



A G E N D A

CIBMTR WORKING COMMITTEE FOR MORBIDITY, RECOVERY AND SURVIVORSHIP WORKING COMMITTEE

Salt Lake City, UT

Saturday, February 7, 2026, 1:00 – 3:00 PM (MT)

Co-Chair:	Seth Rotz, MD; Cleveland Clinic, Cleveland, OH; Telephone: 216-442-8806; E-mail: rotzs@ccf.org
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Page Scholar:	Reena Jayani-Kosarzycki, MD, MSCI; Vanderbilt University Medical Center, Nashville, TN; Telephone: 615-875-5751; E-mail: reena.v.jayani@vumc.org

1. Introduction

- a. Minutes from February 2025 ([Attachment 1](#))

2. Accrual summary ([Attachment 2](#))

3. Presentations, Publications or Submitted papers

- a. **LE12-03a** Gupta M, Schoettler ML, Brazauskas R, Bo-Subait S, Orozco G, Battiwalla M, D Buchbinder, Hamilton BK, Savani BN, Schoemans H, Sorrow ML, Ahmed S, Badawy SM, Bhushan V, Birdsey K, Couriel D, Doherty EE, Donato M, Farag SS, Gutman J, Horwitz M, El Jurdi N, Maakaron JE, Maziarz RT, Pineiro L, Schiller G, Weisdorf DJ, William BM, Shaw BE, Phelan R, Porter DL, Abt PL, Levine M. Risk factors for solid organ graft failure and death in hematopoietic cell transplant recipients undergoing solid organ transplantation: A retrospective Center for International Blood and Marrow Transplant Research and Organ Procurement and

- Transplantation Network Study. **Transplantation. 2025 Oct 1; 109(10):1626-1638. doi:10.1097/TP.0000000000005397. Epub 2025 Jun 23. PMC12353406.**
- b. **LE12-03b** Gupta M, Schoettler ML, Orozco G, Brazauskas R, Bo-Subait S, Battiwalla M, Buchbinder D, Hamilton BK, Savani BN, Schoemans H, Sorror ML, Ahmed S, Badawy SM, Bhushan V, Birdsey K, Couriel D, Doherty EE, Donato M, Farag SS, Gutman J, Horwitz M, El Jurdi N, Maakaron JE, Maziarz RT, Pineiro L, Schiller G, Weisdorf DJ, William BM, Shaw BE, Phelan R, Porter DL, Abt PL, Levine M. Risk factors for solid organ graft failure and death in solid organ transplant recipients undergoing hematopoietic Cell transplantation- A Center for International Blood and Marrow Transplant Research and Organ Procurement & Transplantation Network (OPTN) Study. **Transplantation. 2025 Oct 1; 109(10):1611-1625. doi:10.1097/TP.0000000000005377. Epub 2025 Jun 23. PMC12353109.**
 - c. **CT23-01** Comparison of fludarabine versus bendamustine as a lymphodepleting chemotherapy prior to CAR-T for large cell lymphoma. (R Kamble/ N Ahmed/ S Ganguly/ A Sieg/ C Strouse/ A Ali/ C Rodriguez-Bonilla/ K Nadiminti/ P Pophali/ S Mirza/ L Gowda). **Submitted.**
 - d. **RT19-01** Can Comorbidities Guide Reduced - Intensity Conditioning Selection in AML and MDS? A Center for International Blood and Marrow Transplant Research (CIBMTR) Analysis (R Shouval/ B Savani/ A Nagler). **Poster Presentation, Tandem Meetings 2025.**
 - e. **LE20-01** Cardiovascular Risk Factors in Survivors of Childhood Hematopoietic Cell Transplantation and their Role in Development of Cardiovascular Disease: A CCSS-CIBMTR Analysis (D Novetsky Friedman/ E Chow). **Oral Presentation, ISLCCC 2025.**
 - f. **RT20-01** Toxicities of older adults receiving allogeneic hematopoietic cell transplant compared to younger patients (R Jayani/H Murff). **Poster Presentation, Tandem Meetings 2026.**

4. Studies in progress (Attachment 3)

- a. **AC16-01** Pattern of use and outcomes with donor lymphocyte infusion after human leukocyte antigen haploidentical allogeneic hematopoietic stem cell transplant (E Gupta/ J Foran/ V Roy). **Manuscript Preparation.**
- b. **LE17-01** Late effects after hematopoietic stem cell transplantation for sickle cell disease (E Stenger/L Krishnamurti/S Shenoy). **Manuscript Preparation/Analysis.**
- c. **LE18-01** Trends in late mortality amongst two year survivors of pediatric allogeneic hematopoietic cell transplantation for hematologic malignancies (P Satwani/ L Broglie). **Manuscript Preparation/Submit.**
- d. **CT19-02** Prolonged cytopenia following CD-19 targeted chimeric antigen receptor T therapy for diffuse large B-cell lymphoma (M Shadman). **Manuscript Preparation.**
- e. **LE20-01** Cardiometabolic risk after total body irradiation during childhood (D Novetsky Friedman/E Chow). **Manuscript Preparation.**
- f. **CT20-03c** Determinants of effectiveness of CAR T cells for lymphoma (H Hashmi/ R Shouval/ K Wudhikarn). **Manuscript Preparation.**
- g. **CT20-04** Determinants of outcomes after chimeric antigen receptor T cells for acute lymphoblastic leukemia (S Mirza/ D Ragoonanan). **Data File Preparation.**
- h. **LE21-01** Risk of subsequent neoplasms in patients with post-transplant cyclophosphamide use for graft-versus-host disease prophylaxis (A Tomas/I Muhsen/L Yanez San Segundo/S K. Hashmi/ M-Angel Perales/A Kansagra). **Data file preparation/Analysis.**
- i. **RT19-01** Analysis of comorbidity-associated toxicity at a regimen-based level (R Shouval/ B Savani/A Nagler). **Manuscript Preparation.**
- j. **RT19-02** Hemorrhagic cystitis (HC) as a complication of hematopoietic cell transplantation with post-transplant cyclophosphamide (PTCy)-based graft-versus-host disease prophylaxis compared to other allogeneic transplants (K Adekola/ N Ali/ O Frankfurt/ L Metheny/ J Moreira/M de Lima). **Protocol Development/Data file preparation.**

