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A G E N D A
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**

1. **Introduction**
   a. Minutes and Overview Plan from February 2018 Tandem meeting (Attachment 1)
   b. Introduction of incoming Co-Chair:
   Bipin Savani, MD; Vanderbilt University Medical Center;
   Email: bipin.savani@vumc.org; Phone: 615-936-8422

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

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

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

a. **PROP 1811-45** Risk factor analysis for early vs intermediate vs late non-relapse mortality (M Battiwalla) (Attachment 4)
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)
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)
d. **PROP 1811-189** Analysis of Comorbidity associated Toxicity at a Regimen based Level (R Shouval/B Savani/A Nagler) (Attachment 7)
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)
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)

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

Biorepository Accruals (Attachment 10)

MINUTES AND OVERVIEW PLAN
CIBMTR WORKING COMMITTEE FOR REGIMEN-RELATED TOXICITY AND SUPPORTIVE CARE
Salt Lake City, Utah
Wednesday, February 21, 2018, 12:15 – 2:15 pm

Co-Chair:	**Andrew Artz, MD, MS, University of Chicago School of Medicine, Chicago, IL; Telephone: 773-834-8980; E-mail: aartz@medicine.bsd.uchicago.edu**
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**
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, Milwaukee, WI; Telephone: 414-805-5745; E-mail: cfretham@mcw.edu**

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1. Introduction

Dr. Loren announced the CIBMTR Regimen-Related Toxicity and Supportive Care Committee (RRTWC) meeting started at 12:15pm on Wednesday, February 21, 2018. She introduced the RRTWC leadership and called Marcelo up to the podium.

Marcelo introduced the RRTWC leadership, the outgoing and incoming chairs, the goals, areas of focus and limitations of the RRTWC. He also briefly mentioned the current status of ongoing RRTWC studies and gave an overview of the proposals we received this year. He mentioned the proposal topics and gave a reminder about the importance of voting for the proposals that you would like to see published.

2. Accrual summary (Attachment 2)

The accrual summary was not presented in order to provide more time for the new proposals' presentation and discussion. The summary was provided as an attachment to the committee members.

3. Presentations, published or submitted papers

Due to the full agenda, the 2017 presentations and published papers were mentioned, but not presented. Two papers were published, one submitted, and five presentations were given during the past year.

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.*

Tandem, Salt Lake City, UT, 2018.

b. **RT12-03** Muffly L, Pasquini MC, Martens M, Brazauskas R, Zhu X, Adekola K, Aljurf M, Ballen KK, Bajel A, Baron F, Battiwalla M, Beitinjaneh A, Cahn JY, Carabasi M, Chen YB, Chhabra S, Ciurea S, Copelan E, D'Souza A, Edwards J, Foran J, Freytes CO, Fung HC, Gale RP, Giralt S, Hashmi SK, Hildebrandt GC, Ho V, Jakubowski A, Lazarus H, Luskin MR, Martino R, Maziarz R, McCarthy P, Nishihori T, Olin R, Olsson RF, Pawarode A, Peres E, Rezvani AR, Rizzieri D, Savani BN, Schouten HC, Sabloff M, Seftel M, Seo S, Sorror ML, Szer J, Wirk BM, Wood WA, Artz A. *Increasing Use of Allogeneic Hematopoietic Cell Transplantation in Patients Age 70 Years and Older in the United States.* ***Blood. 2017 Aug 31; 130(9):1156-1164.***

c. **RT14-01** Parikh S, Ahn KW, Sahr N, Zhu X, Abraham A, Auletta J, Chhabra S, Copelan E, Dvorak C, Fretham C, Gadalla S, Gale RP, Gergis U, Hematti P, Hildebrandt G, Keating A, Myers K, Savani B, Shah N, Pasquini M, Satwani P. *Survival Trends after Allogeneic Hematopoietic Cell Transplant (HCT) in Children less than one-year-old (infants).* ***Tandem, Salt Lake City, UT, 2018.***

d. **RT14-03** Zinter MS, Logan BR, Zhu X, Fretham C, Sapru A, Dvorak CC, Pasquini MC. *Improved Mortality Prognostication for Critically Ill Pediatric Hematopoietic Cell Transplant Patients: Results from a Virtual Pediatric Systems (VPS) and Center for International Blood and Marrow Transplant Research (CIBMTR) Database Merger.* ***Tandem, Salt Lake City, UT, 2018.***

e. **RT16-01** Brunstein C, Pasquini MC, Soyoung K, Fei M, Artz A, Battiwalla M, Bejanyan N, Gale RP, Hematti P, Lahoud OB, de Lima M, Reshef R, Rotz S, Savani B, Schouten HC, Mineishi S, Rogosheske J, Perales MA. *The Effect of Conditioning Regimen Dose Reduction in Obese Patients Undergoing Autologous Hematopoietic Cell Transplantation.* ***ASH, Atlanta, GA, 2017.***

f. **RT09-04b/IB09-06 (1)** E Karaesmen, A Rizvi, L Preus, PL McCarthy, M Pasquini, S Singh, SK Singh, K Onel, X Zhu, S Spellman, CA Haiman, DO Stram, L Pooler, X Sheng, Q Zhu, L Yan, Q Liu, Q Hu, S Liu, AI Clay-Gilmour, S Battaglia, D Tritchler, T Hahn, LE Sucheston-Campbell. *Genome-wide significant donor genetic associations with disease death in AML and MDS patients in the first 1 year after BMT are not modified by Conditioning Intensity or TBI.* ***Tandem, Salt Lake City, UT, 2018.***

g. **RT09-04b/IB09-06 (2)** A Rizvi, E Karaesmen, L Preus, PL McCarthy, M Pasquini, S Singh, SK Singh, K Onel, X Zhu, S Spellman, CA Haiman, DO Stram, L Pooler, X Sheng, Q Zhu, L Yan, Q Liu, Q Hu, S Liu, AI Clay-Gilmour, S Battaglia, D Tritchler, T Hahn, LE Sucheston-Campbell. *Genetic Associations with Day +100 Transplant Related Mortality after HLA-Matched Unrelated Donor Blood and Marrow Transplantation (DISCOVeRY-BMT Study).* ***Tandem, Salt Lake City, UT, 2018.***

h. **RT09-04b/IB09-06 (3)** E Karaesmen, AA Rizvi, L Preus, PL McCarthy, MC Pasquini, K Onel, X Zhu, S Spellman, CA Haiman, DO Stram, L Pooler, X Sheng, Q Zhu, L Yan, Q Liu, Q Hu, A Webb, G Brock, AI Clay-Gilmour, S Battaglia, D Tritchler, S Liu, T Hahn, LE Sucheston-Campbell. *Replication and validation of genetic polymorphisms associated with survival after allogeneic blood or marrow transplant.* ***Blood. 2017 August 2; 130(13): 1585-1596.*** **https://doi.org/10.1182/blood-2017-05-784637**

i. **RT09-04b/IB09-06 (4)** Q Zhu, L Yan, Q Liu, Q Hu, L Preus, AI Clay, K Onel, DO Stram, L Pooler, X Sheng, CA Haiman, X Zhu, SR Spellman, M Pasquini, PL McCarthy, S Liu, T Hahn, LE Sucheston-Campbell *Exomechip Analyses Identify Genes affecting mortality after HLA-Matched Unrelated Donor Blood and Marrow Transplantation.* ***Submitted to Blood (under revision).***

4. Studies in progress (Attachment 3)

The progress of the ongoing studies during the past year was not presented in order to provide more time for the new proposals' presentation and discussion. A summary of the progress was provided as an attachment to the committee members.

a. **RT07-01b** Prospective validation of the impacts of the hematopoietic cell transplantation co-morbidity index, alone and combined with aging on hematopoietic cell transplantation outcomes (M Sorror/M Thakar) **Manuscript preparation**
b. **RT13-02** Safety of high-dose total body irradiation followed by an allogeneic hematopoietic cell transplant for hematologic malignancies (M Sabloff) **Manuscript preparation**
c. **RT14-01** Trends and risk factors for infant mortality following allogeneic hematopoietic cell transplant: Case-Control study (P Satwani/S Parikh) **Manuscript preparation**
d. **RT14-02** Endothelial injury complications after allogeneic hematopoietic cell transplantation (S Davies/ W Chinratanalab/S Jodele/M Ramanathan/B Laskin) **Protocol development**
e. **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) **Manuscript preparation**
f. **RT15-01** Comparison of outcomes for myeloablative conditioning regimens combining busulfan with either cyclophosphamide or fludarabine (A Harris/J Levine) **Manuscript preparation**
g. **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) **Analysis**
h. **RT16-01** Effect of chemotherapy dose adjustments on the outcomes of autologous HCT in patients with lymphoma and multiple myeloma (C Brunstein/ J Rogosheske/ MA Perales) **Manuscript preparation**
i. **RT16-02** Evaluation of lung toxicity following allogeneic stem cell transplant with fludarabine/total body irradiation conditioning regimen (A Saad/ K Minagawa/ Y Kanda/ S Mineishi) **Dropped**
j. **RT17-01** Allogeneic hematopoietic stem cell transplant outcome of patients with end stage renal disease on dialysis (N Farhadfar/ JR Wingard/ H Murthy) **Protocol development**

5. Conditioning regimen summary (Attachment 4)

The conditioning regimen summary was not presented in order to provide more time for the new proposals' presentation and discussion. This summary was provided as an attachment to show committee members the data that is available on conditioning regimens to provide information for future proposals.

6. Future/proposed studies

All chairs led this session.

HCT-CI proposals

a. **PROP 1710-21** Impact of the Composite Refined-Disease Risk Index (DRI-R) and Age-adjusted Hematopoietic Stem Cell Transplantation-specific Comorbidity-Age Index (HCT-CI/Age) on Allogeneic Stem Cell Transplantation Outcomes in Patients with Hematologic Malignancies (SO Ciurea/ P Kongtim / M Sorror/ W Saber/ D Rizzo/ RE Champlin) (Attachment 5)

Dr. Artz introduced Dr. Ciurea up to the podium to present the proposal. The hypothesis is that the combined DRI-R and HCT-CI/Age will be an improved predictor of post-transplant outcomes for patients with hematologic malignancies undergoing alloHCT. The study aims to 1) test a new composite prognostic model combining the DRI-R and the HCT-CI/Age to better stratify and predict OS and/or PFS in patients with hematologic malignancies receiving alloHCT; 2) compare the ability of new composite DRI-R and HCT-CI/Age with the original DRI-R in post-transplant outcome prediction including PFS, OS, relapse and NRM; and 3) assess the impact of the composite model on NRM and relapse.

During the discussion, one person brought up the thought of including economic status as one of the variables in the model. Dr. Ciurea thought it was a good point and it would be beneficial to include if there was enough data available for everyone in the cohort. Another member asked if this study plans to be a validation type study. Dr. Ciurea confirmed it would be ideal to validate the new composite score in some way. A third question was asked about how the presenter plans to combine the DRI and HCT-CI. He responded that it would be discussed with the PhD statistician.

b. **PROP 1711-12** The Effect of Pre-Transplant Composite Disease Risk and Comorbidity Index (DRCI) on Survival after Allogeneic Hematopoietic Cell Transplantation
(N Bejanyan/ Z DeFilipp/ YB Chen/ C Brunstein) (Attachment 6)

Dr. Loren introduced Dr. Bejanyan up to the podium to present the proposal. The hypothesis is that combined DRI and HCT-CI will serve as a single pre-HCT prognostic scoring system to predict OS of adults undergoing alloHCT. The proposal aims to study the effect of DRCI on OS of adult allograft recipients with hematological malignancies.

During the discussion, one member brought up the question of how this would be employed from a patient assessment and patient-care standpoint. Dr. Bejanyan responded that it would be a good way to counsel patients and decide whether to include patients in clinical trials. A follow-up questions was asked regarding asked if this is already employed in practice. Dr. Bejanyan mentioned that it is not at her institution but if it was validated through the CIBMTR there is potential to utilize it.

Another attendee asked whether disease would be considered for the combined score. Dr. Bejanyan replied that since DRI already factors in the transplant recipient's indication for transplant and disease status, this should not be an issue.

c. **PROP 1711-05** Developing a Modified Hematopoietic Stem Cell Transplantation – Comorbidity Index for Adolescents and Young Adults (BD Friend/ GJ Schiller) (Attachment 7)

Dr. Mineishi introduced Dr. Friend up to the podium to present the proposal. The hypothesis of the proposal is that AYAs with a greater number of pre-transplant comorbidities (high risk scores) will have increased rates of NRM following allogeneic HCT. The proposed study aims to: 1) determine the incidence of pre-transplant comorbidities among AYAs that underwent allogeneic HCT; 2) analyze whether comorbidities observed in AYAs are associated with higher NRM and lower OS; 3) develop and test a modified HCT-CI; and 4) determine whether scores of psychosocial assessment of candidates for transplantation (PACT) scale impact outcomes and longer length of hospital stay.

During discussion, one attendee mentioned that there seems to be many HCT-CI proposals that hone in on a specific group and this may be causing the field to be using the HCT-CI in such a way that is very nuanced and not useful in practice.

Another attendee wondered how much of the data would needed to be collected by going back to centers and how much is already on the forms. Dr. Friend responded that he thought most of the variables were on the forms and there wouldn't be a need to go back to centers for most of the variables.

d. **PROP 1711-53** Validation of Hematopoietic Cell Transplantation Comorbidity Index among patients with Hematologic Malignancies undergoing Haploidentical Hematopoietic Cell Transplant using Post-transplant Cyclophosphamide (Attachment 8)

Dr. Artz introduced Dr. Manjappa up to the podium to present the proposal. The hypothesis of the proposal is that HCT-CI predicts NRM in haploidentical HCTs. The aims of the study are to: 1) determine the correlation between HCT-CI and NRM after haploidentical HCT; 2) determine the correlation between HCT-CI and OS, relapse and PFS after haploidentical HCT; and 3) compare the HCT-CI score with the HCT-CI/Age composite index in predicting OS, RFS, NRM and relapse.

During the discussion, Dr. Loren brought up her confusion with the exclusion of post-transplant cyclophosphamide as a single-agent GVHD prophylaxis. Marcelo and the presenter clarified that it is not an exclusion of post-cy alone, but rather post-cy given 1 day vs. 2 days.

e. **PROP 1711-63** A Modified Hematopoietic Cell Transplantation-Comorbidity Index (HCT-CI) for Pediatric Recipients of Allogeneic Transplantation (L Broglie/ M Thakar/ M Sorror) (Attachment 9)

Dr. Loren introduced Dr. Broglie up to the podium to present the proposal. The hypothesis is that increasing HCT-CI scores will be associated with decreased overall survival in pediatric patients and that adjustments to the HCT-CI may result in a comorbidity index that is more clinically relevant to the pediatric population and could outperform the HCT-CI in predicting transplant outcomes in this population.

During discussion, Dr. Claudio Brunstein mentioned there is a significant difference between the malignant and non-malignant disease from a biologic standpoint and in terms of outcomes. Dr. Broglie mentioned that she was aware of this and that she was presenting the data on the analysis of the non-malignant population later that day as an oral presentation. Dr. Nigel Key from UNC Chapel Hill, asked if she planned to include PBSC, UCB, and BM transplants. She confirmed she would include all graft sources. He also asked how many pediatric transplants occur in this population every year. Dr. Broglie responded she is not sure but would estimate between 100-300 a year. Dr. Mineishi questioned how Dr. Broglie plans to cut the age groups to represent the difference in the biology of the diseases. Dr. Broglie mentioned that the table in the program showed her proposed age cut points.

Dr. Pasquini closed out the presentation of the HCT-CI proposals by stating that HCT-CI is an important factor to consider especially considering that it has been proven to be associated with OS in many studies. With that said, we should be cautious about which we should accept and attendees should be clear about which proposal(s) could be most impactful to the community when voting on their choice.

Organ toxicity proposals

f. **PROP 1711-21** An Analysis of Non-Infectious Pulmonary Toxicities in Myeloablative Total Body Irradiation versus Chemotherapy-Based Conditioning Regimens after Allogeneic Hematopoietic Cell Transplantation for Hematologic Malignancies (SS Patel/ BK Hamilton/ N Majhail) (Attachment 10)

Dr. Mineishi introduced Dr. Patel up to the podium to present the proposal. The hypothesis is that myeloablative TBI compared to chemotherapy-based conditioning regimens is associated with a greater risk of non-infectious pulmonary toxicity including COP, DAH, IPS, and BOS. The proposed study aims to: 1) assess the incidence and types of non-infectious pulmonary toxicity and compare the risk in TBI versus commonly used chemotherapy conditioning regimens in a cohort of myeloablative allogeneic HCT recipients; 2) identify risk factors for the development of non-infectious lung toxicity; and 3) evaluate the impact that non-infectious pulmonary toxicity has on NRM and OS.

