CRF and TED with biospecimens available through the CIBMTR Repository

Stratified by availability of paired, recipient only and cord blood only samples

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Number of patients	5444	1351	1276
Source of data			
CRF	4129 (76)	1025 (76)	858 (67)
TED	1315 (24)	326 (24)	418 (33)
Number of centers	146	132	195
Disease at transplant			
AML	2044 (38)	451 (33)	409 (32)
ALL	1121 (21)	287 (21)	289 (23)
Other leukemia	91 (2)	26 (2)	24 (2)
CML	117 (2)	33 (2)	31 (2)
MDS	520 (10)	143 (11)	106 (8)
Other acute leukemia	85 (2)	18 (1)	22 (2)
NHL	378 (7)	83 (6)	85 (7)
Hodgkins Lymphoma	92 (2)	25 (2)	22 (2)
Plasma Cell Disorders, MM	35 (1)	10 (1)	7 (1)
Other malignancies	10 (<1)	0	1 (<1)
SAA	89 (2)	31 (2)	24 (2)
Inherited abnormalities erythrocyte diff fxn	157 (3)	48 (4)	31 (2)
SCIDs	236 (4)	71 (5)	97 (8)
Inherited abnormalities of platelets	17 (<1)	4 (<1)	5 (<1)
Inherited disorders of metabolism	332 (6)	93 (7)	84 (7)
Histiocytic disorders	100 (2)	26 (2)	33 (3)
Autoimmune disorders	9 (<1)	0	1 (<1)
Other	11 (<1)	2 (<1)	5 (<1)
AML Disease status at transplant			
CR1	1048 (51)	242 (54)	199 (49)
CR2	569 (28)	114 (25)	116 (28)
CR3+	50 (2)	6 (1)	12 (3)
Advanced or active disease	370 (18)	86 (19)	80 (20)
Missing	7 (<1)	2 (<1)	2 (<1)
ALL Disease status at transplant			
CR1	507 (45)	122 (43)	130 (45)
CR2	421 (38)	108 (38)	103 (36)
CR3+	120 (11)	39 (14)	31 (11)
Advanced or active disease	72 (6)	18 (6)	25 (9)
Missing	1 (<1)	0	0
MDS Disease status at transplant			
Early	163 (31)	36 (26)	48 (46)
Advanced	323 (62)	99 (70)	46 (44)
Missing	33 (6)	6 (4)	11 (10)
NHL Disease status at transplant			
CR1	59 (16)	5 (6)	16 (19)
CR2	71 (19)	18 (22)	24 (29)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
CR3+	42 (11)	10 (12)	9 (11)
PR	65 (17)	12 (14)	11 (13)
Advanced	138 (37)	37 (45)	23 (27)
Missing	0	1 (1)	1 (1)
Recipient age at transplant			
0-9 years	1635 (30)	499 (37)	474 (37)
10-19 years	705 (13)	145 (11)	175 (14)
20-29 years	515 (9)	96 (7)	104 (8)
30-39 years	526 (10)	119 (9)	123 (10)
40-49 years	578 (11)	132 (10)	116 (9)
50-59 years	763 (14)	163 (12)	150 (12)
60-69 years	629 (12)	170 (13)	125 (10)
70+ years	93 (2)	27 (2)	9 (1)
Median (Range)	27 (0-83)	23 (0-77)	19 (0-78)
Recipient race/ethnicity			
Caucasian, non-Hispanic	3033 (59)	802 (62)	704 (62)
African-American, non-Hispanic	783 (15)	181 (14)	147 (13)
Asian, non-Hispanic	315 (6)	85 (7)	81 (7)
Pacific islander, non-Hispanic	27 (1)	3 (<1)	14 (1)
Native American, non-Hispanic	36 (1)	6 (<1)	13 (1)
Hispanic	981 (19)	208 (16)	174 (15)
Other	0	1 (<1)	1 (<1)
Unknown	269 (N/A)	65 (N/A)	142 (N/A)
Recipient sex			
Male	3007 (55)	783 (58)	736 (58)
Female	2437 (45)	568 (42)	540 (42)