Not for publication or presentation

- k. **RT20-01** Toxicities of older adults receiving allogeneic hematopoietic cell transplant compared to younger patients (R Jayani/H Murff). **Analysis.**
- l. **CT22-01** CD19-CAR-T therapy failure: Impact of subsequent therapy in patients with B-cell malignancies (L Gowda/ G Murthy). **Protocol Development/Data file preparation.**
- m. **CT22-02** Machine learning for predicting toxicity and early clinical outcomes in DLBCL and B-ALL patients treated with commercial CAR T products in the real-world setting: an analysis of the CIBMTR registry (A Tomas/ L Appell/ E Bezerra/ A Mirza/ M Perales/ A Sharma/ Y Lin/ L Gowda/ G Murthy). **Analysis.**
- n. **MRS22-01** Racial/ethnic disparities and role of poverty in long-term health outcomes among survivors of allogeneic hematopoietic cell transplant performed in childhood (N Bhatt/A Sharma/L Jimenez-Kurlander/C Duncan). **Protocol Development.**
- o. **MRS22-02** Incidence, risk factors and outcomes of acute cardiac complications after post-transplant cyclophosphamide based GVHD prophylaxis: A retrospective analysis from the CIBMTR database (K Poonsombudlert/C Strouse/H Rangarajan/P Satwani/D Modi). **Protocol Development.**
- p. **MRS23-01** Updated Analysis of Long-Term Survival and Late Deaths after Allogeneic Hematopoietic Cell Transplantation for Hematologic Malignancies and Severe Aplastic Anemia (M Battiwalla/U Rao). **Protocol development.**
- q. **MRS24-01** Toxicity profile and survival of patients with body mass index >30 undergoing allogeneic stem cell transplantation (N Tijaro Ovalle/ A Jakubowski). **Protocol Development.**
- r. **MRS24-02** Determinants of immune effector cell-associated hematotoxicity following CAR-T therapy across disease entities (K Rejeski/ R Shouval). **Analysis.**
- s. **MRS25-01** Association of fludarabine exposure on car-t outcomes (K Sweiss/ S Ahmed). **Protocol development.**
- t. **MRS25-02** CIBMTR Validation of the Transplant Conditioning Intensity (TCI) Classification System in Patients with Acute Myeloid Leukemia and Myelodysplastic Syndrome receiving GVHD prophylaxis with or without Post-Transplant Cyclophosphamide (A Jimenez Jimenez/ B Shaffer/ C Jackson/ L Muffly). **Protocol development.**
- u. **MRS25-03** Real World Experience of Immune Effector Cell Associated Hemophagocytic Lymphohistiocytosis-like Syndrome (IEC HS) in CAR T-cell Recipients (K McNerney/ T Jain/ N Vojjala/ N Ahmed). **Protocol development.**

5. Future/proposed studies

- a. **PROP 2509-47** Use of Anakinra for the Treatment of ICANS after Anti-CD19 Autologous CART in B-cell Lymphoma (Z Hunzeker/ P Strati) ([Attachment 4](#))
- b. **PROP 2509-75; 2509-133; 2509-159** Epidemiology and predictors of non-infectious pulmonary toxicities of contemporary allogeneic transplantation, 2017-2024 (N Tijaro Ovalle/ C Sauter/ A Bao/ J Van Galen/ U Gergis) ([Attachment 5](#))
- c. **PROP 2509-79** Incidence and Causes of Non-Relapse Mortality Following CAR T-cell Therapy in Pediatric and Young Adult B-ALL (A Lambale/ N Shah) ([Attachment 6](#))
- d. **PROP 2509-81** Delayed engraftment and graft rejection in pediatric patients after CAR T-cell therapy (A Dreyzin/ A Keating) ([Attachment 7](#))
- e. **PROP 2509-120** Machine Learning Predictive Modeling of Autologous Mobilization Success and Transplant Outcomes (S Hurwitz) ([Attachment 8](#))
- f. **PROP 2509-153** Developing a Novel Composite Mortality Prediction Score Incorporating Hemoglobinopathy Specific Clinical Biomarkers with the HCT-CI in Allogeneic Transplant Recipients with Sickle Cell Disease (G Raman/ M Thakar) ([Attachment 9](#))
- g. **PROP 2509-209** Comparing patient reported outcomes in allogeneic stem cell transplant recipients who receive myeloablative (MAC) versus reduced intensity conditioning (RIC)

Not for publication or presentation

- (S Usman/ G Shah) ([Attachment 10](#))
- h. **PROP 2509-214** Comparative Prognostic Value of Clinical (HCT-CI, Performance Status) and Structural (Area Deprivation Index, Rurality, Distance to Center) Risk for 1-Year Patient-Reported Recovery After Hematopoietic Cell Transplantation (M-M Sainvil/ S Hong) ([Attachment 11](#))
 - i. **PROP 2509-222** Incidence and risk factors of head and neck cancers in HCT recipients (J Epstein) ([Attachment 12](#))