Discussion was opened and one member mentioned that they were not sure if TBI-based regimens were the only conditioning influence on non-infectious pulmonary toxicity; It is possible that BuCy may also cause an increased risk. Another person asked about the amount of missing data for the incidence of the pulmonary toxicities. Marcelo addressed this by explaining that these variables are difficult to collect fully due to the way data managers fill out the forms. These toxicities are also hard to define which may make it more difficult to accurately represent the incidence. As a follow-up question, one attendee asked about the data quality and if we have any way to validate the reporting of these outcomes. Dr. Artz responded that it is completely dependent on the reporting by the data manager or person completing the form. Dr. Effie Petersdorf from Seattle raised a question regarding how the PI would incorporate the HCT-CI in this proposal and if the PI would be interested in investigating if there was a correlation between pre-transplant pulmonary co-morbidities and HCT-CI.

g. **PROP 1710-08** Incidence and outcomes of hemorrhagic cystic (HC) in patients undergoing Haploidentical Hematopoietic Stem Cell Transplant (AHSCT) with Post Transplant Cyclophosphamide (PT/Cy) used as Graft Versus Host Disease (GVHD) prophylaxis. (AJ Kansagra/ S Ciurea/ A Bashey/ S Hashmi) (Attachment 11)

Dr. Artz introduced Dr. Kansagra up to the podium to present the proposal. The hypothesis is that post-transplant cyclophosphamide when used as a GVHD prophylaxis strategy, will lead to increased risk of hemorrhagic cystitis in patients undergoing allo HCT. Th aims of the proposed study are to: 1) evaluate the incidence and risk factors for developing HC in patients undergoing allo HCT for hematologic malignancies who received PT/Cy as GVHD prophylaxis; 2) identify predictors of HC in patients receiving PT/Cy; 3) identify incidence of second malignancies; and 4) assess OS, DFS and TRM in patients who develop HC.

During the discussion, Dr. Ciurea asked whether the PI could include BK virus as a factor in the study. Dr. Pasquini mentioned that we did not directly collect that information and we do not collect grade of hemorrhagic cystitis either. Dr. Ciurea mentioned that we then should go back to center if we do not have that information as it is very important. Another attendee asked whether it was possible to include transfusions post-HC development but Marcelo said we did not collect transfusion data. Another attendee asked if there is any data on outcomes post-HC development. Marcelo responded that we do not have this data but we could consider going to centers for this information although he is wary to do so because it extends the length of the study significantly. Another attendee mentioned that another way to look at severity of HC would be to check their length of stay during the hospitalization.

h. **PROP 1711-160** Diffuse Alveolar Hemorrhage: The Effect of Graft Source and Conditioning Regimen (C Ustun) (Attachment 12)

Dr. Loren introduced Dr. Artz up to the podium to present the proposal on behalf of Dr. Ustun who could not attend the meeting. The hypothesis is that DAH is a result of a complex interaction between conditioning regimen, graft source and platelet engraftment. The proposed study aims to: 1) evaluate the effect of conditioning intensity, TBI dose and graft source as risk factors for DAH; 2) evaluate the relationship between each neutrophil and platelet engraftment and DAH; 3) evaluate DAH associated with NRM; and 4) evaluate the incidence of DAH.

One attendee asked whether we collect information on viral infections as well to see if they are associated with DAH or confused with DAH. Dr. Artz said we could cross-tabulate the reporting of viral infections and reporting of DAH to see what is shown in the data.

Graft failure proposals

i. **PROP 1711-94/1711-105** Late Graft Failure in Patients Following Myeloablative Allogeneic Hematopoietic Stem Cell Transplantation (RF Olsson / O Ringdén) (Attachment 13)

Dr. Mineishi introduced Dr. Yngvar Flöisand up to the podium to present the proposal on behalf of Dr. Olsson and Dr. Ringden who were not able to attend the meeting. No hypothesis was provided. The proposed study aims to describe the incidence, treatment and risk factors for late graft failure in patients undergoing myeloablative allogeneic HCT.

During the discussion, Dr. Loren asked how late graft failure is defined from a time standpoint; Dr. Flöisand said that they define it as engraftment at any time followed up by the loss of the graft at any time. One attendee mentioned that it seems we do not have very much data on chimerism. Marcelo responded that it is not a readily available set of data and therefore we do have very low information on chimerism. He also explained how we retrieved this information and how we arrived at the number of those who had late graft failure and chimerism simultaneously, provided in the report. Another attendee asked if there was any assessment about if those who had late graft failure were assessed to see what happened after the late graft failure i.e. improvement after a second transplant. Marcelo responded that this was not something we had yet assessed and furthermore, we had excluded those who had relapsed as well. Dr. Ciurea mentioned that late graft failure during a period near the time post-transplant is likely very different than late graft failure further down the road. He thought that any late graft failure before 100 days post-transplant should not be considered. Another attendee mentioned that chimerism is difficult because the biology is also different depending on the graft source. Dr. Effie Petersdorf commented that it would be important to include any data on sensitization or panel reactive antibodies as she thought this data may be associated with the outcomes.

j. **PROP 1711-103** The Risk Factors and Outcomes of Primary Graft Failure after Allogeneic Hematopoietic Cell Transplantation for Hematologic Malignancies (B Wirk) (Attachment 14)

Dr. Artz invited Dr. Wirk up to the podium to present her proposal. No hypothesis was presented. The aims of the proposed study are to: 1) determine the risk factors for primary graft failure (PGF) in a contemporary cohort of patients with hematologic malignancies undergoing myeloablative or RIC allogeneic HCT with related or unrelated donors; 2)

determine theOS with or without second allogeneic HCT for PGF; 3) determine the optimal conditioning regimen for the second allogeneic HCT; and 4) determine whether to use the same or different donors for the second HCT.

Discussion was opened and one attendee asked whether it was important to look at different types of graft sources and donor types. Dr. Wirk said the numbers were robust for these groups in preliminary analysis. Dr. Bejanyan mentioned the differences between conditioning regimens may be of interest and asked how Dr. Wirk will assess engraftment given they may show autologous recovery but no engraftment. Dr. Wirk responded she will utilize donor chimerism data to fully categorize engraftment. Another attendee asked if there is any data on antibodies and the leadership responded that we do not have that and an attendee stated that they will then need to go back to centers for this information as it will be important.

Pre-existing condition proposals

k. **PROP 1711-32** The effect of obesity on outcomes after alternative donor stem cell transplants (MY Abou-Ismail/ G Ravi/ L Metheny/ M de Lima) (Attachment 15)

Dr. Loren introduced Dr. Abou-Ismail up to the podium to present the proposal. The proposal hypothesizes that the increased risk of adverse outcomes related to obesity is greater after haploidentical or umbilical cord transplants vs MUD or MRD transplant. The proposed study aims to: 1) investigate the difference in NRM risk related to obesity after MUD/MRD transplants, haploidentical transplants, and umbilical cord transplants; and 2) determine impact of height, weight and BSA on NRM, OS, and RFS outcomes after alternative donor HCT.

Discussion was opened and an attendee suggested adding stratification of the BMI in more granular groups. Another attendee asked if the proponent has any knowledge from the field if there is an interaction between BMI and donor type for outcomes of HCT and what the hypothesis is for this interaction if the PI believes there is a difference. Dr. Abou-Ismail stated that he wasn't sure and this was a large factor into why he is interested in this study. Another attendee asked if the proponent was considering dose adjusted weight or the actual weight. Marcelo responded that we do use adjusted weight and we could look at both adjusted weight and actual weight for this proposal.

Conditioning regimen proposals

l. **PROP 1711-145** Comparison of transplant outcomes using higher vs. lower dose of melphalan (140 mg/m2 vs. 100 mg/m2) for patients undergoing reduced-intensity conditioning (RIC) transplant for elderly patients with myelodysplastic syndrome (MDS) or acute myeloid leukemia (AML) (HB Alkhateeb/ MV Shah/ MR Litzow) (Attachment 16)

Dr. Mineishi introduce Dr. Alkhateeb up to the podium to present the proposal. The hypothesis is that elderly MDS/AML patients undergoing RIC HCT with FluMel100 is more beneficial than the higher dose FluMel140. The aims of the proposed study are to: 1) study 3-year RFS and OS; 2) assess TRM at day 100, 1-year and 3-years post-transplant; 3) study 3-year cumulative incidence of relapse; 4) study time to neutrophil and platelet engraftment; and 5) assess the cumulative incidence of aGVHD and cGVHD.

A member asked if there is anticipation of bias in selection of FM100 vs. FM140 for patients.

The proponent said this is possible and there could be a center effect but this is also the driving factor of the study. Marcelo commented that this is a valid comment and that we assess the distributions of the doses in order to create these groups and the distribution around the FM100 group showed there may be a center effect occurring. Another member mentioned a similar study that is ongoing in the CIBMTR that is comparing RIC FluMel to RIC BuFlu. Marcelo commented that there is enough distinction between the two studies to continue with this proposed study. Another member mentioned that MPNs should be excluded from the analysis.

Dropped proposed studies

These proposals were not discussed during the meeting. Marcelo commented on the committee's busy portfolio and encouraged attendees to submit ideas again if not accepted at this time.

a. **PROP 1711-18** Racial Disparities and Vascular Injury in Hematopoietic Cell Transplantation (SJ Rotz/ P Bodas/ S Jodele) *Dropped due to overlap with current RRTWC study RT14-02.*
b. **PROP 1711-49** Correlation of pre-hematopoietic stem cell transplant (HSCT) ferritin levels with post-HSCT outcomes and a candidate gene, unbiased SNP approach to identify patients at risk for hyperferritinemia (JA Craddock/ AK Keating) *Dropped due to feasibility. DISCOVeRY-BMT cohort does not align with years serum ferritin values were collected.*
c. **PROP 1711-83** Pre-existing chronic kidney disease in patients undergoing an allogeneic stem cell transplant and its long-term outcomes (A Dias/ N Dunavin/ S Ganguly) *Dropped due to overlap with current RRTWC study RT17-01.*
d. **PROP 1711-137** Outcomes of pediatric acute leukemia patients requiring intensive care after hematopoietic cell transplant (RM Myers/ R Aplenc/ A Seif) *Dropped due to overlap with current RRTWC study RT14-03.*
e. **PROP 1711-146** Conditioning regimen related acute organ toxicities and deaths in the pediatric patients undergoing hematopoietic stem cell transplant for non-malignant diseases (DC Shyr/ M Boyer/ A Petrovic) *Dropped due to overlap with current RRTWC study RT14-01.*

7. Other business

Dr. Artz adjourned the meeting and thanked members for attending.

Study Proposal Acceptance:

Prior to meeting the CIBMTR Advisory Committee released recommendations for each committee with the numbers of proposals to be approved 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 studies RT18-01 (proposals 1711-05/1711-63 combined), RT18-02 (proposal 1711-32) and RT18-03 (proposal 1711-21/1711-160) were accepted based on voting scores, scientific impact in the HCT community and feasibility.

Working Committee Overview Plan for 2018-2019

a. **RT07-01b**: Prospective validation of the impacts of the hematopoietic cell transplantation co-morbidity index, alone and combined with aging on hematopoietic cell transplantation outcomes. We anticipate completing the manuscript by March 2018 and submit to JAMA. (Total hour: 0; Allocated for the fiscal year: 0)

b. **RT13-02**: Safety of high-dose total body irradiation followed by an allogeneic hematopoietic cell transplant for hematologic malignancies. We will complete and submit manuscript to BBMT by April 2018. (Total hour: 10; Allocated for the fiscal year: 10)

c. **RT14-01**: Trends and risk factors for infant mortality following allogeneic hematopoietic cell transplant: Case-Control study. We will complete and submit manuscript March 2018. (Total hour: 10; Allocated for the fiscal year: 10)

d. **RT14-02**: Endothelial injury complications after allogeneic hematopoietic cell transplantation. We will complete data analysis by June 2018, prepare manuscript in July 2018 and submit manuscript by June 2019. (Total hour: 50; Allocated for the fiscal year: 50)

e. **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. We will complete manuscript and submit to peer-review journal by April 2018. (Total hour: 10; Allocated for the fiscal year: 10)

f. **RT15-01**: Comparison of outcomes for myeloablative conditioning regimens combining busulfan with either cyclophosphamide or fludarabine. The manuscript was submitted to Blood Advances in February of 2018. (Total hour: 0; Allocated for the fiscal year: 0)

g. **RT15-02**: Association of anti-epileptic medication with outcomes after conditioning with targeted busulfan followed by cyclophosphamide before allogeneic hematopoietic cell transplantation. Propose a survey to assess antiepileptic uses by centers to assess the feasibility of this study. We anticipate completing analysis in March 2018 and preparing manuscript by June 2018. (Total hour: 10; Allocated for the fiscal year: 10)

h. **RT16-01:** Effect of BEAM dose adjustments on the outcomes of patients with lymphoma or multiple myeloma. We anticipate completing manuscript and submitting to BBMT by March 2018. (Total hour: 70; Allocated for the fiscal year: 10)

i. **16-02:** Evaluation of lung toxicity following allogeneic stem cell transplant with fludarabine/total body irradiation conditioning regimen. This study was dropped.

j. **RT17-01** (proposal 1611-67): Allogeneic hematopoietic stem cell transplant outcome for patients with end stage renal disease on dialysis. We anticipate having the protocol finalized by April 2018, the analysis completed by August 2018, and to submit the manuscript by June 2019. (Total hour: 250; Allocated for the fiscal year: 250)

k. **RT18-01** (proposal 1711-05/1711-63): A Modified Hematopoietic Cell Transplantation-Comorbidity Index (HCT-CI) for Pediatric Recipients of Allogeneic Transplantation/Developing a Modified Hematopoietic Stem Cell Transplantation – Comorbidity Index for Adolescents and Young Adults. We anticipate to having a draft protocol by June 2018. (Total hour: 310; Allocated for the fiscal year: 240)

l. **RT18-02** (proposal 1711-32): The effect of obesity on outcomes after alternative donor stem cell transplants. We anticipate to having a draft protocol by June 2018. (Total hour: 310; Allocated for the fiscal year: 240)

m. **RT18-03** (proposal 1711-21/1711-160): We anticipate to having a draft protocol by June 2018. (Total hour: 310; Allocated for the fiscal year: 160)

Oversight Assignments for Working Committee Leadership (March 2018)	
Alison Loren	**RT14-01:** Trends and Risk Factors for Infant Mortality Following Allogeneic Hematopoietic Cell Transplant: Case-Control study. **RT14-02**: Endothelial injury complication after allogeneic hematopoietic cell transplantation. **RT16-01:** Effect of BEAM dose adjustments on the outcomes of patients with lymphoma or multiple myeloma. **RT18-01** (proposals 1711-05/1711-63): A Modified Hematopoietic Cell Transplantation-Comorbidity Index (HCT-CI) for Pediatric Recipients of Allogeneic Transplantation/Developing a Modified Hematopoietic Stem Cell Transplantation – Comorbidity Index for Adolescents and Young Adults.
Shin Mineishi	**RT13-02**: Safety of high-dose total body irradiation followed by an allogeneic hematopoietic cell transplant for hematologic malignancies. **RT15-01**: Comparison of outcomes for myeloablative conditioning regimens combining busulfan with either cyclophosphamide or fludarabine. **RT15-02:** Association of anti-epileptic medication with outcomes after conditioning with targeted busulfan followed by cyclophosphamide before allogeneic hematopoietic cell transplantation. **RT18-03** (proposals 1711-21/1711-160): An Analysis of Non-Infectious Pulmonary Toxicities in Myeloablative Total Body Irradiation versus Chemotherapy-Based Conditioning Regimens after Allogeneic Hematopoietic Cell Transplantation for Hematologic Malignancies/Diffuse alveolar hemorrhage (DAH) is a result of complex interaction between conditioning regimen (MAC>RIC and TBI>noTBI), graft source (UCB >others), and engraftment (delayed>early).
Edward Stadtmauer	**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.

	RT18-02 (proposal 1711-32): The effect of obesity on outcomes after alternative donor stem cell transplants.
Marcelo Pasquini	**RT07-01b:** Prospective validation of the impacts of the hematopoietic cell transplantation co-morbidity index, alone and combined with aging on hematopoietic cell transplantation outcomes.
	RT17-01: Allogeneic hematopoietic stem cell transplant outcome for patients with end stage renal disease on dialysis.