Karnofsky score			
10-80	1408 (26)	332 (25)	311 (24)
90-100	3885 (71)	928 (69)	886 (69)
Missing	151 (3)	91 (7)	79 (6)
HLA-A B DRB1 groups - low resolution			
<=3/6	73 (1)	33 (3)	8 (1)
4/6	2139 (41)	433 (41)	444 (37)
5/6	2324 (45)	430 (41)	566 (48)
6/6	666 (13)	150 (14)	168 (14)
Unknown	242 (N/A)	305 (N/A)	90 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	2560 (56)	440 (57)	510 (54)
6/8	1104 (24)	172 (22)	237 (25)
7/8	621 (14)	101 (13)	134 (14)
8/8	304 (7)	53 (7)	70 (7)
Unknown	855 (N/A)	585 (N/A)	325 (N/A)
HLA-DPB1 Match			
Double allele mismatch	725 (40)	55 (41)	55 (37)
Single allele mismatch	924 (51)	67 (50)	76 (52)
Full allele matched	169 (9)	12 (9)	16 (11)
Unknown	3626 (N/A)	1217 (N/A)	1129 (N/A)
High resolution release score			
No	3954 (73)	1301 (96)	1262 (99)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Yes	1490 (27)	50 (4)	14 (1)
KIR typing available			
No	4194 (77)	1345 (>99)	1264 (99)
Yes	1250 (23)	6 (<1)	12 (1)
Graft type			
UCB	5135 (94)	1234 (91)	1213 (95)
BM+UCB	1 (<1)	0	0
PBSC+UCB	279 (5)	117 (9)	54 (4)
Others	29 (1)	0	9 (1)
Number of cord units			
1	4572 (84)	0	1066 (84)
2	870 (16)	0	210 (16)
3	2 (<1)	0	0
Unknown	0 (N/A)	1351 (N/A)	0 (N/A)
Conditioning regimen			
Myeloablative	3579 (66)	870 (64)	828 (65)
RIC/Nonmyeloablative	1855 (34)	476 (35)	444 (35)
TBD	10 (<1)	5 (<1)	4 (<1)
Donor age at donation			
To Be Determined/NA	173 (3)	86 (6)	72 (6)
0-9 years	4843 (89)	1055 (78)	1117 (88)
10-19 years	254 (5)	116 (9)	51 (4)
20-29 years	50 (1)	30 (2)	6 (<1)
30-39 years	50 (1)	29 (2)	13 (1)
40-49 years	33 (1)	16 (1)	5 (<1)
50+ years	41 (1)	19 (1)	12 (1)
Median (Range)	3 (0-72)	5 (0-73)	3 (0-72)
Donor/Recipient CMV serostatus			
+/+	1259 (23)	273 (20)	260 (20)
+/-	543 (10)	129 (10)	116 (9)
-/+	1011 (19)	249 (18)	238 (19)
-/-	681 (13)	165 (12)	173 (14)
CB - recipient +	1112 (20)	285 (21)	246 (19)
CB - recipient -	755 (14)	201 (15)	198 (16)
CB - recipient CMV unknown	83 (2)	49 (4)	45 (4)
GvHD Prophylaxis			
Ex vivo T-cell depletion	28 (1)	9 (1)	4 (<1)
CD34 selection	219 (4)	93 (7)	45 (4)
Post-CY + other(s)	7 (<1)	6 (<1)	2 (<1)
Tacrolimus + MMF +- others	1476 (27)	357 (26)	210 (16)
Tacrolimus + MTX +- others (except MMF)	202 (4)	53 (4)	57 (4)
Tacrolimus + others (except MTX, MMF)	213 (4)	55 (4)	48 (4)
Tacrolimus alone	135 (2)	43 (3)	23 (2)
CSA + MMF +- others (except Tacrolimus)	2549 (47)	557 (41)	636 (50)
CSA + MTX +- others (except Tacrolimus, MMF)	93 (2)	27 (2)	38 (3)
CSA + others (except Tacrolimus, MTX, MMF)	313 (6)	109 (8)	138 (11)
CSA alone	56 (1)	16 (1)	44 (3)
Other GVHD prophylaxis	127 (2)	16 (1)	19 (1)
Missing	26 (<1)	10 (1)	12 (1)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Donor/Recipient sex match			