Proposed studies; not accepted for consideration at this time

- j. **PROP 2506-03** The risk of ICANS in APOE4 allele carriers (K Javanshiri). **Dropped due to small sample size.**
- k. **PROP 2509-04** Evaluation of major cardiovascular and thrombotic events following allogeneic transplantation for myelofibrosis (A Coltoff/ A Keyzner). **Dropped due to overlap with current study/publication.**
- l. **PROP 2509-12** Comparative Analysis of Long-term Cognitive Impairment Following BCMA-targeted CAR-T Cell Therapy versus Autologous Stem Cell Transplantation in Multiple Myeloma: A CIBMTR Registry Study (C-H Lee). **Dropped due to small sample size.**
- m. **PROP 2509-18** Comparative impact on ICANS of tocilizumab vs siltuximab in B-cell lymphoma patients treated with CAR T-cell Therapy (C Zhang/ P Strati). **Dropped due to small sample size.**
- n. **PROP 2509-50** Immune effector cell-associated gastrointestinal toxicities following chimeric antigen receptor T-cell therapy in B-cell non-Hodgkin lymphoma (A Tun/ P Johnston). **Dropped due to small sample size.**
- o. **PROP 2509-60** Real-World Outcomes of Lifileucel in Advanced Melanoma (C Lin) **Dropped due to need of supplemental data.**
- p. **PROP 2509-72** Real-World Evidence for the use of Afamitresgene Autoleucel, a Novel Autologous TCR T cell Therapy Targeting MAGE-A4, in Adults with Synovial Sarcoma (C Lin). **Dropped due to small sample size.**
- q. **PROP 2509-98** Validating the predictive power of the expanded and simplified youth nonmalignant hematopoietic cell transplantation comorbidity index (ynHCT-CI) in a contemporary nonmalignant patient cohort treated with hematopoietic cell transplantation and gene therapy (O Williams/ M Thakar). **Dropped due to small sample size.**
- r. **PROP 2509-100** The incidence, risk factors, and outcomes of non-ICANS neurotoxicity in BCMA-directed CAR T-cell therapy for Multiple Myeloma. (B Wirk). **Dropped due to small sample size.**
- s. **PROP 2509-104** To determine the incidence and assess outcomes of Multiple Myeloma Patients who develop non-ICANS Neurotoxicity related to BCMA directed CAR-T therapy. (A Desai/ R Maziarz). **Dropped due to small sample size.**
- t. **PROP 2509-108** Long-term Outcomes of Adolescent and Young Adult Allogeneic Hematopoietic Cell Transplantation Patients After Undergoing Total Body Irradiation Myeloablative Conditioning (M Kashif Amin). **Dropped due to low scientific impact.**
- u. **PROP 2509-109** Thiotepa or TBI-based conditioning regimens and incidence of graft failure in mismatch unrelated donor or haploidentical transplant (A Aljundi/ T Bahar/ S Farhan). **Dropped due to low scientific impact.**
- v. **PROP 2509-110** Incidence of Thrombotic Microangiopathy In PTCy-Based GVHD Prophylaxis Regimens (T Bahar/ A Aljundi/ S Farhan). **Dropped due to overlap with current study/publication.**
- w. **PROP 2509-146** Isolating systematic differences in immune effector cell-associated encephalopathy (ICE) scoring among institutions as an investigation of consistency for immune effector-cell associated neurotoxicity syndrome (ICANS) diagnosis. (J Van Galen/ U Gergis). **Dropped due to low scientific impact.**

Not for publication or presentation

- x. **PROP 2509-150** Impact of Body Mass Index on Chimeric Antigen Receptor T Cell Therapy Outcomes in Multiple Myeloma (K Miller/ D Cirstea). ***Dropped due to low scientific impact.***
- y. **PROP 2509-151** Financial Toxicity and Return to Work in AYA Patients Receiving CD19 CAR T-cell Therapy (H Lust/ R Faramand). ***Dropped due to small sample size.***
- z. **PROP 2509-157** Myeloablative vs reduced intensity conditioning in matched related and unrelated donor transplants with post-transplant cyclophosphamide-based graft versus host disease prophylaxis (A K Mehta/ M Gooptu). ***Dropped due to overlap with current study/publication.***
- aa. **PROP 2509-178** Health-Related Quality of Life (HRQoL) Following Chimeric Antigen Receptor T-Cell Therapy for Hematological Malignancies. (S Gupta/ N Abdallah). ***Dropped due to small sample size.***
- bb. **PROP 2509-191** Real-World Safety and Efficacy of Patients with Large B-Cell Lymphoma Treated With Axicabtagene Ciloleucel and Prophylactic Corticosteroids. (R Shah/ P Strati). ***Dropped due to small sample size.***
- cc. **PROP 2509-220** Prognostic Utility of Pre-Transplant Pulmonary Function Tests in Multiple Myeloma Undergoing Autologous Stem Cell Transplantation or Chimeric Antigen Receptor Therapy (H Shaikh/ Y Efebera/ A Vogel). ***Dropped due to need of supplemental data.***
- dd. **PROP 2509-227** Impact of pre-transplant cardiovascular risk on non-relapse mortality in patients receiving post-transplant cyclophosphamide and non-post-transplant cyclophosphamide-based GVHD prophylaxis (A K Mehta/ R Shapiro). ***Dropped due to overlap with current study/publication.***
- ee. **PROP 2509-230** The Impact of Primary Language on Outcomes After Allogeneic Hematopoietic Cell Transplantation: A Retrospective Analysis Using CIBMTR Data (M Walji). ***Dropped due to need of supplemental data.***
- ff. **PROP 2509-231** Return to Work after Allogeneic Hematopoietic Stem Cell Transplantation in Adults (P Grover). ***Dropped due to low scientific impact.***

6. Other business



A G E N D A

CIBMTR WORKING COMMITTEE FOR MORBIDITY, RECOVERY AND SURVIVORSHIP WORKING COMMITTEE

Honolulu, HI

Saturday, February 15, 2025, 1:00 – 3:00 PM

Co-Chair:	Hélène Schoemans, MD, PhD; University Hospitals Leuven and KU Leuven; Telephone: 321-634-6889; Email: helene.schoemans@uzleuven.be
Co-Chair:	Mohamed Sorrow, MD, MSc; Fred Hutchinson Cancer Research Center; Phone: 206-667-6298; Email: msorrow@fredhutch.org
Co-Chair:	Seth Rotz, MD; Cleveland Clinic, Cleveland, OH; Telephone: 216-442-8806; E-mail: rotzs@ccf.org
Co-Chair:	Sairah Ahmed, MD; University of Texas, MD Anderson Cancer Center, Houston, TX; Telephone: 713-794-5745; E-mail: sahmed3@mdanderson.org
Scientific Director:	Rachel Phelan, MD, MPH; CIBMTR® (Center for International Blood and Marrow Transplant Research), Milwaukee, WI; Telephone: 414-955-4610 E-mail: rphelan@mcw.edu
Scientific Director:	Amy Moskop, MD, MS; CIBMTR® (Center for International Blood and Marrow Transplant Research), Milwaukee, WI; Telephone: 414-805-0747 E-mail: amoskop@mcw.edu
Statistical Director:	Ruta Brazauskas, PhD; CIBMTR® (Center for International Blood and Marrow Transplant Research), Milwaukee, WI; Telephone: 414-456-8687; E-mail: ruta@mcw.edu
Statistician:	Andrew Peterson, MS; CIBMTR® (Center for International Blood and Marrow Transplant Research), Milwaukee, WI; Telephone: 414-805-8163; E-mail: andpeterson@mcw.edu

1. Introduction

a. Minutes from February 2024 (Attachment 1)

The CIBMTR Morbidity Recovery and Survivorship Working Committee (MRSWC) meeting was called to order at 1:00 HST on Friday, February 15, 2025 by Dr. Amy Moskop. She began by welcoming all the in-person and virtual attendees and providing the CIBMTR's Industry Funding Disclosure. Then, she introduced our committee's leadership, including Dr. Annie Im as our incoming chair, Dr. Michelle Schoettler as our Page Scholar, and Rebecca Higgins and Brandon Nuechterlein as our CAC representatives. After reviewing the committee's COI disclosures, she explained the sources of our HCT/CT data and their corresponding forms.