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 2018 in research retrieval

Characteristics of autologous HCT recipients	**N (%)**
Number of patients	23305
Number of centers	345
Age, median (range), years	56 (<1-83)
Sex	
Male	13813 (59)
Female	9492 (41)
Disease	
AML	762 (3)
ALL	68 (<1)
Other leukemia	43 (<1)
CML	13 (<1)
MDS/MPN	39 (<1)
Non-Hodgkin lymphoma	6086 (26)
Hodgkin lymphoma	2085 (9)
PCD/MM	12218 (52)
Other Malignancies	1839 (8)
SAA	5 (<1)
Inherited abnormalities of erythrocyte differentiation or function	3 (<1)
SCID and other immune system disorders	32 (<1)
Inherited disorders of metabolism	2 (<1)
Histiocytic disorders	2 (<1)
Autoimmune Diseases	99 (<1)
Other	9 (<1)
HCT-CI	
0	4793 (21)
1	1806 (8)
2	1940 (8)
3+	4562 (20)
Missing	164 (<1)
NA, pre-TED not completed before 2008	10040 (43)
IPn or ARDS/IPS	
No	21236 (91)
Yes	1092 (5)
Missing	977 (4)

Characteristics of autologous HCT recipients	**N (%)**
Bronchiolitis obliterans	
No	22124 (95)
Yes	147 (<1)
Missing	1034 (4)
Pulmonary hemorrhage	
No	21600 (93)
Yes	133 (<1)
Missing	1572 (7)
Cryptogenic organizing pneumonia	
No	21028 (90)
Yes	36 (<1)
Missing	2241 (10)
VOD/SOS	
No	22107 (95)
Yes	173 (<1)
Missing	1025 (4)
TMA	
No	22107 (95)
Yes	184 (<1)
Missing	1014 (4)
Renal failure severe enough to warrant dialysis	
No	21076 (90)
Yes	1173 (5)
Missing	1056 (5)
Year of transplant	
2000-2003	4556 (20)
2004-2007	5792 (25)
2008-2011	4595 (20)
2012-2015	4930 (21)
2016-2018	3432 (15)

Characteristics of recipients of allogeneic transplant reported to the CIBMTR between 2000 and 2018 in research retrieval

Characteristics of allogeneic HCT recipients	N (%)
Number of patients	62861
Number of centers	422
Age, median (range), years	42 (<1-88)
Sex	
Male	36984 (59)
Female	25877 (41)
Disease	
AML	19489 (31)
ALL	8968 (14)
Other leukemia	1721 (3)
CML	4011 (6)
MDS/MPN	10392 (17)
Non-Hodgkin lymphoma	5372 (9)
Hodgkin lymphoma	1144 (2)
PCD/MM	1428 (2)
Other Malignancies	375 (<1)
SAA	3324 (5)
Inherited abnormalities of erythrocyte differentiation or function	2840 (5)
SCID and other immune system disorders	2008 (3)
Inherited abnormalities of platelets	89 (<1)
Inherited disorders of metabolism	989 (2)
Histiocytic disorders	589 (<1)
Autoimmune Diseases	42 (<1)
Other	80 (<1)
HCT-CI	
0	12333 (20)
1	4203 (7)
2	3601 (6)
3+	11143 (18)
Missing	838 (1)
NA, pre-TED not completed before 2008	30743 (49)
IPn or ARDS/IPS	
No	53033 (84)
Yes	8201 (13)
Missing	1627 (3)

Characteristics of allogeneic HCT recipients	**N (%)**
Bronchiolitis obliterans	
No	58840 (94)
Yes	1792 (3)
Missing	2229 (4)
Pulmonary hemorrhage	
No	51355 (82)
Yes	1480 (2)
Missing	10026 (16)
Cryptogenic organizing pneumonia	
No	49506 (79)
Yes	306 (<1)
Missing	13049 (21)
VOD/SOS	
No	57034 (91)
Yes	3334 (5)
Missing	2493 (4)
TMA	
No	58166 (93)
Yes	1954 (3)
Missing	2741 (4)
Renal failure severe enough to warrant dialysis	
No	52829 (84)
Yes	6000 (10)
Missing	4032 (6)
Hemorrhagic cystitis	
No	55025 (88)
Yes	3732 (6)
Missing	4104 (7)
Year of transplant	
2000-2003	14555 (23)
2004-2007	16545 (26)
2008-2011	11689 (19)
2012-2015	12616 (20)
2016-2018	7456 (12)

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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; Scientific Director for the Regimen-Related Toxicity and Supportive Care Working Committee

RE: Studies in Progress Summary

RT13-02: Safety of high-dose TBI followed by an allogeneic stem cell transplant for hematologic malignancies (M Sabloff) The specific aims were 1) To describe the toxicity profile of those patients receiving high dose TBI (>12Gy) compared to those who had a myeloablative transplant with TBI ≤12, with or without chemotherapy. To study if any pre BMT characteristics might have an influence on the type of toxicity in either group; 2) To compare the toxicity profile of those patients who received high dose TBI (>12Gy) with chemotherapy to those who received high dose TBI (>12Gy) without chemotherapy. To study if any pre BMT characteristics might have an influence on the type of toxicity in either group; 3) To describe the overall and progression free survival of those receiving high dose TBI (>12Gy) compared to patients who received a myeloablative transplant with TBI ≤ 12, with or without chemotherapy; 4) To describe the overall and progression free survival of those receiving high dose TBI (>12Gy) with chemotherapy to patients who received conditioning with high dose TBI (>12Gy), without chemotherapy. Manuscript preparation is underway and the goal of the study is to submit the manuscript to BBMT by March 2019.

RT14-01: Trends and Risk Factors for Infant Mortality Following Allogeneic Hematopoietic Cell Transplant: A Case-Control study (P Satwani/ S Parikh) The primary objectives were 1) to compare transplant related mortality in infants (<1-year-old) following allogeneic hematopoietic stem cell transplant (AlloHCT) between the period of 2001-2005 and 2006-2011; 2) to compare the transplant related mortality in infants (<1-year-old) vs. children >1-10 years old following AlloHCT between the period of 2001-2005 and 2006-2011. The secondary objectives were 1) to compare the incidence of day+30, +100 and 1 year TRM between two-time periods for patients <1 year at the time of start of conditioning. Measure the incidence of TRM in patients receiving AlloHCT for malignant (ALL, AML and MDS/MPS) and non-malignant diseases (SCID, HLH & other immune system disorders, metabolic disorders) between the period of 2001-2005 and 2006-2011; 2) to compare the incidence of day+30, +100 and 1 year TRM between patients <1 year vs. >1-10 years. Measure the incidence of TRM in patients receiving AlloHCT for malignant (ALL, AML and MDS/MPS) and non-malignant diseases (SCID, HLH & other immune system disorders, metabolic disorders) between the period of 2001-2005 and 2006-2011; 3) to calculate the incidence of acute and chronic graft versus host disease, incidence of veno-occlusive disease (VOD), pulmonary toxicity and graft failure; 4) to identify risk factors associated with transplant-related mortality in infants following AlloHCT. The study was submitted to JAMA pediatrics in December 2018.

RT14-02: Endothelial injury complications after allogeneic hematopoietic cell transplantation (N Epperla/A Li) The specific aims were 1) to report outcomes of children and adults who developed transplant-associated thrombotic microangiopathy (TA-TMA) after allogeneic and autologous HSCT in comparison to HCT patients without TMA; 2) to study the risk factors for VOD in the current era of

reduced intensity conditioning regimens and reduced toxicity myeloablative conditioning regimens. The study is in manuscript preparation stage with the goal to submit to BBMT by April 2019.

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) The specific aims were: 1) to identify transplant-related risk factors for PICU mortality through multivariate regression; 2) to identify transplant-related risk factors for life-threatening infections in the PICU, including sepsis, gram-positive and gram-negative bacterial infections, fungal infections, and viral infections; 3) to identify transplant-related risk factors for organ dysfunction and life-saving interventions both on PICU admission and throughout PICU stay. The study was submitted to Intensive Care Medicine in January 2019.

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) The specific aims were to evaluate the safety of using levetiracetam as a replacement for phenytoin in preventing seizures caused by high-dose busulfan (BU)when followed by high-dose cyclophosphamide (CY) 60 mg/kg on two successive days as the conditioning regimen before allogeneic hematopoietic cell transplantation. Safety was evaluated through measures of hepatic toxicity, interstitial pneumonia, renal failure requiring dialysis, non-relapse mortality, relapse or progression of malignant disease, and overall survival. The study was submitted to BBMT in November 2018.

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 study is in data file preparation with the goal to move to analysis in March 2019.

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 is in protocol development with the goal to move to data file preparation in February 2019.

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 protocol development with goal to move to data file preparation by July 2019.

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 protocol development with the goal to move to data file preparation by July 2019.

Proposal: 1811-45

Title:
Risk factor analysis for early versus intermediate versus late non-relapse mortality (NRM)

Minoo Battiwalla, MD, MS, minoo.battiwalla@hcahealthcare.com, Sarah Cannon Blood Cancer Network

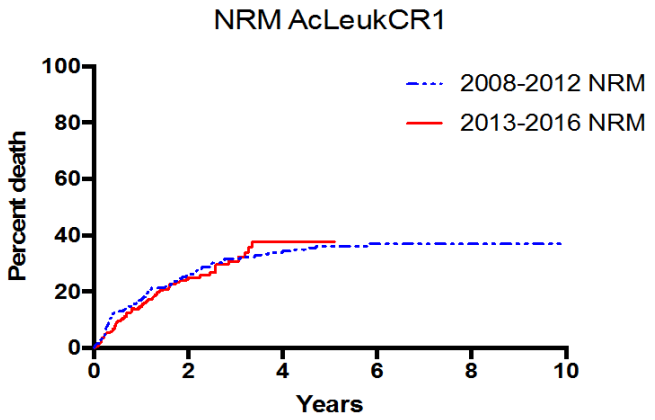
Hypothesis:
- Hypothesis #1: Risk factors differentially impact early (<1 year) versus intermediate (1-3 years) versus late (>3 years) non-relapse mortality following allogeneic transplant.
- Hypothesis #2: While early non-relapse mortality has declined significantly over the past two decades, intermediate and late non-relapse mortality have not declined as much.

Specific aims:
- Aim #1: Evaluate the different clinical risk factors that predict early (<1 year) versus intermediate (1-3 years) versus delayed (>3 years) non-relapse mortality.
- Aim #2: Understand which phase of NRM (early versus intermediate versus late) has most improved over recent years

Scientific impact:
Improvement in survival after allogeneic HCT has occurred predominantly because of reduction in NRM while relapse mortality has remained relatively stagnant. Nowadays, most transplant centers routinely succeed in restricting the cumulative incidence of NRM to <20% at 1 year post HCT. However, the cumulative incidence of NRM continues to increase from 1 year to about 3 to 4 years before plateauing. There are two important conclusions from this observation. First, there is scope for continued improvements in NRM. Secondly, it is notable that the bulk of NRM now occurs once patients have left the immediate supervision of their transplant center and returned to their home physicians. Reducing NRM will require a targeted approach, which in turn depends upon identifying the relative impact of different risk factors for NRM depending upon time post transplant.

Scientific justification:
It is difficult to parse out the precise cause of death (COD) after allogeneic HCT, which is why the composite endpoint of NRM is popular. Nevertheless, there is variance in non-relapse COD based upon time post HCT. In the first year after HCT, the major contributors to NRM are organ-failure from regimen-related toxicity, non-engraftment, acute GVHD and infection. From 1-3 years, major contributors are infection and chronic GVHD. Beyond 3 years, infection, pulmonary, cardiovascular and subsequent neoplasm predominate. Therefore, risk factors would be expected to differentially impact each phase of NRM. Knowing the most impactful risk factors at each phase of the transplant process would allow accurate risk assessment for targeted approaches to reducing NRM.
It is not enough to identify the relevant risk factors for NRM, it is also important to understand at which phase centers need to provide the most attention. We know that there has been continued improvement in NRM over recent years through improvements in supportive care and patient selection. Most centers have observed an improvement in NRM in the first year after transplant but there is limited data to show that this reduction in early NRM carries over to subsequent years. For instance, unpublished data from our network shows that the incidence of NRM has not improved in recent years. Allogeneic HCT for acute leukemia in CR1: n=572 subjects with median follow up >3 years. For patients transplanted between 2008 to 2012, NRM at 1 year was 17% but went up to 32% at 3 years. For patients transplanted between 2013 to 2016, NRM at 1 year was 15%, but increased to 31% at 3 years. If this

finding of lack of improvement in intermediate and late NRM is found in the CIBMTR, then this should support the development of robust survivorship programs in centers where this is currently lacking.



Patient eligibility population:

- Allogeneic HCT recipients from 2000-2017
- Standard transplant indications for hematologic malignancy.
- First HCT
- PBSC or marrow graft
- HLA-identical or fully matched unrelated donor grafts.
- Centers with a high completeness index

Study design:

Specific Aim 1: Evaluate the impact of disease-related factors, patient-related factors, therapy-related factors, graft-related factors, center-related factors and post transplant variables on each individual phase of NRM, early, intermediate or late.

Disease-related factors:

- DRI
- Time from dx to HCT

Patient-related factors:

- Age
- CMV status
- BMI
- Race/eth
- KPS
- HCT-CI

Therapy-related:

- Intensity
- TBI
- GVHD prophy

Graft-related:

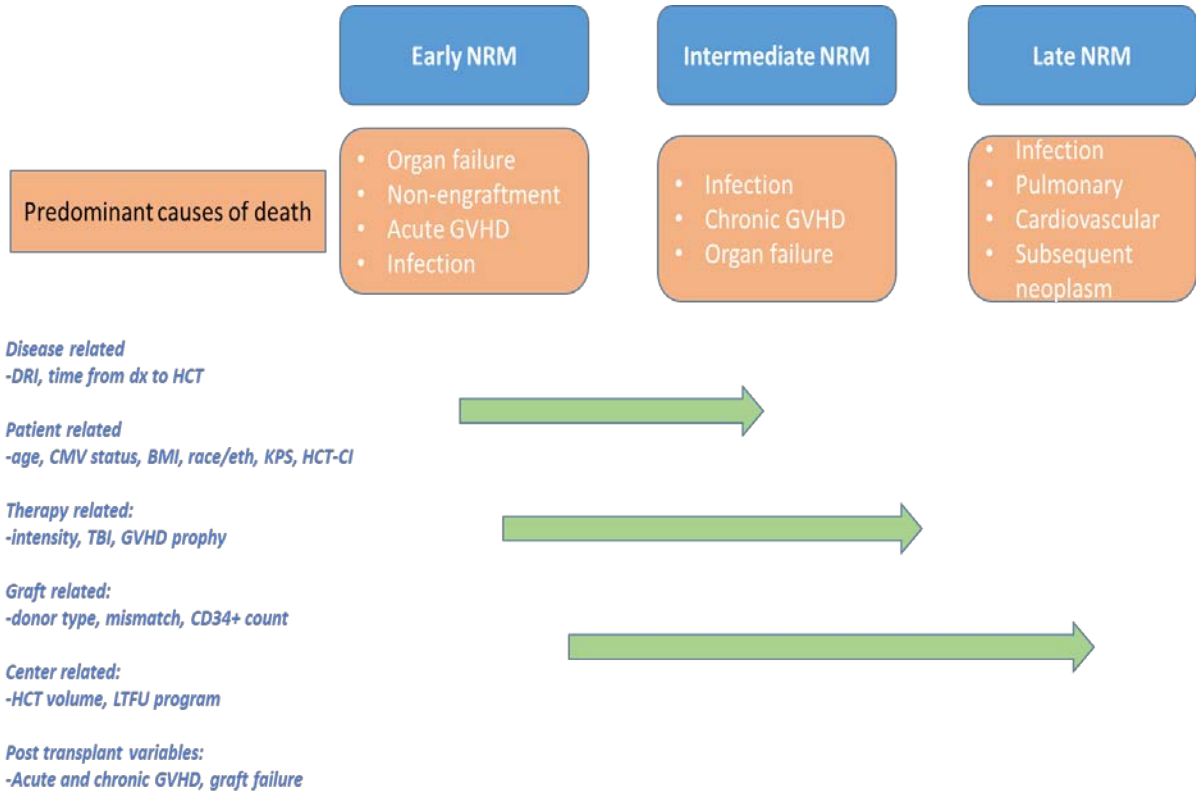
- Donor type
- Mismatch
- CD34+ count

Center-related:

- HCT volume
- LTFU program

Post-transplant variables:

- Max grade of acute and chronic GVHD
- Graft failure



Specific Aim 2: Look at impact of transplantation era (prior to 2010 versus beyond 2010) on overall NRM and then individually for early, intermediate and late NRM. Compare the magnitude of changes by transplantation era between early vs intermediate vs late NRM.

Characteristics of patients who received first alloHCT for hematologic malignancy with PBSC or marrow from 2000-2017 (HLA-identical sibling and Well-matched donors only)

Characteristic	N (%)
Number of patients	30074
Number of centers	362
Age, median (range), years	50 (<1-83)
Age group	
0-9	1260 (4)
10-19	2088 (7)
20-29	2950 (10)
30-39	3553 (12)
40-49	5515 (18)
50-59	7823 (26)
60-69	5940 (20)
≥70	945 (3)
Sex	
Male	17849 (59)
Female	12225 (41)
Race	
Caucasian	25634 (85)
African-American	1065 (4)
Asian	1940 (6)
Pacific islander	71 (<1)
Native American	108 (<1)
Other	487 (2)
More than one race	107 (<1)
Missing	662 (2)
Ethnicity	
Hispanic or Latino	2117 (7)
Not Hispanic or Latino	21178 (70)
NA, non-resident of USA	3827 (13)
Missing	2952 (10)
Karnofsky/Lansky performance score	
90-100	19099 (64)
< 90	9672 (32)
Missing	1303 (4)

Characteristic	N (%)
Disease	
AML	10812 (36)
ALL	4114 (14)
Other leukemia	1242 (4)
CML	2491 (8)
MDS/MPN	6499 (22)
Other acute leukemia	228 (<1)
NHL	3089 (10)
HD	478 (2)
PCD/MM	944 (3)
Other Malignancies	148 (<1)
Breast Cancer	29 (<1)
HCT-CI	
0	4151 (14)
1	1854 (6)
2	1866 (6)
3+	5787 (19)
NA, pre-TED not completed before 2008	16176 (54)
Missing	240 (<1)
Donor type	
HLA-identical sibling	13720 (46)
Well-matched unrelated	16354 (54)
Donor/recipient sex match	
M-M	11460 (38)
M-F	6940 (23)
F-M	5850 (19)
F-F	4868 (16)
Missing	956 (3)
Donor/recipient CMV serostatus	
+/+	9596 (32)
+/-	3172 (11)
-/+	8106 (27)
-/-	8041 (27)
Missing	1159 (4)
Graft source	

Characteristic	N (%)
Bone marrow	7177 (24)
Peripheral blood	22897 (76)
Conditioning regimen intensity	
MAC	17926 (60)
RIC	7797 (26)
NMA	2853 (9)
Missing	1498 (5)
GVHD prophylaxis	
No GVHD prophylaxis	311 (1)
Ex-vivo T-cell depletion	700 (2)
CD34 selection	640 (2)
Post-CY + other(s)	409 (1)
Post-CY alone	55 (<1)
TAC + MMF +- other(s) (except post-CY)	3552 (12)
TAC + MTX +- other(s) (except MMF, post-CY)	11097 (37)
TAC + other(s) (except MMF, MTX, post-CY)	1276 (4)
TAC alone	653 (2)
CSA + MMF +- other(s) (except post-CY)	2572 (9)
CSA + MTX +- other(s) (except MMF, post-CY)	6922 (23)
CSA + other(s) (except MMF, MTX, post-CY)	618 (2)
CSA alone	932 (3)
Other(s)	302 (1)
Missing	35 (<1)
ATG/Campath	
ATG + CAMPATH	7 (<1)
ATG alone	6535 (22)
CAMPATH alone	1183 (4)
No ATG or CAMPATH	21932 (73)
Missing	417 (1)
Year of transplant	
2000	1763 (6)
2001	1818 (6)
2002	1901 (6)
2003	1876 (6)
2004	2367 (8)
2005	2428 (8)

Characteristic	N (%)
2006	2325 (8)
2007	1865 (6)
2008	1767 (6)
2009	1638 (5)
2010	1051 (3)
2011	709 (2)
2012	730 (2)
2013	1482 (5)
2014	1963 (7)
2015	1719 (6)
2016	1510 (5)
2017	1162 (4)
Median follow-up of survivors (range), months	74 (3-221)

Source: November 2018 CRF retrieval

Proposal: 1811-124

Title:
Second allogeneic hematopoietic cell transplantation for primary graft failure: effect of conditioning regimen, graft source and GVHD prophylaxis on outcome.