CB - recipient M	3007 (55)	783 (58)	734 (58)
CB - recipient F	2437 (45)	568 (42)	540 (42)
CB - recipient sex unknown	0	0	2 (<1)
Year of transplant			
1996-2000	0	2 (<1)	4 (<1)
2001-2005	105 (2)	82 (6)	30 (2)
2006-2010	1757 (32)	406 (30)	438 (34)
2011-2015	2574 (47)	494 (37)	575 (45)
2016-2019	1008 (19)	367 (27)	229 (18)
Follow-up among survivors, Months			
N Eval	2649	729	653
Median (Range)	60 (1-168)	47 (3-192)	51 (1-217)

Related Donor HCT Research Sample Inventory

Summary for first alloHCT in CRF and TED with biospecimens available through the CIBMTR Repository

Stratified by availability of paired, recipient only and donor only samples

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Number of patients	7714	1121	483
Source of data			
CRF	2971 (39)	349 (31)	219 (45)
TED	4743 (61)	772 (69)	264 (55)
Number of centers	86	68	52
Disease at transplant			
AML	2519 (33)	367 (33)	140 (29)
ALL	1219 (16)	215 (19)	83 (17)
Other leukemia	170 (2)	30 (3)	18 (4)
CML	256 (3)	26 (2)	11 (2)
MDS	1294 (17)	182 (16)	85 (18)
Other acute leukemia	102 (1)	16 (1)	3 (1)
NHL	747 (10)	102 (9)	65 (13)
Hodgkins Lymphoma	161 (2)	24 (2)	18 (4)
Plasma Cell Disorders, MM	230 (3)	33 (3)	18 (4)
Other malignancies	21 (<1)	0	0
Breast cancer	1 (<1)	0	0
SAA	346 (4)	40 (4)	13 (3)
Inherited abnormalities erythrocyte diff fxn	413 (5)	51 (5)	18 (4)
SCIDs	160 (2)	28 (2)	7 (1)
Inherited abnormalities of platelets	9 (<1)	0	0
Inherited disorders of metabolism	12 (<1)	2 (<1)	1 (<1)
Histiocytic disorders	38 (<1)	5 (<1)	2 (<1)
Autoimmune disorders	7 (<1)	0	1 (<1)
Other	9 (<1)	0	0
AML Disease status at transplant			
CR1	1570 (62)	243 (66)	86 (61)
CR2	391 (16)	42 (11)	15 (11)
CR3+	28 (1)	6 (2)	1 (1)
Advanced or active disease	520 (21)	73 (20)	36 (26)
Missing	10 (<1)	3 (1)	2 (1)
ALL Disease status at transplant			
CR1	765 (63)	136 (63)	56 (67)
CR2	326 (27)	49 (23)	16 (19)
CR3+	62 (5)	9 (4)	6 (7)
Advanced or active disease	66 (5)	20 (9)	5 (6)
Missing	0	1 (<1)	0
MDS Disease status at transplant			
Early	203 (16)	21 (12)	16 (19)
Advanced	1051 (81)	151 (83)	67 (79)
Missing	40 (3)	10 (5)	2 (2)
NHL Disease status at transplant			
CR1	126 (17)	19 (19)	11 (17)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
CR2	141 (19)	20 (20)	11 (17)
CR3+	84 (11)	9 (9)	2 (3)
PR	65 (9)	13 (13)	7 (11)
Advanced	324 (44)	40 (40)	34 (52)
Missing	2 (<1)	0	0
Recipient age at transplant			
0-9 years	754 (10)	91 (8)	27 (6)
10-19 years	866 (11)	90 (8)	39 (8)
20-29 years	632 (8)	123 (11)	41 (8)
30-39 years	589 (8)	98 (9)	43 (9)
40-49 years	1006 (13)	150 (13)	66 (14)
50-59 years	1785 (23)	253 (23)	115 (24)
60-69 years	1817 (24)	278 (25)	139 (29)
70+ years	265 (3)	38 (3)	13 (3)
Median (Range)	50 (0-78)	50 (0-76)	53 (0-77)