Dr. Michelle Schoettler then took over and explained some of the CIBMTR's resources, including PRO data, public datasets, and study summaries on our website. She then explained MRS committee membership, and that anyone that scanned their badge is now a member! Dr. Schoettler explained our goals of publishing high impact studies in a timely manner. As a Page scholar, she explained the program and her experience getting involved with CIBMTR. Lastly, she highlighted changes and additional restrictions with submitting proposals.

Dr. Seth Rotz introduced our studies' recent publications, as well as our current studies in progress. Please find them listed in sections 3 and 4.

Dr. Rachel Phelan introduced the scoring process for our 8 accepted proposals this year. Each presentation is about 5 minutes in length with about 5 minutes for questions. The proposals accepted to become studies boils down to their scientific impact, prioritization, and score. As these studies progress, those that are members of our working committee can contribute as authors, assuming substantial contributions to all steps of the study are made.

Dr. Mohamed Sorrow and Dr. Sairah Ahmed then introduced the proposals listed in section 5. Please find their corresponding notes below.

2. Accrual summary (Attachment 2)

3. Presentations, Publications or Submitted papers

- a. **LE19-01d** Smith MA, Cheng G, Phelan R, Brazauskas R, Strom J, Ahn KW, Hamilton BK, Peterson A, Savani B, Schoemans H, Schoettler ML, Sorrow M, Keller RL, Higham CS, Dvorak CC, Fineman JR, Zinter MS. Pulmonary hypertension in the intensive care unit after pediatric allogeneic hematopoietic stem cell transplant: Incidence, risk factors, and outcomes. *Frontiers in Oncology*. 14:1415984. doi:10.3389/fonc.2024.1415984. Epub 2024 May 29. PMC11167102.
- b. **LE19-01c** Cheng G, Smith M, Phelan R, Brazauskas R, Strom J, Ahn KW, Hamilton B, Peterson A, Savani B, Schoemans H, Schoettler M, Sorrow M, Higham C, Kharbanda S, Dvorak C, Zinter M. Epidemiology of diffuse alveolar hemorrhage in pediatric allogeneic hematopoietic cell transplant recipients. *Transplantation and Cellular Therapy*. 2024 Oct 1; 10(30):1017.e1-1017.e12. doi:10.1016/j.jtct.2024.07.022. Epub 2024 Jul 31.
- c. **LE16-02b** Kahn J, Brazauskas R, Bo-Subait S, Buchbinder D, Hamilton BK, Schoemans H, Abraham AA, Agrawal V, Auletta JJ, Badawy SM, Beitinjaneh A, Bhatt NS, Broglie LA, Diaz M, Farhadfar N, Freytes CO, Gale RP, Ganguly S, Hayashi RJ, Hematti P, Hildebrandt GC, Inamoto Y, Kamble RT, Koo J, Lazarus HM, Mayo SJ, Mehta PA, Myers KC, Nishihori T, Prestidge T, Rotz SJ, Savani BN, Schears RM, Sharma A, Stenger E, Ustun C, Williams KM, Vrooman LM, Satwani P, Phelan R. Late effects after allogeneic hematopoietic cell transplantation in children and adolescents with non-malignant disorders: a retrospective cohort study. *The Lancet. Child & Adolescent Health*. doi:10.1016/S2352-4642(24)00167-6. Epub 2024 Aug 30.
- d. **LE12-03a** Risk Factors for Solid Organ Graft Failure and Death in Hematopoietic Cell Transplant Recipients Undergoing Solid Organ Transplantation- A Retrospective Center for International Blood and Marrow Transplant Research (CIBMTR) and Organ Procurement & Transplantation Network Study. *In Press*.
- e. **LE19-01c** Cheng G, Smith M, Phelan R, Brazauskas R, Strom J, Ahn KW, Hamilton B, Peterson A, Savani B, Schoemans H, Schoettler M, Sorrow M, Higham C, Kharbanda S, Dvorak C, Zinter M. Epidemiology of diffuse alveolar hemorrhage in pediatric allogeneic hematopoietic cell transplant recipients. *Transplantation and Cellular Therapy*. 2024 Oct 1; 10(30):1017.e1-1017.e12. doi:10.1016/j.jtct.2024.07.022. Epub 2024 Jul 31.
- f. **LE12-03b** Risk Factors for Solid Organ Graft Failure and Death in Solid Organ Transplant Recipients Undergoing Hematopoietic Cell Transplantation- A Retrospective Center for International Blood and Marrow Transplant Research (CIBMTR) and Organ Procurement & Transplantation Network (OPTN) Study. *In Press*.
- g. **CT20-03a** New Comorbidity Index Predicts Survival After Chimeric Antigen Receptor T Cell Therapy for Large B-Cell Lymphoma. *Submitted*.

- h. **CT20-03b** Cytokine release syndrome and neurotoxicity following CD19-CAR T-cell therapy in aggressive B-cell lymphoma: a CIBMTR analysis. **Submitted.**