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Specific aims:

- To study the effect of conditioning regimen on outcome of second hematopoietic cell transplantation (HCT) for primary graft failure.
- To assess impact of GVHD prophylaxis regimen, primary disease, and stem cell source in outcomes after second HCT for primary graft failure

Scientific justification:
Question:
Second allogeneic hematopoietic cell transplantation for primary graft failure: does the choice of conditioning regime, GVHD prophylaxis, or graft source affect outcome?
Literature:
While hematopoietic stem cell transplantation (HCT) has become safer with improved outcomes, graft failure (GF) still occurs with an incidence of 5–30% (1). Strategies to successfully re-transplant such patients are of high priority as primary GF carries high mortality without second transplant. Second transplants for GF have used both myeloablative (MA) and non-myeloablative (NMA)/reduced intensity conditioning (RIC) regimens and various hematopoietic stem cell sources.
A prior CIBMTR study (2) looks at outcomes of second transplants for primary graft failure in 122 patients transplanted between 1990 to 2005, but did not report effect of conditioning regimens, GVHD prophylaxis or stem cell source on outcome (though it compared same vs different donor, fresh vs cryopreserved cells, no conditioning vs some conditioning strategies and effect of cell dose)**.** The reported outcomes after second HCT are wide-ranging, with overall survival (OS) ranging from 11 to 70% (1,3). Studies in the setting of thalassemia major (4) and hematological malignancies (5) have reported that conditioning regimen used for second transplant and use of TBI as part of the conditioning regime can affect the outcome. Additionally, the use of PBSC has been reported in one small series to result in faster engraftment (6) in patients undergoing second transplants. This has prompted us to propose this study to evaluate the effect of conditioning regimens, GVHD prophylaxis and stem cell source used for salvage HCT on outcomes (in a more recent cohort of patients from 2006-2017 compared to the initial CIBMTR study).

Patient eligibility population:
Data on patients who have undergone their second HLA matched or mismatched HCT for primary graft failure from 2006-2017 will be analyzed, to avoid overlap with the prior CIBMTR study which looked at outcomes of second transplant for primary graft failure in patients transplanted from 1990 to 2005. Analysis of more recent data is relevant in this scenario as supportive care and conditioning regimes have improved considerably in the last 2 decades.

Data will include the following:

- Patient characteristics-age, gender, prior immune-suppressive therapy/chemotherapy
- Disease characteristics-malignant/non-malignant
- Year of Transplant
- Conditioning regimen for first transplant (NMA vs RIC vs MA)
- Duration from first transplant to second transplant for primary graft failure
- Autologous recovery after primary graft failure-yes/no
- Donor characteristics for second transplant including degree of match and donor-recipient gender
- Conditioning regime for second transplant (NMA vs RIC vs MA)
- Stem cell source (BM/PB) for second transplant
- Use of fresh vs frozen cells
- CD34 dose for second transplant
- GVHD prophylaxis, use of T cell depletion strategies for either transplant
- Neutrophil recovery
- Platelet recovery
- Acute GVHD
- Chronic GVHD
- Relapse/ graft failure
- Mortality/Survival data

Study design:

The CIBMTR data base would provide data for the variables of interest. A cohort of patients who have undergone second HSCT for primary graft failure from 2006-2017 will be analyzed. By comparing the difference in early and late outcomes using different conditioning regimes, it will be possible to determine whether choice of conditioning regime plays a role in survival. If a non-myeloablative regimen has similar outcome to a higher intensity regimen, then that would justify use of less toxic regimens in patients undergoing second transplant.

Statistical methods:

Time to event analyses will be done using the Kaplan-Meier method. Cox proportional hazards regression model will be used for identifying variables which affect survival and calculating hazard ratios. Variables of interest include: patient age, gender, disease diagnosis, prior chemo or IST, donor match type and characteristics for first and second transplant, autologous recovery before second transplant, conditioning regimes used for first and second transplants, GVHD prophylaxis for first and second transplants including use of T cell depletion strategies, year of transplant, active infections at time of second transplant, CD34 dose for first and second transplant, fresh or frozen cells used, bone marrow or peripheral blood as graft source. Other variables like engraftment data, acute and chronic GVHD, relapse, infectious complications post-transplant would also be captured.

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Characteristics of patients who received 2nd alloHCT for primary graft failure, transplanted from 2006-2017

Characteristic	N (%)
Number of patients	1097
Number of centers	205
Age, median (range), years	25 (<1-77)
Age group	
0-9	341 (31)
10-19	165 (15)
20-29	84 (8)
30-39	77 (7)
40-49	93 (8)
50-59	168 (15)
60-69	150 (14)
≥70	19 (2)
Sex	
Male	678 (62)
Female	419 (38)
Race	
Caucasian	725 (66)
African-American	156 (14)
Asian	65 (6)
Pacific islander	5 (<1)
Native American	11 (1)
Other	2 (<1)
More than one race	11 (1)
Missing	122 (11)
Ethnicity	
Hispanic or Latino	137 (12)
Not Hispanic or Latino	759 (69)
NA, non-resident of USA	178 (16)
Missing	23 (2)
Karnofsky/Lansky performance score	
90-100	421 (38)
< 90	529 (48)
Missing	147 (13)

Characteristic	N (%)
Disease	
AML	240 (22)
ALL	51 (5)
Other leukemia	21 (2)
CML	49 (4)
MDS/MPN	200 (18)
Other acute leukemia	11 (1)
NHL	37 (3)
HD	6 (<1)
PCD/MM	9 (<1)
Other malignancy	1 (<1)
SAA	136 (12)
Inherited abnormality of erythrocyte differentiation or function	123 (11)
SCID or other immune system disorder	117 (11)
Inherited abnormality of platelets	2 (<1)
Metabolic disorder	60 (5)
Histiocytic disorder	19 (2)
Autoimmune disease	2 (<1)
Other, specify	13 (1)
HCT-CI	
0	281 (26)
1	122 (11)
2	73 (7)
3+	250 (23)
NA, pre-TED not completed before 2008	364 (33)
Missing	7 (<1)
Donor type (current transplant)	
HLA-identical sibling	159 (14)
Other related	295 (27)
Well-matched unrelated	166 (15)
Partially-matched unrelated	76 (7)
Mis-matched unrelated	11 (1)
Multi-donor	10 (<1)
Unrelated (matching TBD)	215 (20)
Cord blood	161 (15)
Missing	4 (<1)

Characteristic	N (%)
Donor type (first alloHCT)	
HLA-identical sibling	176 (16)
Other related	213 (19)
Well-matched unrelated	260 (24)
Partially-matched unrelated	117 (11)
Mis-matched unrelated	14 (1)
Multi-donor	7 (<1)
Unrelated (matching TBD)	55 (5)
Cord blood	254 (23)
Missing	1 (<1)
Donor/recipient sex match	
M-M	302 (28)
M-F	143 (13)
F-M	175 (16)
F-F	135 (12)
CB - recipient M	101 (9)
CB - recipient F	60 (5)
Missing	181 (16)
Donor/recipient CMV serostatus	
+/+	359 (33)
+/-	80 (7)
-/+	194 (18)
-/-	129 (12)
CB - recipient +	96 (9)
CB - recipient -	48 (4)
CB - recipient CMV unknown	17 (2)
Missing	174 (16)
Graft source	
Bone marrow	240 (22)
Peripheral blood	695 (63)
Umbilical cord blood	161 (15)
Missing	1 (<1)
Conditioning regimen intensity (current transplant)	
MAC	291 (27)
RIC/NMA	645 (59)
Missing	161 (15)

Characteristic	N (%)
Conditioning regimen intensity (first alloHCT)	
MAC	545 (50)
RIC/NMA	520 (47)
Missing	32 (3)
GVHD prophylaxis	
Ex-vivo T-cell depletion	33 (3)
CD34 selection	98 (9)
Post-CY + other(s)	134 (12)
Post-CY alone	1 (<1)
TAC + MMF +- other(s) (except post-CY)	169 (15)
TAC + MTX +- other(s) (except MMF, post-CY)	111 (10)
TAC + other(s) (except MMF, MTX, post-CY)	36 (3)
TAC alone	60 (5)
CSA + MMF +- other(s) (except post-CY)	169 (15)
CSA + MTX +- other(s) (except MMF, post-CY)	68 (6)
CSA + other(s) (except MMF, MTX, post-CY)	40 (4)
CSA alone	48 (4)
Other(s)	35 (3)
Missing	95 (9)
ATG/Campath	
ATG alone	370 (34)
CAMPATH alone	129 (12)
No ATG or CAMPATH	444 (40)
Missing	154 (14)
Year of transplant	
2006-2008	186 (17)
2009-2011	170 (15)
2012-2014	270 (25)
2015-2017	471 (43)
Median follow-up of survivors (range), months	36 (3-143)

Source: November 2018 TED retrieval

Proposal: 1811-160

Title:
Exploring Ensemble Machine Learning Methods to Better Predict Veno-Occlusive Disease Following Allogeneic Hematopoietic Stem Cell Transplantation

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Hypothesis:
We hypothesize that ensemble machine learning (ML) methods can be used to make robust predictions of the occurrence of veno-occlusive disease (VOD) in patients receiving allogeneic hematopoietic cell transplant (alloHCT) prior to a clinical diagnosis. This prediction model will allow early interventions aimed at reducing the occurrence of VOD that include transplant modifications in conditioning regimens, defibrotide prophylaxis and/or preemptive defibrotide treatment in cases where the benefit of defibrotide prophylaxis may not be obvious.

Specific aims:
To determine if ensemble machine learning methods to predict VOD is feasible. Problems in the prediction of transplant related complications arise from the non-linear, complex relationship between the outcome and patient and treatment covariables. While some specific patient populations have been recognized for being at much higher risk to develop VOD, a significant portion of patients who develop VOD do not have any individual characteristics that indicate high risk, requiring risk assessment to be made based on multiple weaker predictive features. In addition, the risk of developing VOD is further adjusted by minute changes in biometric measures (weight, fluid balance) as well as laboratory testing (T. bili, serum creatinie) early in the post-transplant course. Ensemble machine learning (ML) approaches are a suite of methods designed to tackle classification and regression problems. They represent an alternative to classical linear and generalized models and have been shown to provide more robust predictive models with complex, high-dimensional datasets.[1] They rely on the collective strength of simple, weak models built on different subsets of data, allowing a more precise and personalized risk prediction. A transplant course provides an ideal test case to explore the use of ML techniques to create predictive models of adverse outcomes, e.g. VOD. Each transplant goes through similar distinct phases where a patient's risk of developing a given complication (e.g. VOD) is modified by specific events including primary diagnosis, treatment prior to transplant, pre-transplant liver injury, conditioning regimen, stem cell source, GVHD prophylaxis and other hepatotoxic/nephrotoxic agents, all of which are predictive features for VOD.

Scientific impact:
The impact of this study is focused on identifying patients at high risk of developing VOD so that disease modifying interventions can occur prior to the clinical diagnosis of VOD. The long-term significance includes improving morbidity and mortality secondary to VOD among alloHCT recipients. Furthermore, the use of this prediction model may be more cost-effective than using defibrotide as prophylaxis at the time of transplant conditioning or as treatment after VOD onset. Lastly, if this prediction model for VOD is successful, this may lead to the development of other ML methods to more accurately predict other transplant-related complications.

Scientific justification:

VOD is a transplant-related complication associated with high risk for both mortality and morbidity.[2] VOD is a clinical diagnosis, conventionally made by either the modified Seattle criteria or the Baltimore Criteria. However, many criteria used are subjective, operator-dependent and confounded by underlying diagnosis.

Recent published work from EBMT on VOD have focused expanding the diagnostic criteria aimed at improving the VOD diagnosis in consideration of difference between pediatric and adult patients with the goal of improving timely intervention with defibrotide.[3,4] The new diagnostic criteria are summarized in the table below (Table 1). While the new EBMT diagnostic criteria for VOD are likely to capture more VOD cases, it is still a reactive approach instead of a preemptive one. Many of the expended criteria are still fairly subjective and likely to be inconsistent between clinicians. The major problem with this reactive approach is that by the time the diagnostic criteria are met, the disease process is likely to have progressed to the stage where the risk for morbidity and mortality is too high.

Table 1.

Pediatrics	Adults
• No limitation of time of onset • Two or more of the following o Unexplained consumptive and transfusion-refractory thrombocytopenia o Otherwise unexplained weight gain on three consecutive days despite the use of diuretics or weight gain >5% above baseline value o Hepatomegaly o Ascites o Rising bilirubin from baseline value on 3 consecutive days or bilirubin ≥2 mg/dL within 72 hours	• Classical VOD—Baltimore criteria in the first 21 days • Late VOD—21 days after HSCT • Classical VOD, or • Histologically proven VOD, or • Two or more of the following o Bilirubin ≥ 2 o Painful hepatomegaly o Weight gain > 5% o Ascites • AND hemodynamical or/and US evidence of the SOS/VOD

While defibrotide is an effective treatment, its optimal use remains to be determined. There is evidence suggesting that earlier treatment after diagnosis improves survival.[5] On the other hand, defibrotide prophylaxis is currently in trial and its efficacy or cost value remains a subject of debate.[6,7] It would seem that the optimal timing of initiating defibrotide therapy lies somewhere between the beginning of transplant and the VOD diagnosis. Accurate real-time prediction of those at increasing risk of developing VOD would likely yield increased benefit and cost-effectiveness with early preemptive defibrotide treatment. Predictive models of VOD and other transplant related complications that incorporate early post-transplant information are very much need to minimize post-transplant complications beyond our current practices.

Recent studies on VOD have shown a strong interest toward a more predictive approach of this transplant complication. Rocker et al. evaluated different parameters in the 7 days preceding VOD in a single center and found that platelet refractoriness, higher serum tacrolimus level and higher serum creatinine level are associated with higher risk of VOD. This is an interesting example where the investigator chose to focus on predicting VOD prior to the clinical diagnosis using Cox regression analysis

in which a backward selection method was used to identify the final set of risk factors.[8] Strouse et al have also constructed risk score based model predicting VOD that demonstrated strong discriminatory ability to identify high-risk cohort using methodologies including multivariate analysis and maximum likelihood estimates.[9] These works are largely based on traditional logistic regression methods, which may have limitations when modeling complex system with nonparametric relationships, which is more reflective of alloHCT biology and physiology.

ML methods, e.g. random forests or other decision tree ensembles, are used across a range of different disciplines to obtain robust predictive models in nonparametric regression problems[10]. Ensemble ML methods have been studied in recent medical research, with promising results found across clinical, translational and basic science research; including applications predicting post-traumatic stress disorder, Parkinson's diseases, gene-gene interaction in colorectal cancer and methylation sites in prostate cancer.[11-14]

We propose to explore the use of ML methods to forecast the occurrence of VOD based on a large set of potential predictive features. We will start by building models based on the entire suite of features, then use this in a modeling framework that allows forecasting of VOD outcome based on different scenarios of treatment over the transplant course.

Patient eligibility population:

All allogeneic transplant from 2008 to present.