Recipient race/ethnicity			
Caucasian, non-Hispanic	4973 (67)	622 (59)	323 (70)
African-American, non-Hispanic	906 (12)	118 (11)	45 (10)
Asian, non-Hispanic	342 (5)	90 (9)	20 (4)
Pacific islander, non-Hispanic	26 (<1)	3 (<1)	1 (<1)
Native American, non-Hispanic	29 (<1)	2 (<1)	1 (<1)
Hispanic	1119 (15)	214 (20)	71 (15)
Unknown	319 (N/A)	72 (N/A)	22 (N/A)
Recipient sex			
Male	4528 (59)	665 (59)	285 (59)
Female	3186 (41)	456 (41)	198 (41)
Karnofsky score			
10-80	2680 (35)	462 (41)	194 (40)
90-100	4846 (63)	628 (56)	266 (55)
Missing	188 (2)	31 (3)	23 (5)
Graft type			
Marrow	2221 (29)	259 (23)	137 (28)
PBSC	5443 (71)	841 (75)	336 (70)
BM+PBSC	6 (<1)	4 (<1)	0
BM+UCB	26 (<1)	7 (1)	1 (<1)
PBSC+UCB	0	0	8 (2)
Others	18 (<1)	10 (1)	0
Conditioning regimen			
Myeloablative	4418 (57)	649 (58)	257 (53)
RIC/Nonmyeloablative	3256 (42)	464 (41)	220 (46)
TBD	40 (1)	8 (1)	6 (1)
Donor age at donation			
To Be Determined/NA	18 (<1)	4 (<1)	3 (1)
0-9 years	535 (7)	60 (5)	21 (4)
10-19 years	770 (10)	95 (8)	38 (8)
20-29 years	980 (13)	151 (13)	60 (12)
30-39 years	1004 (13)	178 (16)	79 (16)
40-49 years	1247 (16)	185 (17)	69 (14)
50+ years	3160 (41)	448 (40)	213 (44)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Median (Range)	45 (0-81)	44 (0-79)	46 (0-76)
Donor/Recipient CMV serostatus			
+/+	3114 (41)	509 (46)	201 (43)
+/-	872 (11)	87 (8)	48 (10)
-/+	1890 (25)	264 (24)	110 (24)
-/-	1719 (23)	239 (22)	104 (22)
Unknown	119 (N/A)	22 (N/A)	20 (N/A)
GvHD Prophylaxis			
Ex vivo T-cell depletion	93 (1)	28 (2)	8 (2)
CD34 selection	123 (2)	32 (3)	9 (2)
Post-CY + other(s)	1568 (20)	215 (19)	107 (22)
Post-CY alone	34 (<1)	8 (1)	3 (1)
Tacrolimus + MMF +- others	793 (10)	70 (6)	27 (6)
Tacrolimus + MTX +- others (except MMF)	3165 (41)	392 (35)	217 (45)
Tacrolimus + others (except MTX, MMF)	619 (8)	224 (20)	49 (10)
Tacrolimus alone	64 (1)	6 (1)	2 (<1)
CSA + MMF +- others (except Tacrolimus)	206 (3)	27 (2)	7 (1)
CSA + MTX +- others (except Tacrolimus, MMF)	623 (8)	76 (7)	31 (6)
CSA + others (except Tacrolimus, MTX, MMF)	80 (1)	9 (1)	2 (<1)
CSA alone	68 (1)	9 (1)	1 (<1)
Other GVHD prophylaxis	118 (2)	12 (1)	8 (2)
Missing	160 (2)	13 (1)	12 (2)
Donor/Recipient sex match			
Male-Male	2525 (33)	399 (36)	159 (33)
Male-Female	1662 (22)	219 (20)	97 (20)
Female-Male	1978 (26)	253 (23)	120 (25)
Female-Female	1516 (20)	233 (21)	97 (20)
CB - recipient M	20 (<1)	12 (1)	6 (1)
CB - recipient F	8 (<1)	4 (<1)	4 (1)
Unknown	5 (N/A)	1 (N/A)	0 (N/A)
Year of transplant			
2006-2010	570 (7)	66 (6)	49 (10)
2011-2015	3617 (47)	469 (42)	194 (40)
2016-2019	3527 (46)	586 (52)	240 (50)
Follow-up among survivors, Months			
N Eval	4876	688	306
Median (Range)	33 (1-131)	24 (2-124)	26 (2-124)