4. Studies in progress (Attachment 3)

- a. **AC16-01** Pattern of use and outcomes with donor lymphocyte infusion after human leukocyte antigen haploidentical allogeneic hematopoietic stem cell transplant (E Gupta/ J Foran/ V Roy). **Manuscript Preparation.**
- b. **LE17-01** Late effects after hematopoietic stem cell transplantation for sickle cell disease (E Stenger/ L Krishnamurti/ S Shenoy). **Analysis.**
- c. **LE18-01** Trends in late mortality amongst two year survivors of pediatric allogeneic hematopoietic cell transplantation for hematologic malignancies (Prakash Satwani/ Larisa Broglie). **Manuscript Preparation.**
- d. **CT19-02** Prolonged cytopenia following CD-19 targeted chimeric antigen receptor T therapy for diffuse large B-cell lymphoma (M Shadman). **Manuscript Preparation.**
- e. **LE19-02** Incidence and predictors of long-term toxicities and late side effects in elderly patients (≥ 50 years) receiving allogeneic hematopoietic cell transplantation for hematological malignancies (M Veeraputhiran/S Pingali/A Mukherjee/L Muffly). **Analysis.**
- f. **LE20-01** Cardiometabolic risk after total body irradiation during childhood (D Novetsky Friedman/E Chow). **Manuscript preparation.**
- g. **CT20-03c** Determinants of effectiveness of CAR T cells for lymphoma (H Hashmi/ R Shouval/ K Wudhikarn). **Manuscript Preparation.**
- h. **CT20-04** Determinants of outcomes after chimeric antigen receptor T cells for acute lymphoblastic leukemia (S Mirza/ D Ragoonanan). **Data File Preparation.**
- i. **LE21-01** Risk of subsequent neoplasms in patients with post-transplant cyclophosphamide use for graft-versus-host disease prophylaxis (A Tomas/I Muhsen/L Yanez San Segundo/S K. Hashmi/ M-Angel Perales/A Kansagra). **Data File Preparation.**
- j. **RT19-01** Analysis of comorbidity-associated toxicity at a regimen-based level (R Shouval/ B Savani/A Nagler). **Analysis.**
- k. **RT19-02** Hemorrhagic cystitis (HC) as a complication of hematopoietic cell transplantation with post-transplant cyclophosphamide (PTCy)-based graft-versus-host disease prophylaxis compared to other allogeneic transplants (K Adekola/ N Ali/ O Frankfurt/ L Metheny/ J Moreira/ M de Lima). **Protocol Development.**
- l. **RT20-01** Toxicities of older adults receiving allogeneic hematopoietic cell transplant compared to younger patients (R Jayani/H Murff). **Data File Preparation.**
- m. **CT22-01** CD19-CAR-T therapy failure: Impact of subsequent therapy in patients with B-cell malignancies (L Gowda/ G Murthy). **Protocol Development.**
- n. **CT22-02** Machine learning for predicting toxicity and early clinical outcomes in DLBCL and B-ALL patients treated with commercial CAR T products in the real-world setting: an analysis of the CIBMTR registry (A Tomas/ L Appell/ E Bezerra/ A Mirza/ M Perales/ A Sharma/ Y Lin/ L Gowda/ G Murthy). **Protocol Received.**
- o. **MRS22-01** Racial/ethnic disparities and role of poverty in long-term health outcomes among survivors of allogeneic hematopoietic cell transplant performed in childhood (N Bhatt/A Sharma/L Jimenez-Kurlander/C Duncan). **Protocol Development.**
- p. **MRS22-02** Incidence, risk factors and outcomes of acute cardiac complications after post-transplant cyclophosphamide based GVHD prophylaxis: A retrospective analysis from the CIBMTR database (K Poonsombudlert/C Strouse/H Rangarajan/P Satwani/D Modi). **Protocol Received.**
- q. **CT23-01** Outcomes of CD19 CAR-T in patients who received lymphodepleting chemotherapy using fludarabine-containing versus other regimens (R Kamble/ N Ahmed/ S Ganguly/ A Sieg/ C

Strouse/ A Ali/ C Rodriguez-Bonilla/ K Nadiminti/ P Pophali/ S Mirza/ L Gowda). **Manuscript Preparation.**

- r. **MRS23-01** Updated Analysis of Long-Term Survival and Late Deaths after Allogeneic Hematopoietic Cell Transplantation for Hematologic Malignancies and Severe Aplastic Anemia (M Battiwalla/U Rao). **Protocol Pending.**
- s. **MRS24-01** Toxicity profile and survival of patients with body mass index >30 undergoing allogeneic stem cell transplantation (N Tijaro Ovalle/ A Jakubowski). **Protocol Received.**
- t. **MRS24-02** Determinants of immune effector cell-associated hematotoxicity following CAR-T therapy across disease entities (K Rejeski/ R Shouval). **Protocol Received.**

5. Future/proposed studies

- a. **PROP 2410-02** Association of fludarabine exposure on car-t outcomes (K Sweiss/ S Ahmed) (Attachment 4)

Dr. Karen Sweiss gave this presentation virtually. Since fludarabine exhibits wide PK variability after dosing, it leads to unpredictable dose-exposure (AUC) profiles. This study aims to assess the variability of AUC and model the outcomes for patients with MM or LBCL that have fludarabine.

The first question asked why ALL patients will not be included in this study. Dr. Sweiss said that MM and LBCL are good starting points, but ALL can be included. This echoes another comment to include a pediatric population.

The second comment addresses the variability of dosing based on product. It will be important to investigate this as a confounding factor.

Dr. Moskop mentioned that we only capture total dose and start date, not dosing on each day. The number of doses is not specified. Dr. Sweiss noted that they would still be able to run the model even without daily dosing data.

An additional comment asked that if this model becomes finalized, can this model become available through all centers associated with CIBMTR? Dr. Sweiss said that the next steps would be to validate the model with measured PK data. If the convergence is good, this may be used as a good dosing guide.

- b. **PROP 2410-10/2410-232** Comparing the Toxicity Profile of AYA Patients vs Older Patients following anti-CD19 CAR T-cell Therapy for B-cell malignancies (I Sheikh/ P Kebriaei/ S Ahmed) (Attachment 5)

Dr. Irtiza Sheikh gave this presentation. This study aims to further our understanding of the impact of CAR-T cell toxicities in AYA patients with B-cell malignancies. This study includes LBCL and ALL patients.

The first question asked if LBCL includes primary mediastinal lymphoma. These patients are AYA and there is a confounding factor of the checkpoint inhibitors. They are not included for now but will gladly be considered.

The second question asked if we know disease burden and infection prior to infusion. Disease burden is captured on the forms. Infection pre-CAR T is captured only within the context of the comorbidity index.

The third comment mentions that there is some discrepancy in product. Also, they have enough patients to explore differences within the AYA group. Lastly, they are encouraged to explore the differences between patients treated in pediatric vs primarily adult hospitals.

- c. **PROP 2410-14/2410-102/2410-124/2410-165** Impact of Baseline Co-Morbidities including HCT-CI and Renal Dysfunction on Non-Relapse Mortality and Survival in Myeloma Patients Treated with Chimeric Antigen Receptor T (CAR T) Cell Therapy and Developing a Co-Morbidity Score to Predict Outcomes (M Mohan/ C Schinke/ H Shaikh/ H Hashmi/ S Usmani/ M Janakiram/ G Kaur/ S Sidana/ D Hansen) (Attachment 6)

This presentation was given by Dr. Gurbakhash Kaur. The goal of this study is to create a validated risk prediction tool to assess the impact of comorbidities on treatment outcomes for CAR-T patients.