Data requirements :

Forms:

- 2000
- 2100
- 2400
- 2450

Variables to be described and/or analyzed:

Patient related (pre-transplant characteristics):

- Age
- Patient gender: male vs. female
- Race/ethnicity: White vs. African American vs. Hispanics vs. others
- Obesity
- Clinically significant coexisting diseases or organ impairment (renal and hepatic)
- Organ function prior to the preparative regimen (serum creatinine, T. bili, AST, ALT)
- Performance Karnofsky/Lansky score
- HCT comorbidity index: 0-1 vs. 2-3 vs. 4+

Disease related (pre-transplant characteristics):

- Nonmalignant diseases including severe aplastic anemia, hemophagocytic syndromes, sickle cell disease, thalassemia, congenial amegakaryocytic thrombocytopenia, severe combined immunodeficiency, T cell immunodeficiency, severe congenital neutropenia, chronic granulomatous disease, mucopolysaccharoidoses, globoid cell leukodystrophy, metachromatic leukodystrophy, cerebral X-linked aderenoleukodystrophy, osteopetrosis, fanconi anemia, dyskeratosis congenital and other DNA repair defects

- Malignant diseases including leukemia, lymphoma, MDS, MPNs
    - Remission status (CR#)
    - Prior high-risk chemotherapy drugs (gemtuzumab, inotuzumab, etc)

Transplant related:

- Graft Type: BM vs. PB vs. Cord, graft manipulation if used (e.g. CD34 selection.)
- Number of allo-transplant—first, second, etc.
- Conditioning regimen
    - Drug/drug combination used (number of alkylating agent used)
    - Drug dose given
    - Total Body Radiation dose delivered
    - GVHD prophylaxis used
    - Serotherapy used

Outcomes

- VOD—Yes or no, post-transplant day of VOD diagnosis

Study design:

We will adopt the data analysis strategy outlined in Papini's work since the prediction model of posttraumatic stress disorder resembles VOD well.13 Predictive features are likely to include age, primary diagnosis, performance score, disease status (for malignancies), prior treatment, pretransplant hepatic and renal function, conditioning regimen, and GVHD prophylaxis. Categorical and continuous variables will be coded accordingly. We will first perform a preliminary analysis of a representative subset of data using regression models (logistic or Cox regression) to identify VOD predictors. We plan to expand on the prior work by Strouse et al for this step. This preliminary model will be used to validate previously reported predictors and reduce the number of features by eliminating variables with non-significant predictive value, by minimizing the AIC. The final model will provide a baseline traditional method to compare the ML methods.

We will then produce models of VOD occurrence based on ensemble ML methods, including random forests and gradient boosted decision trees. In parallel, we will also investigate the use of Bayesian Additive Regression Trees, to help in the selection of model hyperparameters. Models will be based on the full set of potential predictive features, removing only those with negligible variance.

Model predictive skill will be tested using cross-validation for both the traditional and ML methods. We will use a nested cross-validation, with a 5-fold cross-validation used for both inner and outer cross-validation nests. The inner corss-validation will be used to tune model parameters and the outer cross-validation used to estimate predictive skill on independent data. This will be repeated 10 times under different randomizations to ensure that model prediction metrics are not dependent on a single chance data partition and to estimate a confidence interval around the mean of these prediction metrics based on the observed variability among the 50 outer cross-validation resamples. Model accuracy will be tested using the area under the curve (AUC) score of the receiver operator curve, which incorporates sensitivity and specificity. Feature importance and partial dependency will also be analyzed.

We will then build on these results by establishing a framework to allow 'scenario' testing with the method that has the best predictive skill. This will take the pre-transplant characteristics for a given patient and produce the probability of VOD occurrence under a set of transplant options, to predict the expected VOD outcome if that course of treatment is followed. This same approach can also be iterated over a set of different transplant options, in order to estimate which has the lowest risk of VOD onset.

If time permits, we will also investigate the use of these method in a dynamic framework, where post-transplant information can be used to signal an increased risk of VOD. In addition to the pre-transplant and transplant variables described above, this will require, if feasible, additional data on time since

transplant, daily weight, fluid balance, T. bili, serum creatinine, platelet count and calcineurin inhibitor level 7 days prior to VOD diagnosis. We will calibrate and validate an ML model on this dataset, which may then be subsequently used for prediction of the changing risk of VOD following transplantation. Initial predictions can be made based on pre-transplant and transplant features, and the value of the post-transplant variables over the preceding 7 days. Subsequently, updated risk predictions can be made every day, as new values of the post-transplant variables are monitored and recorded.
We will access for Center for High Performance Computing at University of Utah for data analysis and computer modelling, as well as the code base developed in Dr. Brewer's group for various machine learning applications.

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Characteristics of patients who received first alloHCT between from 2008-2017

Characteristic	N (%)
Number of patients	26557
Number of centers	269
Age, median (range), years	49 (<1-88)
Age group	
0-9	3313 (12)
10-19	2409 (9)
20-29	2232 (8)
30-39	2248 (8)
40-49	3350 (13)
50-59	5608 (21)
60-69	6166 (23)
≥70	1231 (5)
Sex	
Male	15620 (59)
Female	10937 (41)
Race	
Caucasian	20632 (78)
African-American	2470 (9)
Asian	1514 (6)
Pacific islander	133 (<1)
Native American	179 (<1)
Other	1 (<1)
More than one race	275 (1)
Missing	1353 (5)
Ethnicity	
Hispanic or Latino	2840 (11)
Not Hispanic or Latino	21114 (80)
NA, non-resident of USA	2197 (8)
Missing	406 (2)
Karnofsky performance score	
90-100	17030 (64)
< 90	8978 (34)
Missing	549 (2)

Characteristic	N (%)
Disease	
AML	9113 (34)
ALL	3448 (13)
Other leukemia	775 (3)
CML	791 (3)
MDS/MPN	6198 (23)
Other acute leukemia	279 (1)
NHL	1803 (7)
HD	346 (1)
PCD/MM	396 (1)
Other malignancy	14 (<1)
SAA	1341 (5)
Inherited abnormality of erythrocyte differentiation or function	914 (3)
SCID or other immune system disorder	927 (3)
Metabolic disorder	198 (<1)
Histiocytic disorder	13 (<1)
Autoimmune disease	1 (<1)
HCT-CI	
0	9385 (35)
1	3623 (14)
2	3131 (12)
3+	9678 (36)
NA, pre-TED not completed	341 (1)
Missing	399 (2)
Donor type	
HLA-identical sibling	6498 (24)
Twin	225 (<1)
Other related	3063 (12)
Well-matched unrelated	9027 (34)
Partially-matched unrelated	2050 (8)
Mis-matched unrelated	135 (<1)
Multi-donor	48 (<1)
Unrelated (matching TBD)	300 (1)
Cord blood	5069 (19)
Missing	142 (<1)
Donor/recipient sex match	

Characteristic	N (%)
M-M	8299 (31)
M-F	4998 (19)
F-M	4328 (16)
F-F	3637 (14)
CB - recipient M	2848 (11)
CB - recipient F	2221 (8)
Missing	226 (<1)
Donor/recipient CMV serostatus	
+/+	7269 (27)
+/-	2350 (9)
-/+	5907 (22)
-/-	5353 (20)
CB - recipient +	3197 (12)
CB - recipient -	1796 (7)
CB - recipient CMV unknown	76 (<1)
Missing	609 (2)
Graft source	
Bone marrow	5525 (21)
Peripheral blood	15961 (60)
Umbilical cord blood	5069 (19)
Missing	2 (<1)
Conditioning regimen intensity	
MAC	14059 (53)
RIC	7292 (27)
NMA	4259 (16)
Missing	947 (4)
GVHD prophylaxis	
No GVHD prophylaxis	551 (2)
Ex-vivo T-cell depletion	308 (1)
CD34 selection	647 (2)
Post-CY + other(s)	2076 (8)
Post-CY alone	63 (<1)
TAC + MMF +- other(s) (except post-CY)	4413 (17)
TAC + MTX +- other(s) (except MMF, post-CY)	8997 (34)
TAC + other(s) (except MMF, MTX, post-CY)	1408 (5)
TAC alone	572 (2)

Characteristic	N (%)
CSA + MMF +- other(s) (except post-CY)	3698 (14)
CSA + MTX +- other(s) (except MMF, post-CY)	2343 (9)
CSA + other(s) (except MMF, MTX, post-CY)	605 (2)
CSA alone	371 (1)
Other(s)	395 (1)
Missing	110 (<1)
ATG/Campath	
ATG + CAMPATH	16 (<1)
ATG alone	8132 (31)
CAMPATH alone	1269 (5)
No ATG or CAMPATH	16936 (64)
Missing	204 (<1)
Year of transplant	
2008	3374 (13)
2009	3109 (12)
2010	1955 (7)
2011	1429 (5)
2012	1473 (6)
2013	2725 (10)
2014	3495 (13)
2015	3356 (13)
2016	3124 (12)
2017	2517 (9)
Median follow-up of survivors (range), months	46 (3-128)

Source: November 2018 CRF retrieval

Table 2. 100-day incidence of VOD in proposed population

	Study Population (N = 26557)	
Outcomes	**Number Evaluable**	**Prob (95% CI)**
VOD	26225	
100-day		3 (3-3)%

Proposal 1811-189

Title:
Analysis of Comorbidity associated Toxicity at a Regimen based Level

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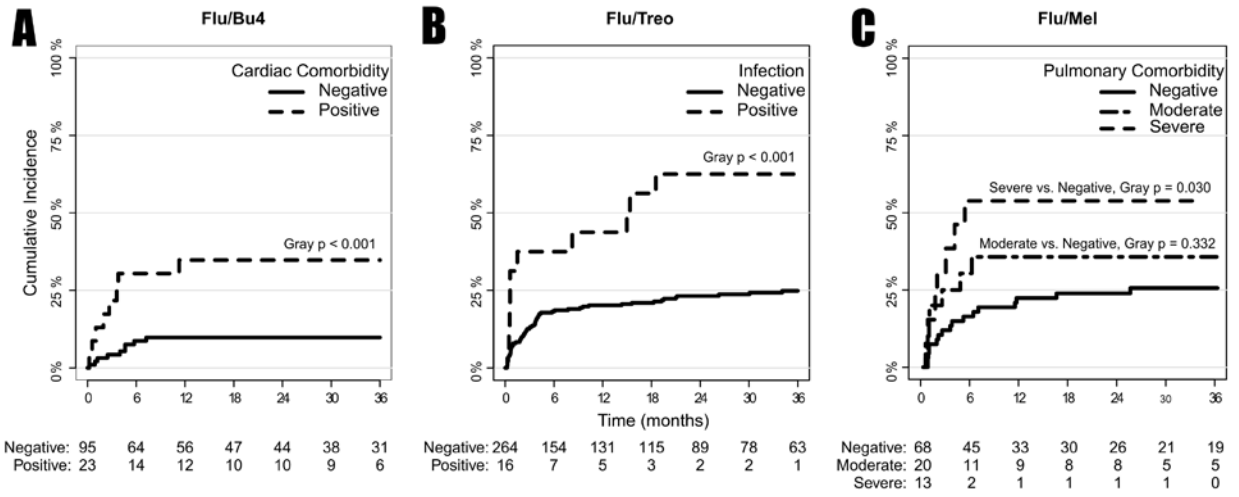
Hypothesis:
Given the differing mechanisms and toxicity profiles of the conditioning agents administered prior to allogeneic hematopoietic stem cell transplantation (HSCT)[1,2] and based on preliminary results,[3] we hypothesized that the hazard of comorbidities is exerted in a regimen-specific manner.

Specific aims:
- Evaluation of the non-relapse mortality (NRM) hazard (primary outcome) associated with pre-transplantation comorbidities in predefined conditioning regimens
- Evaluation of the NRM hazard associated with pre-transplantation comorbidities in conditioning intensity categories (non-myeloablative, reduced intensity conditioning, myeloablative conditioning)
- Explore toxicities associated with specific conditioning regimen stratified by preexisting comorbidities

Scientific justification:
Comorbidities have long been understood to be an integral component in the evaluation of stem cell transplantation candidates. Typically, the cumulative comorbidity burden of comorbidities, as measured by the HCT-CI, is used as a marker of risk for non-relapse mortality.[4] Such an approach has been well validated, but may lead to loss of important prognostic information. Since individual conditioning regimens carry unique toxicity profiles and act through differing mechanism, it is likely that the risk of regimen-associated toxicity (RAT) is dependent on quality and not only the quantity of comorbidities. In a recent single center retrospective analysis including 875 patients who underwent allogeneic HSCT,[3] our group has demonstrated a differential effect of pre-transplantation comorbidities within a variety of conditioning regimens. For instance, severe pulmonary comorbidity (per HCT-CI definition) had a detrimental impact in patients receiving fludarbine and melaphalane but not in those conditioned with fuldarabine and treosulfan (Figure). Findings were consistent in a univariate and multivariable analysis.



Given the theoretical considerations of the interaction between regimen and comorbidities discussed above and our preliminary data, there is compelling rational to further study the hypothesis that RAT are exerted in a regimen specific manner.

Patient eligibility population:

- Adults (age≥18 years)
- Transplantation from 2006-2016
- 1st allogeneic HSCT in CR1
- Disease: acute myeloid leukemia and acute lymphoblastic leukemia
- Donor: HLA matched sibling donors, HLA matching unrelated donors, Haploidentical donor
- Conditioning regimens: Flu/Bu2, Flu/Bu4. CY/TBI, BU/CY, Flu/Mel, Flu/Treo, FLU/TBI, Theiothepa [plus other common CR regimens] VP16-TBI….haplo conditioning regimens
- Graft source: bone marrow and peripheral blood

Data requirements:

- Recipients
    - Demographic: age, sex, ethnicity
    - Comorbidities as defined by HCT-CI
    - HCT-CI score
    - If available: ejection fraction, creatinine, body mass index, AST, ALT, bilirubin, pulmonary function tests
    - Recipient CMV serostatus
- Disease
    - Diagnosis
    - Disease risk
    - Remission status at transplantation
    - Time from diagnosis to transplantation
- Donor
    - Donor type
    - Graft source
    - Donor sex
    - Donor CMV serostatus
- Transplantation

  - Transplantation year
  - Conditioning regimen
  - Conditioning regimen intensity by category
  - GVHD prophylaxis
  - T-cell depletion strategy
- Outcomes
  - Overall survival, non-relapse mortality, relapse
  - Cause of death
  - Neutrophil and platelet engraftment
  - Acute and chronic GVHD
  - GRFS

Study design:
Retrospective analysis of the CIBMTR registry data. Association of comorbidities with NRM and additional outcomes will be evaluated in a univariate and multivariable analysis (cause specific Cox) in the entire population and within each regimen and within conditioning intensity groups. The analysis will also be stratified by age groups (depending on the distribution of age),disease, and donor type. Covariates included in the multivariable analysis: age, sex, disease risk, time from diagnosis to transplantation, donor type, recipient-donor sex match, recipient-donor CMV status, GVHD prophylaxis, and T-cell depletion strategy.
Additional analyses:

- Evaluation of comorbidities impact by conditioning intensity groups (NMA, RIC, MAC)
- If available, association between contentious measure of comorbidities (ejection fraction, creatinine, BMI, etc) and NRM using cubic splines.
- Cause of death associated with each comorbidity within each regimen

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Characteristics of adults (≥18) receiving first alloHCT for AML or ALL in CR1 transplanted between 2006-2017

Characteristics	N (%)
Number of patients	5246
Number of centers	218
Age, median (range), years	52 (18-78)
Age group	
18-29	725 (14)
30-39	619 (12)
40-49	1015 (19)
50-59	1470 (28)
60-69	1222 (23)
≥70	195 (4)
Sex	
Male	2848 (54)
Female	2398 (46)
Race	
Caucasian	4391 (84)
African-American	268 (5)
Asian	354 (7)
Pacific islander	12 (<1)
Native American	22 (<1)
Other	7 (<1)
More than one race	14 (<1)
Missing	178 (3)
Ethnicity	
Hispanic or Latino	399 (8)
Not Hispanic or Latino	4488 (86)
NA, non-resident of USA	281 (5)
Missing	78 (1)
Karnofsky performance score	
90-100	3325 (63)
< 90	1837 (35)
Missing	84 (2)

Characteristics	N (%)
Disease	
AML	3987 (76)
ALL	1259 (24)
HCT-CI	
0	1252 (24)
1	638 (12)
2	668 (13)
3+	1704 (32)
NA, pre-TED not completed before 2008	921 (18)
Missing	63 (1)
Donor type	
HLA-identical sibling	2050 (39)
Haploidentical	450 (9)
Well-matched unrelated	2746 (52)
Donor/recipient sex match	
M-M	1898 (36)
M-F	1417 (27)
F-M	930 (18)
F-F	963 (18)
Missing	38 (<1)
Donor/recipient CMV serostatus	
+/+	1731 (33)
+/-	565 (11)
-/+	1579 (30)
-/-	1278 (24)
Missing	93 (2)
Graft source	
Bone marrow	935 (18)
Peripheral blood	4311 (82)
Conditioning regimen intensity	
MAC	3320 (63)
RIC	1331 (25)
NMA	471 (9)
Missing	124 (2)
GVHD prophylaxis	

Characteristics	N (%)
No GVHD prophylaxis	34 (<1)
Ex-vivo T-cell depletion	87 (2)
CD34 selection	120 (2)
Post-CY + other(s)	415 (8)
Post-CY alone	34 (<1)
TAC + MMF +- other(s) (except post-CY)	712 (14)
TAC + MTX +- other(s) (except MMF, post-CY)	2455 (47)
TAC + other(s) (except MMF, MTX, post-CY)	311 (6)
TAC alone	111 (2)
CSA + MMF +- other(s) (except post-CY)	254 (5)
CSA + MTX +- other(s) (except MMF, post-CY)	577 (11)
CSA + other(s) (except MMF, MTX, post-CY)	36 (<1)
CSA alone	54 (1)
Other(s)	44 (<1)
Missing	2 (<1)
ATG/Campath	
ATG alone	1116 (21)
CAMPATH alone	108 (2)
No ATG or CAMPATH	3995 (76)
Missing	27 (<1)
Year of transplant	
2006	520 (10)
2007	456 (9)
2008	530 (10)
2009	459 (9)
2010	367 (7)
2011	206 (4)
2012	177 (3)
2013	454 (9)
2014	630 (12)
2015	567 (11)
2016	532 (10)
2017	348 (7)
Median follow-up of survivors (range), months	51 (3-149)

Source: November 2018 CRF retrieval

Proposal: 1811-35/1811-167

Title:
Outcomes of Patients with Inflammatory Bowel Disease After Hematopoietic Cell Transplantation

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Hypothesis:
- Outcomes after allogeneic (allo-HCT) and autologous (auto-HCT) hematopoietic cell transplantation will be comparable among patients with inflammatory bowel disease (IBD) as compared to matched patients without IBD undergoing HCT
- IBD activity will improve after HCT, including higher remission rates and lower need for post-transplant immunosuppressive therapy

Specific aims:
- Aim 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.