The first comment alluded to a presentation at ASH that created a CT-CI for patients with lymphoma. It is suggested to take this and if it works well with myeloma patients. Dr. Kaur mentioned that we would need to account for additional disease-specific details outside of comorbidities (which CT-CI is based on) so there remains value of creating a new score for these patients.

The second WC participant mentioned that NRM will likely be low and that looking at overall survival as a primary endpoint may be better. Dr. Sorror agrees to look at OS and disease features. The HCT-CI does not translate as well to myeloma; CAR-T is more about relapse and relapse-related mortality.

The last comment it was that it would be interesting to include malnutrition, if available in the registry, as one of the comorbidities.

- d. **PROP 2410-16/2410-154** CIBMTR Validation of the Transplant Conditioning Intensity (TCI) Classification System in Patients with Acute Myeloid Leukemia and Myelodysplastic Syndrome receiving GVHD prophylaxis with or without Post-Transplant Cyclophosphamide (A Jimenez Jimenez/ B Shaffer/ C Jackson/ L Muffly) (Attachment 7)

This presentation was given by Dr. Clayton Jackson. The TCI score is a score developed by EBMT as a refinement to the classic RIC/MAC strata. Each regimen is assigned an intensity rate, and is used to calculate the score. This study hopes to validate the TCI score as a predictive measurement of conditioning intensity compared to RIC/MAC.

The first comment mentioned that we may not need to have our endpoints as long, since NRM has been improving throughout the years. Also, we may need to separate PTCy into a separate cohort.

Since this score was not originally data driven, the second comment suggested to not only validate the score, but to develop something better as well.

The third question addressed that era is a confounder in NRM. So when comparing the PTCy cohort, how do we know differences are due to the confounder or PTCy? Given that the dataset is large, it will be feasible to narrow something down to more in-line with the current era.

- e. **PROP 2410-99/2410-260** Real World Experience of Immune Effector Cell Associated Hemophagocytic Lymphohistiocytosis-like Syndrome (IEC HS) in CAR T-cell Recipients (K McNerney/ T Jain/ N Vojjala/ N Ahmed) (Attachment 8)

This presentation was given by Dr. Kevin McNerney. The goal of this study is to provide a descriptive analysis of IEC-HS, as well as a multivariate analysis to determine associated factors.

The first question asked how confident we are that all IEC-HS reported is accurate, and not severe CRS with MOD. Also, how confident that our registry identifies what was used to treat the HLH? Dr. Moskop added that HLH was previously captured within the context of CRS (child question) but has since been separated from CRS so ideally we are capturing these patients better. However, past data will likely not be clean. Additionally, organ toxicity collection is very limited within the registry so will likely not be useful for IEC-HS grading purposes.

There are dates for resolution of IEC-HS collected. Also, there are grade 3 organ toxicities and peak ferritin collected to help with diagnosis. For the treatments, there is a field that asks for the specific HLH treatment, separate from CRS data collected.

The second comment said that these numbers are likely underreported. We may need to come up with our own criteria to define this outside of the ASTCT consensus criteria.

- f. **PROP 2410-248** Impact of Li Fraumeni syndrome upon outcomes of Hematopoietic stem cell transplant recipients of hematologic malignancies (K Singh Sandhu/ R Nakamura) (Attachment 9)

Dr. Karamjeet S Sandhu gave this presentation. Li-Fraumeni syndrome is an autosomal dominant disorder characterized by a germline TP53 mutation, and about 4% of these patients will go on to develop hematologic malignancies. This study aims to evaluate EFS and other outcomes in this cohort.

The first comment from the audience brings up that the primary endpoint is at 4 years, but about 25% of the population won't have 4-year follow-up. It is agreed that by the time we would run the analysis, the data may mature some more.

The second question asked if we have samples for these patients in the repository. We do not know the number currently, but it is a number that we would be able to pull.

- g. **PROP 2410-249** Clonal Cytopenia Mutations: The Impact of the Recipient's Underlying Malignant Disease Biology on Posttransplant Engraftment of Donor-derived Clonal Cytopenia (CH) Clones (M Kulasekaran/ G Hildebrandt) (Attachment 10)

This presentation was given by Dr. Monika Kulasekaran. The goal of this study is to evaluate the impact of disease biology in the engraftment of donor CH clones in select diseases, perform a comparative analysis of pre-HCT bone marrow molecular profiling, and post-HCT molecular testing to identify the acquisition of novel mutations.

The first comment addresses that CHIP mutations are driven by age. Therefore, it may make sense to restrict it to older donor-recipient pairs.

The second question asked if we would collect samples randomly and evaluate? The PIs will restrict by donor age (40+ years) and then would test the donor samples randomly. There is no plan to test the recipient samples.

The third comment mentions that we will need to look at the data closely and make sure we have all of the donors that we need as samples. It was suggested to look at available specimens on the BMT CTN public website for post-HCT sample availability

- h. **PROP 2410-258** The Risk of Engraftment Syndrome in Multiple Myeloma Patients Undergoing Autologous Stem Cell Transplantation: A Comparison of Plerixafor + G-CSF vs. G-CSF Alone (N Tiwari/ J Holter Chakrabarty/ P Vallabhaneni) (Attachment 11)

This presentation was given by Dr. Nishant Tiwari. The goal of this study is to study the association of incidence of ES in patients receiving ASCT for MM who were treated with Plerixafor + G-CSF vs. G-CSF alone.

A question was asked if we should shorten the time-period of data collected. Over time, their cell populations that are mobilized may begin to differ. This is definitely something that can be looked into.

Proposed studies; not accepted for consideration at this time

- i. **PROP 2407-03** Assessing the Risk of Secondary Breast Cancer Malignancy in Survivors Following Radiation Therapy Post- pediatric bone marrow Transplantation (BMT) (M Gabriel/ I Twist). ***Dropped due to small sample size.***
- j. **PROP 2408-11** Endocrine impairments after hematopoietic stem cell transplantation based on the big database, CIBMTR (M Pamukcuoglu). ***Dropped due to overlap with current study/publication.***
- k. **PROP 2408-12** Which Treatment is Best for Hematopoietic Stem Cell Transplantation Associated Thrombotic Microangiopathy? (M Pamukcuoglu). ***Dropped due to low scientific impact.***
- l. **PROP 2409-03** CRS-related and driving-related restriction durations following BCMA CAR-T therapy (R Banerjee). ***Dropped due to overlap with current study/publication.***
- m. **PROP 2409-10** Incidence, Causes and Outcome of End Stage Renal Disease Post-Allogeneic HSCT (F Andreozzi/ G Gambino). ***Dropped due to supplemental data needed.***
- n. **PROP 2409-24** Late effects in allogeneic HCT patients receiving post-transplant cyclophosphamide for hematological malignancies. (P Munshi/ N Hossain). ***Dropped due to overlap with current study/publication.***
- o. **PROP 2409-28** Identifying Patients Who Derive Survival Benefits from Reduced Intensity Conditioning Regimen (Y Akahoshi/ J Levine). ***Dropped due to overlap with current study/publication.***

- p. **PROP 2409-34** Molecular origin of second primary malignancy after CAR19 therapy for B-cell lymphoma. (D Miklos/ M Hamilton). ***Dropped due to overlap with current study/publication***
- q. **PROP 2410-20** What is the risk of subsequent neoplasm in the modern era of hematopoietic cell transplantation? (O Ringden/ B Sadeghi). ***Dropped due to overlap with current study/publication***
- r. **PROP 2410-39** Safety and Effectiveness of CAR-T Cell Therapy in Patients with B-Cell Malignancies and Heart Failure (G Sanchez-Petitto/ P Strati). ***Dropped due to supplemental data needed.***
- s. **PROP 2410-48** Outcomes of Grade 3 & 4 Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS) in patients who receive CD-19 - directed CAR-T cell therapy for Large B-Cell Lymphoma (LBCL) (A Gradone/ U Gergis). ***Dropped due to overlap with current study/publication.***
- t. **PROP 2410-49** Outcomes of Grade 3 and 4 Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS) in patients who receive BCMA -directed CAR-T cell therapy for Multiple Myeloma (A Gradone/ U Gergis). ***Dropped due to overlap with current study/publication.***
- u. **PROP 2410-51** Patient Reported Outcomes of Grade 3 & 4 Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS) in patients who receive CAR-T cell therapy for hematologic malignancies (A Gradone/ U Gergis). ***Dropped due to small sample size.***
- v. **PROP 2410-59** Evaluation of the Incidence of Pregnancy and Outcomes Post CAR-T Cell Therapy (S Raghunandan/ V Bachanova). ***Dropped due to small sample size.***
- w. **PROP 2410-92** Safety and Efficacy of CAR-T in Multiple Myeloma Patients with Pre-existing Heart Failure (H Shaikh/ Y Efebera). ***Dropped due to supplemental data needed.***
- x. **PROP 2410-95** Second Primary Malignancies in Patients with Relapsed/Refractory Multiple Myeloma after Commercial BCMA-directed CAR T-cell therapy (D Dima/ D Hansen). ***Dropped due to overlap with current study/publication.***
- y. **PROP 2410-96** Real world data for lifileucel (J Wagner). ***Dropped due to small sample size.***
- z. **PROP 2410-104** Neurologic and Cognitive Health of Survivors of Chimeric Antigen Receptor Therapy in the United States. (V Irizarry Gatell/ R Faramand). ***Dropped due to small sample size.***
- aa. **PROP 2410-109** Post-transplant toxicity and non-relapse mortality in recipients of low-intensity therapies before allogeneic stem cell transplant. (L Gowda/ K Chetlapalli). ***Dropped due to small sample size.***
- bb. **PROP 2410-118** Incidence and risk factors for therapy-associated myeloid neoplasms following chimeric antigen receptor T-cell therapy (R Stubbins/ H Cherniawsky). ***Dropped due to overlap with current study/publication.***
- cc. **PROP 2410-119** Incidence of secondary malignancies following commercial chimeric antigen receptor T-cell (CAR-T) therapy. (B Gattas/ U Gergis). ***Dropped due to overlap with current study/publication.***
- dd. **PROP 2410-122** Pulmonary function testing to predict the risk of complications after CAR-T therapies in hematologic malignancies (A Sheshadri/ S Ahmed). ***Dropped due to supplemental data needed.***
- ee. **PROP 2410-129** The Cardiac Toll of CART-T Therapy: Long-Term Implications (D Jamil/ S Farhan/ M Reddy). ***Dropped due to supplemental data needed.***
- ff. **PROP 2410-142** Treatment related mortality according to post infusion time in recipients of FDA approved BCMA and CD 19 CART therapy (N Vojjala/ N Ahmed). ***Dropped due to low scientific impact.***
- gg. **PROP 2410-146** An assessment of conditioning dose intensity dosing in the setting of post-transplant cyclophosphamide (PTCy) (T Wang/ A Jimenez Jimenez). ***Dropped due to overlap with current study/publication.***

- hh. **PROP 2410-173** Understanding updates to prognosis as complications accumulate in pediatric stem cell transplantation (J O'Brien/ G Chain/ E Frint). **Dropped due to overlap with current study/publication.**
- ii. **PROP 2410-183** Real-world experience of Second Primary Malignancies post treatment with CAR-T cell therapy in patients with Multiple Myeloma, ALL, Lymphoma (N Vojjala/ N Ahmed). **Dropped due to overlap with current study/publication.**
- jj. **PROP 2410-188** Impact of Pre-treatment Liver-related Factors on Clinical Outcomes after CAR T-cell Therapy for Lymphoma. (S Ahmed/ A Lionel). **Dropped due to supplemental data needed.**
- kk. **PROP 2410-196** Health-Related Quality of Life (HRQoL) Following Chimeric Antigen Receptor T-Cell Therapy for Hematological Malignancies. (N Abdallah/ S Gupta). **Dropped due to small sample size.**
- ll. **PROP 2410-209** Incidence and Treatment of Movement and Neuro-cognitive treatment emergent adverse events (MNTs) following BCMA CAR-T cell therapy in patients with multiple myeloma. (N Vojjala/ N Ahmed). **Dropped due to supplemental data needed**
- mm. **PROP 2410-240** Role of baseline inflammatory markers in toxicities and outcomes post CD19 CAR-T cell therapy in lymphoma (M Junaid Tariq). **Dropped due to overlap with current study/publication.**

6. Other business

a. Update on Female-Specific Systematic Review

Dr. Phelan closed out to give an update on our Female-Specific Systematic Review. Also, a big thank you to Dr. Mohamed Sorror and Dr. Hélène Schoemans for serving on our committee as chairs! Lastly, thank you to everyone for joining in person or virtually!