- Aim 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.

Scientific impact:
Inflammatory bowel disease (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), is characterized by chronic, relapsing intestinal inflammation that affects over 1.5 million people in the USA. IBD is considered an adverse risk factor for HCT yet there is a paucity of data on general and IBD-specific outcomes among patients with IBD who undergo HCT. Furthermore, both allo-HCT and auto-SCT have been seen to benefit patients' underlying IBD. Given the complex interplay between HCT and IBD, further evaluation and characterization of these patients' clinical outcomes is warranted via a large registry analysis using CIBMTR data.

Scientific justification:
Inflammatory bowel diseases (IBD), and immunosuppressive therapies used to manage IBD, are associated with increased risk of hematologic malignancies.[1-5] Comorbid IBD is also considered an adverse risk factor for patients undergoing hematopoietic stem cell transplantation (HCT). In the development of the hematopoietic cell transplantation-specific comorbidity index (HCT-CI), IBD was found to convey a hazard ratio (HR) of 1.3 for 2-year NRM.[6] However, the overall prevalence of IBD in the derivation cohort of 1,055 patients was low (1%) and the true impact of comorbid IBD on HCT has not been well-studied.
Few studies have investigated the hematologic outcomes after allo-HCT in patients with IBD. In a retrospective review of the national French SCT database, 18 IBD patients who underwent allo-HCT between 2004-2015 were compared to 50 age- and disease-matched controls.[7] After a median follow-up

of 33 months, they found no differences in the cumulative incidence of acute or chronic GVHD. There was a trend towards higher NRM at 48 months in IBD patients as compared to matched controls (19% vs 11%, respectively, p=0.067), but no difference in OS at 48 months (59% vs 60%, p=0.56). Based on these findings, they concluded that the negative impact of comorbid IBD should be reduced in considering transplant candidacy.

In contrast, a recent cross-sectional study using the Nationwide Inpatient Sample database from 1998-2011 compared the outcomes of inpatient auto-HCT and allo-HCT patients with different co-morbid immune-mediated inflammatory diseases (IMID) to matched non-IMID controls.[8] On review of over 36,000 HCT patients, the cohort of IMID patients included a total of 78 patients with UC and 72 patients with CD. The study found that patients with UC were at higher risk for adverse outcomes, including higher inpatient peri-HCT mortality related to bacteremia, opportunistic infections, intubation and death as compared to matched controls and other IMIDs. Limitations of this large analysis include its focus on inpatient outcomes and lack of longitudinal follow-up. A more comprehensive analysis of the CIBMTR database would provide baseline donor information as well as long term follow up regarding post-HCT outcomes that could be used to determine the impact of IBD on patients undergoing HCT. Furthermore, there are potential benefits of HCT to patients' underlying IBD. Case reports have noted instances of sustained clinical remission of IBD after patients undergo allo-HCT[9-12] and auto-HCT has been used as salvage therapy for patients with refractory Crohn's disease.[13-15]

Patient eligibility population:

- Individuals with IBD (Crohn's Disease [ICD10 K50] or Ulcerative colitis [ICD10 K51]) who underwent allo-HCT or auto-HCT between 2008-2016 for any indication.
- Matched cohort (3:1) of individuals without IBD who underwent allo-HCT or auto-HCT between 2008-2016.

Data requirements:

The collection of IBD-related pre- and post-HCT data will require contact with individual centers, with a focus on those centers with highest number of IBD patients undergoing HCT.

Patient-specific characteristics, including:

- Age at the time of HCT
- Gender
- Race
- Karnofsky performance status
- Hematopoietic cell transplantation-comorbidity index
- Disease type and classification
- Disease risk
- Disease status at the time of HCT (CR/CRu, PR, etc.)
- CMV serostatus

IBD-specific characteristics, including:

- Age at IBD diagnosis
- Montreal classification[16] of Crohn's disease and ulcerative colitis
- Pre and post-transplant labs, imaging, endoscopy and pathology reports
- Pre and post-transplant medical and surgical IBD management

Transplantation-specific characteristics, including:

- Conditioning regimen used
- Date of HCT
- GVHD prophylaxis regimen

Outcome measures, including:

- PFS and OS at 1, 3 and 5 years post-HCT
- Cumulative incidence of relapse
- Cumulative incidence and severity of acute and chronic GVHD
- Cumulative incidence of NRM at 1, 3 and 5 years post-HCT
- IBD outcomes post-transplant, including need for immunosuppressive therapy, IBD-related hospitalization, surgery
- CMV reactivation with end-organ involvement (if present)
- Adverse events, if available
- Cause of death

Study design:

This study is a retrospective analysis using observational CIBMTR registry data to identify a cohort of patients with IBD who underwent HCT, and to compare their outcomes to matched patients without IBD. 3:1 matching for control:IBD patients will be performed based on:

- Center
- Time period of HCT
- Gender
- Age
- Disease
- Disease risk (or DRI)
- Type of transplant (allo-HCT or auto-HCT)
- Conditioning type/intensity
- Disparity between donor and recipient
- Donor type
- Stem cell source
- CMV serostatus donor/recipient
- GVHD prophylaxis

Time-to-event analyses will be used to compare incidence of GVHD, NRM and PFS/OS. Acute GVHD will be censored at 100 days. NRM will be defined as death before disease relapse or progression. Death will be considered a competing event for GVHD, NRM and relapse and progression will be considered mutually competing risk. Survival distribution will be estimated using Kaplan-Meier methods and difference between/among groups will be tested using log rank. Group comparisons using stratified Cox proportional hazard model will be used for overall survival and stratified cause-specific proportional models for NRM and GVHD. Multivariable analysis for overall survival, non-relapse mortality, and relapse incidence will be performed on all patients in the cohort. Center effect will be adjusted in the final multivariable models.

Non-CIBMTR Data Source:

- IBD baseline and outcomes data from individual centers

The collection of IBD-specific data will be an important adjunct to this study, to allow for more detailed pre-transplant risk assessment and stratification and for evaluation of IBD-specific outcomes post-transplantation. However, if data acquisition from outside CIBMTR is not feasible, this study is still of significant importance to patients with IBD to properly advise them on the risks, benefits and likely outcomes of HCT.

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Characteristics of patients who received first alloHCT or autoHCT from 2008-2016, split by IBD diagnosis pre-transplant

	IBD pre-transplant N (%)	
Characteristic	**No**	**Yes**
Number of patients	174593	1555
Number of centers	411	219
Age, median (range), years	53 (<1-86)	56 (<1-78)
Age group		
0-9	13512 (8)	43 (3)
10-19	10056 (6)	61 (4)
20-29	13038 (7)	92 (6)
30-39	14091 (8)	122 (8)
40-49	23981 (14)	222 (14)
50-59	44348 (25)	463 (30)
60-69	46626 (27)	450 (29)
70+	8941 (5)	102 (7)
Sex		
Male	103303 (59)	825 (53)
Female	71290 (41)	730 (47)
Race		
Caucasian	125124 (72)	1354 (87)
African-American	14874 (9)	83 (5)
Asian	9515 (5)	31 (2)
Pacific islander	512 (<1)	1 (<1)
Native American	769 (<1)	5 (<1)
Other	2 (<1)	0
More than one race	736 (<1)	7 (<1)
Missing	23061 (13)	74 (5)
Ethnicity		
Hispanic or Latino	16284 (9)	68 (4)
Not Hispanic or Latino	131100 (75)	1356 (87)
NA, non-resident of USA	24997 (14)	110 (7)
Missing	2212 (1)	21 (1)

	IBD pre-transplant N (%)	
Characteristic	**No**	**Yes**
Karnofsky/Lansky performance score		
90-100	112525 (64)	872 (56)
< 90	56852 (33)	637 (41)
Missing	5216 (3)	46 (3)
Disease		
AML	31740 (18)	345 (22)
ALL	13539 (8)	79 (5)
Other leukemia	2892 (2)	27 (2)
CML	2942 (2)	28 (2)
MDS/MPN	12959 (7)	159 (10)
Other acute leukemia	1103 (<1)	8 (<1)
NHL	32725 (19)	288 (19)
HD	10148 (6)	45 (3)
PCD/MM	49062 (28)	442 (28)
Other malignancy	5995 (3)	10 (<1)
Breast cancer	45 (<1)	0
SAA	3986 (2)	11 (<1)
Inherited abnormality of erythrocyte differentiation or function	3291 (2)	6 (<1)
SCID or other PID	2099 (1)	80 (5)
Inherited abnormality of platelets	88 (<1)	0
Metabolic disorder	811 (<1)	0
Histiocytic disorder	759 (<1)	6 (<1)
Autoimmune disease	258 (<1)	19 (1)
Other	151 (<1)	2 (<1)
HCT-CI		
0	68624 (39)	0
1	21624 (12)	397 (26)
2	21099 (12)	247 (16)
3+	51659 (30)	910 (59)
NA, pre-TED not completed	436 (<1)	0
Missing	11151 (6)	1 (<1)

	IBD pre-transplant N (%)	
Characteristic	**No**	**Yes**
Transplant type		
Allogeneic	87482 (50)	845 (54)
Autologous	87111 (50)	710 (46)
Donor type		
Autologous	87111 (50)	710 (46)
HLA-identical sibling	30961 (18)	262 (17)
Other related	7149 (4)	64 (4)
Well-matched unrelated	23596 (14)	309 (20)
Partially-matched unrelated	5914 (3)	71 (5)
Mis-matched unrelated	357 (<1)	1 (<1)
Multi-donor	546 (<1)	2 (<1)
Unrelated (matching TBD)	10204 (6)	84 (5)
Cord blood	8005 (5)	46 (3)
Missing	750 (<1)	6 (<1)
Graft source		
Bone marrow	20313 (12)	155 (10)
Peripheral blood	146042 (84)	1354 (87)
Umbilical cord blood	8018 (5)	46 (3)
Missing	220 (<1)	0
Conditioning regimen intensity		
MAC	51389 (29)	423 (27)
RIC/NMA	35117 (20)	417 (27)
Autologous HCT (TBD)	87111 (50)	710 (46)
Missing	976 (<1)	5 (<1)
GVHD prophylaxis		
Ex-vivo T-cell depletion	854 (<1)	6 (<1)
CD34 selection	1596 (<1)	17 (1)
Post-CY + other(s)	3420 (2)	40 (3)
Post-CY alone	172 (<1)	2 (<1)
TAC + MMF +- other(s) (except post-CY)	9784 (6)	132 (8)
TAC + MTX +- other(s) (except MMF, post-CY)	26565 (15)	318 (20)
TAC + other(s) (except MMF, MTX, post-CY)	4087 (2)	41 (3)
TAC alone	1586 (<1)	16 (1)
CSA + MMF +- other(s) (except post-CY)	10786 (6)	102 (7)

	IBD pre-transplant N (%)	
Characteristic	**No**	**Yes**
CSA + MTX +- other(s) (except MMF, post-CY)	18098 (10)	89 (6)
CSA + other(s) (except MMF, MTX, post-CY)	2142 (1)	20 (1)
CSA alone	4734 (3)	24 (2)
Other(s)	2027 (1)	23 (1)
Missing	1631 (<1)	15 (<1)
Autologous HCT	87111 (50)	710 (46)
ATG/Campath		
ATG + CAMPATH	49 (<1)	0
ATG alone	27636 (16)	232 (15)
CAMPATH alone	4509 (3)	69 (4)
No ATG or CAMPATH	52026 (30)	515 (33)
Missing	3271 (2)	29 (2)
Autologous HCT	87111 (50)	710 (46)
Year of transplant		
2008-2010	52095 (30)	381 (25)
2011-2013	60730 (35)	521 (34)
2014-2016	61768 (35)	653 (42)
Median follow-up of survivors (range), months	48 (3-128)	48 (3-122)

*Source: November 2018 TED retrieval

Proposal: 1811-85/1811-159

Title:
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.

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Hypothesis:

- The inclusion of post-transplant cyclophosphamide (post-Cy) as GVHD prophylaxis for patients getting haplo-identical hematopoietic stem cell transplant (haplo-HCT) as well as other allogeneic stem cell transplant (allo-SCT) results in an increase in hemorrhagic cystitis (HC) and BK nephropathy as compared to other allo-SCT without post-Cy.
- There are similar long-term outcomes in regards to HC and BK nephropathy in patients who get post-Cy as GVHD prophylaxis versus those who did not.

Specific aims:
Primary aim:

- 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.

Secondary aims:

- To evaluate the severity of hemorrhagic cystitis and BK nephropathy in patients who received post-Cy as part of GVHD prophylaxis regimen versus those who did not.
- To describe and evaluate disease characteristics and pre-transplant regimens of patients with hematologic malignancies that received post-Cy as part of GVHD prophylaxis.
- To evaluate the impact of HC and BK nephropathy on the rate of acute GVHD in the recipients of haplo-HCT and other allo-SCT who received post-Cy as part of GVHD prophylaxis.
- To evaluate long-term and survival outcomes in patients who received post-Cy as part of GVHD prophylaxis regimen.

Scientific justification:
Hemorrhagic Cystitis is a known complication of allogeneic stem cell transplantation (1), with a varying reported incidence between 10-60%. Clinical manifestations range from microscopic hematuria to gross hematuria which can be associated with significant treatment related morbidity and mortality (2). Predisposing factors implicated in development of HC include conditioning regimen intensity particularly

cyclophosphamide and TBI containing regimens, use of antithymocyte globulin (ATG), viral infections including BK/ JC polyomavirus, adenovirus and cytomegalovirus, GVHD and thrombocytopenia (1, 3). It is however difficult to attribute it to one specific virus as it has been reported that eighty percent of patients in the early post-transplant period excrete BK virus in the urine (4).
Donor type has been found to be an independent risk factor for the development of HC. A retrospective, single center study found higher incidence of HC in patients undergoing matched unrelated (MUD) and umbilical cord blood (UCB) transplantation as compared to matched related donor (MRD). The cumulative incidence of HC was 16%, 40% and 40% in recipients of MRD, MUD and UCB transplantation respectively. Interestingly, cyclophosphamide containing conditioning regimen was not significantly associated with development of HC (HR 0.7 [95% CI, 0.16-2.95]; $p = 0.6$) (5).
Cyclophosphamide was historically one of the first chemotherapeutic agents used as a preparative regimen for bone marrow transplantation given its immunosuppressive properties (6-10). In recent times, it has been re-invented as an agent to be used in the post-preparative regimen of stem cell transplantation as prophylaxis against GVHD (11-13). This was initially in the setting of a haplo-HCT (12). The use of post-transplant cyclophosphamide has been reported to result in comparable outcomes in patients who get haplo-HCT as compared to HLA matched related and unrelated donor stem cell transplantation (13-15). Specifically, there has been an improvement in GVHD outcomes and subsequently non-relapse mortality for patients undergoing haplo-HCT (16). Post-transplant cyclophosphamide is not only being used in the haplo-HCT setting, but also increasingly in other types of HLA mismatch (related or unrelated), single or more, and in matched unrelated donor transplants (17-20).
There is scarcity of data regarding hemorrhagic cystitis in haplo-HCT. Theoretically, the risk of HC is high in recipients of haplo-HCT due to the use of post-Cy which is the cornerstone of GVHD prophylaxis in haplo-HCT, delayed immune reconstitution and viral infections. In one retrospective study, 20 of the 33 patients included developed HC at a median time of 38-days post-transplantation (21). Another retrospective study showed a higher rate of HC in haplo-HCT in comparison to non-haplo-HCT (33% vs 13%; $p = 0.03$) (22). These anecdotal studies are limited in power due to smaller sample size and lack of direct comparison between haplo-HCT and other donor type transplants.
It is therefore of importance to determine if the use of post-transplant cyclophosphamide in the post-preparative regimen (as GVHD prophylaxis) has resulted in an increase in toxic hemorrhagic cystitis and/or BK nephropathy. Hemorrhagic cystitis can result in prolonged and/or repeated hospitalizations, and therefore affect quality of life of stem cell transplant recipients (2). Hence, we propose to conduct a CIBMTR study to elucidate the risk of HC/ BK nephropathy in recipients of post-Cy. As a result, these predisposing factors could potentially be modified to minimize the risk of HC in these patients, for example, guidance in selection of donors, conditioning regimen, and in utilizing pre-transplant characteristics in these selections.

Patient eligibility population:

- All patients aged 18 years and older with a diagnosis of a hematologic malignancy
- Patients who received post-transplant cyclophosphamide as GVHD prophylaxis
- Received hematopoietic transplant from 2008 to 2017
- All donor sources are eligible – haplo-identical, all HLA-mismatch, MUDs, MSDs
- All transplant regimens are eligible

Exclusion criteria:

- Recipients of umbilical cord blood stem cell transplantation
- Recipients of haplo-HCT, MRD or MUD for non-malignant hematological disorders

Data requirements:

Patient specific data:

- Recipient age
- Recipient gender (male/ female)
- Recipient race
- Malignancy

Donor specific data:

- Donor age
- Donor gender (male/ female)
- Type of donor (haplo-identical/ related/ unrelated
- HLA mismatch (yes/ no)
- Number of HLA mismatch

Transplant related data:

- Disease stage at transplant
- Conditioning intensity (MA/ RIC)
- TBI based conditioning (yes/ no)
- Cyclophosphamide based conditioning (yes/ no)
- Graft source (peripheral blood/ bone marrow)
- ATG (yes/ no)
- ATG dose
- GVHD prophylaxis
- Neutrophil engraftment
- Platelet recovery
- Time to development of HC (early [< 2 weeks]/ late [> 2 weeks])
- Severity of HC (mild/ moderate/ severe)
- BK/ JC virus (yes/ no)
- Adenovirus (yes/ no)
- CMV virus (yes/ no)
- Acute GVHD (yes/ no)
- Grade of acute GVHD (I/ II/ III/ IV)
- GVHD organ involved
- Chronic GVHD (yes/ no)
- Grade of chronic GVHD (mild/ moderate/ severe)
- GVHD organ involved
- Treatment-related mortality (yes/ no)
- Graft failure (yes/ no)
- Relapse (yes/ no)
- Overall survival
- GVHD-free/ relapse-free survival

Study design:

This is a retrospective study with review of CIBMTR database with the objective to analyze patients who received post-transplant cyclophosphamide as part of GVHD prophylaxis who met the inclusion criteria.

Outcomes:

Primary outcome analysis:

- Calculation of the incidence of hemorrhagic cystitis and BK nephropathy. All patients deemed evaluable will be included in this analysis. Cumulative incidence of hemorrhagic cystitis will be calculated for haplo-HCT and non-haplo-HCT.

Secondary outcome analysis:

- Calculation of the 1-, 3- and 5-year overall survival probability based on the Kaplan-Meier product limit estimator. The confidence interval will also be calculated. All patients deemed evaluable will be included in this analysis.
- Acute and chronic GVHD rates will be determined
- GVHD-free, relapse-free survival analysis will be conducted
- Relapse rate and/or treatment-related mortality will be calculated from day 0 of transplant. This will be evaluated using cumulative incidence curves.
- Graft failure rates will be calculated from day 0 of transplant. This will also be evaluated using the Kaplan-Meier estimator.
- Factors affecting and predicting outcomes will be evaluated - type of preparative regimen, type of pre-transplant chemotherapy, type of HLA mismatch, number of HLA mismatches, GVHD organ involvement.

Categorical variables will be analyzed using Chi square or Fischer Exact test, while continuous variables using Mann Whitney U test. Risk factors for HC will be evaluated on univariate and multivariate analysis using Cox's regression model. All *p* values will be two-tailed and significant at < 0.05.

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Characteristics of adults (≥18) with first alloHCT for hematologic malignancy who received transplanted from 2008-2017

	Post-CY use N (%)	
Characteristic	**No**	**Yes**
Number of patients	15534	1954
Number of centers	236	141
Age, median (range), years	56 (18-83)	57 (18-88)
Age group		
18-29	1430 (9)	236 (12)
30-39	1421 (9)	188 (10)
40-49	2458 (16)	282 (14)
50-59	4412 (28)	451 (23)
60-69	4838 (31)	641 (33)
≥70	975 (6)	156 (8)
Sex		
Male	9249 (60)	1176 (60)
Female	6285 (40)	778 (40)
Race		
Caucasian	13256 (85)	1412 (72)
African-American	826 (5)	305 (16)
Asian	763 (5)	114 (6)
Pacific islander	50 (<1)	8 (<1)
Native American	72 (<1)	8 (<1)
Other	1 (<1)	0
More than one race	73 (<1)	11 (<1)
Missing	493 (3)	96 (5)
Ethnicity		
Hispanic or Latino	1095 (7)	195 (10)
Not Hispanic or Latino	13370 (86)	1594 (82)
NA, non-resident of USA	872 (6)	137 (7)
Missing	197 (1)	28 (1)
Karnofsky performance score		
90-100	9158 (59)	1093 (56)
< 90	6087 (39)	823 (42)
Missing	289 (2)	38 (2)

	Post-CY use N (%)	
Characteristic	**No**	**Yes**
Disease		
AML	5839 (38)	794 (41)
ALL	1568 (10)	258 (13)
Other leukemia	636 (4)	51 (3)
CML	561 (4)	70 (4)
MDS/MPN	5004 (32)	525 (27)
Other acute leukemia	121 (<1)	34 (2)
NHL	1268 (8)	146 (7)
HD	192 (1)	54 (3)
PCD/MM	342 (2)	19 (<1)
Other malignancy	3 (<1)	3 (<1)
HCT-CI		
0	4292 (28)	479 (25)
1	2079 (13)	282 (14)
2	2107 (14)	268 (14)
3+	6554 (42)	915 (47)
NA, pre-TED not completed	295 (2)	6 (<1)
Missing	207 (1)	4 (<1)
Donor type		
HLA-identical sibling	4921 (32)	171 (9)
Twin	190 (1)	2 (<1)
Haploidentical	364 (2)	1108 (57)
Other related	528 (3)	324 (17)
Well-matched unrelated	7534 (49)	241 (12)
Partially-matched unrelated	1558 (10)	83 (4)
Mis-matched unrelated	90 (<1)	12 (<1)
Multi-donor	32 (<1)	7 (<1)
Unrelated (matching TBD)	182 (1)	5 (<1)
Missing	135 (<1)	1 (<1)
Donor/recipient sex match		
M-M	6137 (40)	760 (39)
M-F	3638 (23)	455 (23)
F-M	2988 (19)	409 (21)
F-F	2576 (17)	320 (16)
Missing	195 (1)	10 (<1)

	Post-CY use N (%)	
Characteristic	**No**	**Yes**
Donor/recipient CMV serostatus		
+/+	5113 (33)	783 (40)
+/-	1722 (11)	197 (10)
-/+	4495 (29)	520 (27)
-/-	4039 (26)	439 (22)
Missing	165 (1)	15 (<1)
Graft source		
Bone marrow	1766 (11)	778 (40)
Peripheral blood	13768 (89)	1176 (60)
Conditioning regimen intensity		
MAC	7989 (51)	814 (42)
RIC	5708 (37)	357 (18)
NMA	1297 (8)	763 (39)
Missing	540 (3)	20 (1)
GVHD prophylaxis		
No GVHD prophylaxis	307 (2)	0
Ex-vivo T-cell depletion	127 (<1)	0
CD34 selection	257 (2)	0
Post-CY + other(s)	0	1892 (97)
Post-CY alone	0	62 (3)
TAC + MMF +- other(s) (except post-CY)	2692 (17)	0
TAC + MTX +- other(s) (except MMF, post-CY)	7897 (51)	0
TAC + other(s) (except MMF, MTX, post-CY)	1096 (7)	0
TAC alone	385 (2)	0
CSA + MMF +- other(s) (except post-CY)	1074 (7)	0
CSA + MTX +- other(s) (except MMF, post-CY)	1182 (8)	0
CSA + other(s) (except MMF, MTX, post-CY)	96 (<1)	0
CSA alone	149 (<1)	0
Other(s)	181 (1)	0
Missing	91 (<1)	0
ATG/Campath		
ATG + CAMPATH	2 (<1)	0
ATG alone	4160 (27)	52 (3)
CAMPATH alone	477 (3)	0
No ATG or CAMPATH	10785 (69)	1895 (97)
Missing	110 (<1)	7 (<1)

	Post-CY use N (%)	
Characteristic	**No**	**Yes**
Year of transplant		
2008	2157 (14)	71 (4)
2009	1923 (12)	53 (3)
2010	1155 (7)	23 (1)
2011	828 (5)	26 (1)
2012	831 (5)	35 (2)
2013	1695 (11)	158 (8)
2014	2170 (14)	235 (12)
2015	1887 (12)	348 (18)
2016	1688 (11)	453 (23)
2017	1200 (8)	552 (28)
Median follow-up of survivors (range), months	48 (3-126)	24 (3-122)

*Source: November 2018 CRF retrieval

Table 2. Incidence of hemorrhagic cystitis in proposed population

	Population (N = 17488)	
Outcomes	**N Eval**	**Prob (95% CI)**
Hemorrhagic cystitis	17461	
100-day		3 (2-3)%
1-year		3 (3-4)%
2-year		3 (3-4)%

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	37744	10623	6882
Source of data			
CRF	21889 (58)	5634 (53)	4225 (61)
TED	15855 (42)	4989 (47)	2657 (39)
Number of centers	249	218	316
Disease at transplant			
AML	12782 (34)	3782 (36)	2223 (32)
ALL	5581 (15)	1464 (14)	1153 (17)
Other leukemia	1312 (3)	328 (3)	227 (3)
CML	3217 (9)	856 (8)	715 (10)
MDS	6063 (16)	1873 (18)	915 (13)
Other acute leukemia	388 (1)	119 (1)	72 (1)
NHL	3579 (9)	951 (9)	559 (8)
Hodgkins Lymphoma	800 (2)	162 (2)	120 (2)
Plasma Cell Disorders, MM	766 (2)	228 (2)	108 (2)
Other malignancies	54 (<1)	13 (<1)	17 (<1)
Breast cancer	7 (<1)	3 (<1)	1 (<1)
SAA	1191 (3)	297 (3)	280 (4)
Inherited abnormalities erythrocyte diff fxn	665 (2)	184 (2)	127 (2)
SCIDs	648 (2)	186 (2)	182 (3)
Inherited abnormalities of platelets	38 (<1)	9 (<1)	9 (<1)
Inherited disorders of metabolism	261 (1)	63 (1)	80 (1)
Histiocytic disorders	332 (1)	83 (1)	71 (1)
Autoimmune disorders	16 (<1)	7 (<1)	4 (<1)
Other	44 (<1)	15 (<1)	19 (<1)
AML Disease status at transplant			
CR1	6446 (50)	1924 (51)	970 (44)
CR2	2591 (20)	762 (20)	469 (21)
CR3+	257 (2)	70 (2)	50 (2)
Advanced or active disease	3341 (26)	989 (26)	687 (31)
Missing	143 (1)	37 (1)	43 (2)
ALL Disease status at transplant			
CR1	2643 (47)	730 (50)	464 (40)
CR2	1641 (29)	402 (27)	344 (30)
CR3+	466 (8)	120 (8)	111 (10)
Advanced or active disease	787 (14)	198 (14)	202 (18)

Refreshed January 2019

Biorepository accruals

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Missing	44 (1)	14 (1)	31 (3)
MDS Disease status at transplant			
Early	1233 (20)	327 (18)	212 (23)
Advanced	4332 (72)	1419 (76)	568 (63)
Missing	457 (8)	114 (6)	124 (14)
NHL Disease status at transplant			
CR1	446 (13)	158 (17)	58 (10)
CR2	664 (19)	166 (18)	93 (17)
CR3+	302 (9)	82 (9)	47 (8)
PR	431 (12)	108 (11)	78 (14)
Advanced	1655 (47)	419 (44)	271 (49)
Missing	50 (1)	9 (1)	9 (2)
Recipient age at transplant			
0-9 years	3381 (9)	833 (8)	898 (13)
10-19 years	3499 (9)	871 (8)	820 (12)
20-29 years	4018 (11)	1092 (10)	855 (12)
30-39 years	4481 (12)	1152 (11)	887 (13)
40-49 years	5945 (16)	1647 (16)	1104 (16)
50-59 years	7884 (21)	2177 (20)	1205 (18)
60-69 years	7285 (19)	2369 (22)	975 (14)
70+ years	1251 (3)	482 (5)	138 (2)
Median (Range)	46 (0-84)	49 (0-79)	40 (0-79)
Recipient race/ethnicity			
Caucasian, non-Hispanic	31488 (85)	8851 (85)	5200 (83)
African-American, non-Hispanic	1728 (5)	446 (4)	296 (5)
Asian, non-Hispanic	809 (2)	351 (3)	233 (4)
Pacific islander, non-Hispanic	49 (<1)	17 (<1)	12 (<1)
Native American, non-Hispanic	143 (<1)	47 (<1)	23 (<1)
Hispanic	2619 (7)	655 (6)	452 (7)
Other	44 (<1)	25 (<1)	21 (<1)
Unknown	864 (N/A)	231 (N/A)	645 (N/A)
Recipient sex			
Male	22065 (58)	6269 (59)	4075 (59)
Female	15679 (42)	4354 (41)	2807 (41)
Karnofsky score			
10-80	12440 (33)	3698 (35)	2071 (30)
90-100	23812 (63)	6374 (60)	4287 (62)
Missing	1492 (4)	551 (5)	524 (8)
HLA-A B DRB1 groups - low resolution			
<=3/6	21 (<1)	25 (<1)	1 (<1)

Refreshed January 2019

Biorepository accruals

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
4/6	204 (1)	75 (1)	29 (<1)
5/6	5329 (14)	1325 (14)	977 (15)
6/6	31770 (85)	7921 (85)	5383 (84)
Unknown	420 (N/A)	1277 (N/A)	492 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	834 (2)	66 (1)	27 (1)
6/8	1639 (4)	105 (2)	117 (3)
7/8	7450 (20)	1297 (19)	934 (23)
8/8	26608 (73)	5482 (79)	3001 (74)
Unknown	1213 (N/A)	3673 (N/A)	2803 (N/A)
HLA-DPB1 Match			
Double allele mismatch	8931 (30)	536 (25)	298 (28)
Single allele mismatch	16049 (54)	1101 (51)	549 (52)
Full allele matched	4646 (16)	522 (24)	206 (20)
Unknown	8118 (N/A)	8464 (N/A)	5829 (N/A)
High resolution release score			
No	397 (1)	156 (43)	362 (67)
Yes	28516 (99)	207 (57)	178 (33)
Unknown	8831 (N/A)	10260 (N/A)	6342 (N/A)
KIR typing available			
No	24082 (64)	10499 (99)	6842 (99)
Yes	13662 (36)	124 (1)	40 (1)
Graft type			
Marrow	14336 (38)	3792 (36)	3234 (47)
PBSC	23388 (62)	6730 (63)	3645 (53)
BM+PBSC	8 (<1)	6 (<1)	2 (<1)
BM+UCB	0	1 (<1)	0
PBSC+UCB	12 (<1)	94 (1)	1 (<1)
Number of cord units			
1	5 (100)	0	1 (100)
Conditioning regimen			
Myeloablative	24422 (65)	6581 (62)	4710 (68)
RIC/Nonmyeloablative	13151 (35)	4000 (38)	2093 (30)
TBD	171 (<1)	42 (<1)	79 (1)
Donor age at donation			
To Be Determined/NA	180 (<1)	1269 (12)	57 (1)
0-9 years	11 (<1)	15 (<1)	0
10-19 years	1043 (3)	307 (3)	145 (2)
20-29 years	16285 (43)	4188 (39)	2531 (37)
30-39 years	10995 (29)	2720 (26)	2168 (32)

Refreshed January 2019

Biorepository accruals

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
40-49 years	7072 (19)	1608 (15)	1499 (22)
50+ years	2158 (6)	516 (5)	482 (7)
Median (Range)	31 (0-69)	30 (0-109)	33 (18-67)
Donor/Recipient CMV serostatus			
+/+	9249 (25)	2887 (28)	1677 (26)
+/-	4528 (12)	1376 (13)	860 (13)
-/+	12323 (33)	3133 (31)	2128 (33)
-/-	11116 (30)	2822 (28)	1874 (29)
CB - recipient +	0	4 (<1)	0
CB - recipient -	0	2 (<1)	0
CB - recipient CMV unknown	0	1 (<1)	0
Unknown	528 (N/A)	398 (N/A)	343 (N/A)
GvHD Prophylaxis			
Ex vivo T-cell depletion	1089 (3)	271 (3)	300 (4)
CD34 selection	665 (2)	282 (3)	105 (2)
Tacrolimus + MMF +- others	4514 (12)	1101 (10)	572 (8)
Tacrolimus + MTX +- others (except MMF)	16190 (43)	4697 (44)	1910 (28)
Tacrolimus + others (except MTX, MMF)	1971 (5)	682 (6)	273 (4)
Tacrolimus alone	919 (2)	285 (3)	117 (2)
CSA + MMF +- others (except Tacrolimus)	2583 (7)	581 (5)	566 (8)
CSA + MTX +- others (except Tacrolimus, MMF)	6473 (17)	1656 (16)	2128 (31)
CSA + others (except Tacrolimus, MTX, MMF)	985 (3)	297 (3)	283 (4)
CSA alone	462 (1)	115 (1)	267 (4)
Other GVHD prophylaxis	687 (2)	202 (2)	116 (2)
Missing	1206 (3)	454 (4)	245 (4)
Donor/Recipient sex match			
Male-Male	15602 (42)	4222 (40)	2727 (40)
Male-Female	9473 (25)	2543 (24)	1586 (23)
Female-Male	6359 (17)	1927 (18)	1323 (19)
Female-Female	6134 (16)	1702 (16)	1201 (18)
CB - recipient M	5 (<1)	53 (1)	0
CB - recipient F	7 (<1)	42 (<1)	1 (<1)
Unknown	164 (N/A)	134 (N/A)	44 (N/A)
Year of transplant			
1986-1990	349 (1)	45 (<1)	85 (1)
1991-1995	1795 (5)	448 (4)	610 (9)
1996-2000	3148 (8)	1113 (10)	894 (13)
2001-2005	5002 (13)	987 (9)	1433 (21)
2006-2010	9213 (24)	1853 (17)	1391 (20)
2011-2015	12850 (34)	3618 (34)	1714 (25)

Refreshed January 2019

Biorepository accruals

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
2016-2019	5387 (14)	2559 (24)	755 (11)
Follow-up among survivors, Months			
N Eval	16177	4874	2672
Median (Range)	53 (0-344)	37 (0-325)	51 (0-337)

*Note: Biospecimens include whole blood, serum/plasma and limited quantities of viable cells and cell lines (collected prior to 2006). Specific inventory queries available upon request through the CIBMTR Immunobiology Research Program.

Refreshed January 2019

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	5199	1233	1179
Source of data			
CRF	3988 (77)	952 (77)	795 (67)
TED	1211 (23)	281 (23)	384 (33)
Number of centers	144	127	188
Disease at transplant			
AML	1937 (37)	411 (33)	381 (32)
ALL	1060 (20)	259 (21)	268 (23)
Other leukemia	91 (2)	25 (2)	23 (2)
CML	112 (2)	29 (2)	28 (2)
MDS	502 (10)	123 (10)	100 (8)
Other acute leukemia	80 (2)	19 (2)	21 (2)
NHL	367 (7)	81 (7)	80 (7)
Hodgkins Lymphoma	93 (2)	25 (2)	21 (2)
Plasma Cell Disorders, MM	34 (1)	10 (1)	5 (<1)
Other malignancies	10 (<1)	0	0
SAA	89 (2)	28 (2)	21 (2)
Inherited abnormalities erythrocyte diff fxn	149 (3)	46 (4)	30 (3)
SCIDs	235 (5)	67 (5)	83 (7)
Inherited abnormalities of platelets	15 (<1)	3 (<1)	4 (<1)
Inherited disorders of metabolism	308 (6)	80 (6)	76 (6)
Histiocytic disorders	97 (2)	25 (2)	31 (3)
Autoimmune disorders	9 (<1)	0	1 (<1)
Other	11 (<1)	2 (<1)	6 (1)
AML Disease status at transplant			
CR1	966 (50)	219 (53)	192 (50)
CR2	548 (28)	104 (25)	104 (27)
CR3+	51 (3)	6 (1)	11 (3)
Advanced or active disease	364 (19)	80 (20)	72 (19)
Missing	8 (<1)	1 (<1)	2 (1)
ALL Disease status at transplant			
CR1	477 (45)	108 (42)	122 (46)
CR2	397 (37)	100 (39)	95 (35)
CR3+	118 (11)	35 (14)	28 (10)
Advanced or active disease	68 (6)	16 (6)	23 (9)
MDS Disease status at transplant			

Refreshed January 2019

Biorepository accruals

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Early	161 (32)	30 (25)	46 (46)
Advanced	306 (61)	86 (71)	43 (43)
Missing	34 (7)	5 (4)	10 (10)
NHL Disease status at transplant			
CR1	56 (15)	5 (6)	17 (22)
CR2	68 (19)	17 (21)	20 (25)
CR3+	42 (12)	10 (12)	9 (11)
PR	65 (18)	12 (15)	10 (13)
Advanced	133 (37)	36 (44)	22 (28)
Missing	0	1 (1)	1 (1)
Recipient age at transplant			
0-9 years	1562 (30)	456 (37)	440 (37)
10-19 years	681 (13)	143 (12)	160 (14)
20-29 years	490 (9)	86 (7)	91 (8)
30-39 years	507 (10)	104 (8)	113 (10)
40-49 years	546 (11)	123 (10)	108 (9)
50-59 years	731 (14)	149 (12)	141 (12)
60-69 years	599 (12)	151 (12)	117 (10)
70+ years	83 (2)	21 (2)	9 (1)
Median (Range)	27 (0-81)	22 (0-75)	19 (0-78)
Recipient race/ethnicity			
Caucasian, non-Hispanic	2908 (59)	739 (63)	650 (62)
African-American, non-Hispanic	743 (15)	167 (14)	136 (13)
Asian, non-Hispanic	300 (6)	70 (6)	74 (7)
Pacific islander, non-Hispanic	23 (<1)	2 (<1)	12 (1)
Native American, non-Hispanic	34 (1)	6 (1)	13 (1)
Hispanic	945 (19)	189 (16)	169 (16)
Other	0	1 (<1)	1 (<1)
Unknown	246 (N/A)	59 (N/A)	124 (N/A)
Recipient sex			
Male	2858 (55)	712 (58)	675 (57)
Female	2341 (45)	521 (42)	504 (43)
Karnofsky score			
10-80	1330 (26)	297 (24)	281 (24)
90-100	3728 (72)	851 (69)	829 (70)
Missing	141 (3)	85 (7)	69 (6)
HLA-A B DRB1 groups - low resolution			
<=3/6	70 (1)	27 (3)	5 (<1)
4/6	2051 (41)	393 (41)	411 (38)
5/6	2231 (45)	401 (42)	522 (48)

Refreshed January 2019

Biorepository accruals

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
6/6	630 (13)	136 (14)	158 (14)
Unknown	217 (N/A)	276 (N/A)	83 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	2478 (56)	405 (58)	474 (54)
6/8	1066 (24)	160 (23)	212 (24)
7/8	594 (13)	89 (13)	127 (14)
8/8	294 (7)	49 (7)	66 (8)
Unknown	767 (N/A)	530 (N/A)	300 (N/A)
HLA-DPB1 Match			
Double allele mismatch	682 (40)	42 (45)	39 (38)
Single allele mismatch	858 (50)	41 (44)	51 (50)
Full allele matched	160 (9)	10 (11)	12 (12)
Unknown	3499 (N/A)	1140 (N/A)	1077 (N/A)
High resolution release score			
No	156 (9)	32 (39)	31 (79)
Yes	1499 (91)	50 (61)	8 (21)
Unknown	3544 (N/A)	1151 (N/A)	1140 (N/A)
KIR typing available			
No	3935 (76)	1227 (>99)	1171 (99)
Yes	1264 (24)	6 (<1)	8 (1)
Cord blood number of units			
1	3609 (69)	0	913 (77)
2	1588 (31)	0	266 (23)
3	2 (<1)	0	0
Unknown	0 (N/A)	1233 (N/A)	0 (N/A)
Graft type			
UCB	4951 (95)	1138 (92)	1127 (96)
BM+UCB	1 (<1)	1 (<1)	0
PBSC+UCB	247 (5)	94 (8)	52 (4)
Conditioning regimen			
Myeloablative	3433 (66)	805 (65)	773 (66)
RIC/Nonmyeloablative	1756 (34)	426 (35)	403 (34)
TBD	10 (<1)	2 (<1)	3 (<1)
Donor age at donation			
To Be Determined/NA	137 (3)	76 (6)	65 (6)
0-9 years	4642 (89)	976 (79)	1029 (87)
10-19 years	273 (5)	104 (8)	52 (4)
20-29 years	44 (1)	21 (2)	7 (1)
30-39 years	43 (1)	27 (2)	12 (1)
40-49 years	24 (<1)	11 (1)	4 (<1)

Refreshed January 2019

Biorepository accruals

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
50+ years	36 (1)	18 (1)	10 (1)
Median (Range)	4 (0-72)	4 (0-73)	3 (0-67)
Donor/Recipient CMV serostatus			
+/+	1204 (23)	251 (20)	245 (21)
+/-	532 (10)	119 (10)	113 (10)
-/+	966 (19)	223 (18)	217 (18)
-/-	655 (13)	153 (12)	165 (14)
CB - recipient +	1045 (20)	252 (20)	218 (18)
CB - recipient -	714 (14)	187 (15)	178 (15)
CB - recipient CMV unknown	83 (2)	48 (4)	43 (4)
GvHD Prophylaxis			
Ex vivo T-cell depletion	23 (<1)	9 (1)	4 (<1)
CD34 selection	182 (4)	70 (6)	39 (3)
Tacrolimus + MMF +- others	1379 (27)	309 (25)	182 (15)
Tacrolimus + MTX +- others (except MMF)	200 (4)	55 (4)	54 (5)
Tacrolimus + others (except MTX, MMF)	214 (4)	54 (4)	47 (4)
Tacrolimus alone	131 (3)	43 (3)	23 (2)
CSA + MMF +- others (except Tacrolimus)	2453 (47)	518 (42)	586 (50)
CSA + MTX +- others (except Tacrolimus, MMF)	92 (2)	27 (2)	39 (3)
CSA + others (except Tacrolimus, MTX, MMF)	311 (6)	104 (8)	134 (11)
CSA alone	57 (1)	15 (1)	44 (4)
Other GVHD prophylaxis	125 (2)	17 (1)	15 (1)
Missing	32 (1)	12 (1)	12 (1)
Donor/Recipient sex match			
CB - recipient M	2858 (55)	712 (58)	674 (57)
CB - recipient F	2341 (45)	521 (42)	504 (43)
CB - recipient sex unknown	0	0	1 (<1)
Year of transplant			
1996-2000	0	2 (<1)	4 (<1)
2001-2005	113 (2)	82 (7)	22 (2)
2006-2010	1783 (34)	406 (33)	425 (36)
2011-2015	2567 (49)	491 (40)	569 (48)
2016-2019	736 (14)	252 (20)	159 (13)
Follow-up among survivors, Months			
N Eval	2515	664	606
Median (Range)	52 (1-176)	37 (2-191)	49 (1-217)

*Note: Biospecimens include whole blood, serum/plasma and limited quantities of viable cells and cell lines (collected prior to 2006-recipient only). Specific inventory queries available upon request through the CIBMTR Immunobiology Research Program.

Refreshed January 2019

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	6033	890	403
Source of data			
CRF	2317 (38)	276 (31)	161 (40)
TED	3716 (62)	614 (69)	242 (60)
Number of centers	82	63	51
Disease at transplant			
AML	1980 (33)	297 (33)	118 (29)
ALL	946 (16)	170 (19)	60 (15)
Other leukemia	141 (2)	26 (3)	19 (5)
CML	206 (3)	20 (2)	14 (3)
MDS	994 (16)	137 (15)	59 (15)
Other acute leukemia	81 (1)	14 (2)	3 (1)
NHL	631 (10)	84 (9)	58 (14)
Hodgkins Lymphoma	134 (2)	18 (2)	17 (4)
Plasma Cell Disorders, MM	182 (3)	30 (3)	15 (4)
Other malignancies	16 (<1)	0	0
Breast cancer	1 (<1)	0	0
SAA	261 (4)	31 (3)	12 (3)
Inherited abnormalities erythrocyte diff fxn	289 (5)	41 (5)	16 (4)
SCIDs	109 (2)	18 (2)	8 (2)
Inherited abnormalities of platelets	9 (<1)	0	0
Inherited disorders of metabolism	8 (<1)	0	0
Histiocytic disorders	31 (1)	2 (<1)	2 (<1)
Autoimmune disorders	5 (<1)	0	0
Other	9 (<1)	2 (<1)	2 (<1)
AML Disease status at transplant			
CR1	1215 (61)	189 (64)	72 (61)
CR2	312 (16)	33 (11)	12 (10)
CR3+	23 (1)	4 (1)	0
Advanced or active disease	423 (21)	69 (23)	32 (27)
Missing	7 (<1)	2 (1)	2 (2)
ALL Disease status at transplant			
CR1	597 (63)	112 (66)	43 (72)
CR2	257 (27)	35 (21)	10 (17)
CR3+	39 (4)	5 (3)	2 (3)

Refreshed January 2019

Biorepository accruals

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Advanced or active disease	53 (6)	18 (11)	5 (8)
MDS Disease status at transplant			
Early	175 (18)	19 (14)	6 (10)
Advanced	789 (79)	114 (83)	51 (86)
Missing	30 (3)	4 (3)	2 (3)
NHL Disease status at transplant			
CR1	103 (16)	19 (23)	8 (14)
CR2	124 (20)	14 (17)	11 (19)
CR3+	70 (11)	6 (7)	2 (3)
PR	58 (9)	11 (13)	6 (10)
Advanced	270 (43)	32 (39)	31 (53)
Missing	2 (<1)	1 (1)	0
Recipient age at transplant			
0-9 years	556 (9)	70 (8)	29 (7)
10-19 years	629 (10)	65 (7)	25 (6)
20-29 years	484 (8)	93 (10)	37 (9)
30-39 years	470 (8)	79 (9)	33 (8)
40-49 years	844 (14)	121 (14)	57 (14)
50-59 years	1450 (24)	208 (23)	102 (25)
60-69 years	1402 (23)	225 (25)	109 (27)
70+ years	198 (3)	29 (3)	11 (3)
Median (Range)	50 (0-78)	51 (0-76)	52 (0-74)
Recipient race/ethnicity			
Caucasian, non-Hispanic	3899 (67)	485 (58)	264 (68)
African-American, non-Hispanic	690 (12)	89 (11)	43 (11)
Asian, non-Hispanic	269 (5)	73 (9)	22 (6)
Pacific islander, non-Hispanic	22 (<1)	3 (<1)	0
Native American, non-Hispanic	23 (<1)	1 (<1)	0
Hispanic	909 (16)	184 (22)	60 (15)
Unknown	221 (N/A)	55 (N/A)	14 (N/A)
Recipient sex			
Male	3540 (59)	533 (60)	235 (58)
Female	2493 (41)	357 (40)	168 (42)
Karnofsky score			
10-80	2091 (35)	367 (41)	164 (41)
90-100	3801 (63)	502 (56)	221 (55)
Missing	141 (2)	21 (2)	18 (4)
Graft type			
Marrow	1660 (28)	209 (23)	115 (29)
PBSC	4348 (72)	673 (76)	284 (70)

Refreshed January 2019

Biorepository accruals

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
BM+PBSC	6 (<1)	3 (<1)	0
BM+UCB	19 (<1)	5 (1)	1 (<1)
PBSC+UCB	0	0	3 (1)
Conditioning regimen			
Myeloablative	3530 (59)	518 (58)	217 (54)
RIC/Nonmyeloablative	2469 (41)	367 (41)	179 (44)
TBD	34 (1)	5 (1)	7 (2)
Donor age at donation			
To Be Determined/NA	34 (1)	4 (<1)	2 (<1)
0-9 years	406 (7)	43 (5)	19 (5)
10-19 years	571 (9)	75 (8)	28 (7)
20-29 years	731 (12)	116 (13)	46 (11)
30-39 years	738 (12)	130 (15)	66 (16)
40-49 years	1004 (17)	148 (17)	57 (14)
50+ years	2549 (42)	374 (42)	185 (46)
Median (Range)	46 (0-81)	45 (0-79)	47 (0-76)
Donor/Recipient CMV serostatus			
+/+	2457 (41)	431 (49)	177 (45)
+/-	650 (11)	62 (7)	49 (13)
-/+	1490 (25)	202 (23)	87 (22)
-/-	1347 (23)	178 (20)	77 (20)
Unknown	89 (N/A)	17 (N/A)	13 (N/A)
GvHD Prophylaxis			
Ex-vivo T-cell depletion	65 (1)	19 (2)	3 (1)
CD34 selection	80 (1)	26 (3)	7 (2)
Post-CY + other(s)	1057 (18)	148 (17)	70 (17)
Post-CY alone	32 (1)	8 (1)	3 (1)
TAC + MMF +- other(s) (except post-CY)	698 (12)	59 (7)	25 (6)
TAC + MTX +- other(s) (except MMF, post-CY)	2520 (42)	331 (37)	196 (49)
TAC + other(s) (except MMF, MTX, post-CY)	557 (9)	195 (22)	45 (11)
TAC alone	51 (1)	7 (1)	2 (<1)
CSA + MMF +- other(s) (except post-CY)	157 (3)	11 (1)	4 (1)
CSA + MTX +- other(s) (except MMF, post-CY)	497 (8)	52 (6)	26 (6)
CSA + other(s) (except MMF, MTX, post-CY)	57 (1)	9 (1)	2 (<1)
CSA alone	53 (1)	8 (1)	2 (<1)
Other(s)	90 (1)	7 (1)	6 (1)
Missing	119 (2)	10 (1)	12 (3)
Donor/Recipient sex match			
Male-Male	1954 (32)	329 (37)	140 (35)
Male-Female	1305 (22)	168 (19)	83 (21)

Refreshed January 2019

Biorepository accruals

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Female-Male	1569 (26)	199 (22)	94 (23)
Female-Female	1184 (20)	188 (21)	82 (20)
CB - recipient M	15 (<1)	4 (<1)	1 (<1)
CB - recipient F	4 (<1)	1 (<1)	3 (1)
Unknown	2 (N/A)	1 (N/A)	0 (N/A)
Year of transplant			
2006-2010	511 (8)	48 (5)	38 (9)
2011-2015	3239 (54)	455 (51)	206 (51)
2016-2019	2283 (38)	387 (43)	159 (39)
Follow-up among survivors, Months			
N Eval	3825	575	258
Median (Range)	25 (1-126)	23 (2-121)	25 (2-109)

*Note: Biospecimens include whole blood, serum/plasma and limited quantities of viable cells and cell lines (collected prior to 2006). Specific inventory queries available upon request through the CIBMTR Immunobiology Research Program.