Working Committee Overview Plan for 2025-2026		
Study number and title	Current status	Chairs priority
AC16-01: Pattern of use and outcomes with donor lymphocyte infusion after human leukocyte antigen haploidentical allogeneic hematopoietic stem cell transplant.	Manuscript preparation	3
LE17-01: Late effects after hematopoietic stem cell transplantation for sickle cell disease.	Analysis	1
LE18-01: Trends in late mortality amongst two-year survivors of pediatric allogeneic hematopoietic cell transplantation for hematologic malignancies	Manuscript preparation	1
CT19-02: Prolonged cytopenia following CD-19 targeted chimeric antigen receptor T therapy for diffuse large B-cell lymphoma.	Manuscript preparation	1
LE19-02: Incidence and predictors of long-term toxicities and late side effects in elderly patients (≥60 years) receiving allogeneic hematopoietic cell transplantation for hematological malignancies	Analysis	2
LE20-01: Cardiometabolic risk after total body irradiation during childhood	Manuscript preparation	2

CT20-03a: New Comorbidity Index Predicts Survival After Chimeric Antigen Receptor T Cell Therapy for Large B-Cell Lymphoma	Submitted	1
CT20-03b: Cytokine release syndrome and neurotoxicity following CD19-CAR T-cell therapy in aggressive B-cell lymphoma: a CIBMTR analysis	Manuscript preparation	1
CT20-03c: Determinants of effectiveness of CAR T cells for lymphoma	Manuscript preparation	1
LE21-01: Risk of subsequent neoplasms in patients with post-transplant cyclophosphamide use for graft-versus-host disease prophylaxis	Data file preparation	2
RT19-01: Analysis of comorbidity-associated toxicity at a regimen-based level	Manuscript prep	1
RT19-02: Hemorrhagic cystitis as a complication of hematopoietic stem cell transplantation in the post-transplant cyclophosphamide graft-versus-host disease prophylaxis era compared to other allogeneic stem cell transplants	Data file preparation	1
RT20-01: Toxicities of older adults receiving allogeneic hematopoietic cell transplant compared to younger patients	Analysis	1
CT22-01: CD19-CAR-T therapy failure: Impact of subsequent therapy in patients with B-cell malignancies	Protocol development	2
CT22-02: Machine learning for predicting toxicity and early clinical outcomes in DLBCL and B-ALL patients treated with commercial CAR T products in the real-world setting: an analysis of the CIBMTR registry	Protocol development	2
MRS22-01: Racial/ethnic disparities and role of poverty in long-term health outcomes among survivors of allogeneic hematopoietic cell transplant performed in childhood	Protocol development	2
MRS22-02: Post-transplant cyclophosphamide related cardiomyopathy; incidence, risk factors and outcome: A retrospective review from CIBMTR database	Protocol development	3
CT23-01: Outcomes of CD19 CAR-T in patients who received lymphodepleting chemotherapy using fludarabine-containing versus other regimens	Manuscript preparation	1
MRS23-01: Updated Analysis of Long-Term Survival and Late Deaths after Allogeneic Hematopoietic Cell Transplantation for Hematologic Malignancies and Severe Aplastic Anemia	Protocol pending	3
MRS24-01: Toxicity profile and survival of patients with BMI >30 undergoing allogeneic stem cell transplantation	Protocol received	3
MRS24-02: Determinants of immune effector cell-associated hematotoxicity (ICAHT) following CAR-T therapy across disease entities	Protocol development	2

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

Variable	<u>Samples</u>		
	<u>Available for Recipient and Donor</u> N (%)	<u>Samples Available for Recipient Only</u> N (%)	<u>Samples Available for Donor Only</u> N (%)
Number of patients	52147	28252	13886
Source of data			
CRF	26120 (50)	9911 (35)	6049 (44)
TED	26027 (50)	18341 (65)	7837 (56)
Number of centers	269	246	400
Disease at transplant			
AML	18232 (35)	10649 (38)	4659 (34)
ALL	7447 (14)	3394 (12)	2177 (16)
Other leukemia	1515 (3)	516 (2)	341 (2)
CML	3644 (7)	1331 (5)	1086 (8)
MDS	8027 (15)	5686 (20)	1874 (13)
Other acute leukemia	594 (1)	340 (1)	163 (1)
NHL	4508 (9)	1890 (7)	1018 (7)
Hodgkin Lymphoma	987 (2)	318 (1)	230 (2)
Plasma Cell Disorders, MM	960 (2)	310 (1)	215 (2)
Other malignancies	61 (<1)	14 (<1)	23 (<1)
Breast cancer	7 (<1)	3 (<1)	1 (<1)
SAA	1706 (3)	856 (3)	609 (4)
Inherited abnormalities erythrocyte diff fxn	733 (1)	256 (1)	226 (2)
Inherited bone marrow failure syndromes	79 (<1)	100 (<1)	47 (<1)
Hemoglobinopathies	48 (<1)	56 (<1)	27 (<1)
Paroxysmal nocturnal hemoglobinuria	6 (<1)	12 (<1)	6 (<1)
SCIDs	918 (2)	473 (2)	417 (3)
Inherited abnormalities of platelets	45 (<1)	22 (<1)	13 (<1)
Inherited disorders of metabolism	316 (1)	108 (<1)	172 (1)
Histiocytic disorders	415 (1)	164 (1)	150 (1)
Autoimmune disorders	36 (<1)	44 (<1)	18 (<1)
MPN	1811 (3)	1693 (6)	392 (3)
Others	52 (<1)	17 (<1)	22 (<1)
AML Disease status at transplant			
CR1	10313 (57)	7148 (67)	2436 (52)
CR2	3375 (19)	1683 (16)	904 (19)
CR3+	364 (2)	139 (1)	106 (2)
Advanced or active disease	3996 (22)	1639 (15)	1066 (23)

Refresh Date: Dec 2025

Variable	<u>Samples</u>		
	<u>Available for</u>	<u>Samples</u>	<u>Samples</u>
	<u>Recipient and</u>	<u>Available for</u>	<u>Available for</u>
	<u>Donor</u>	<u>Recipient Only</u>	<u>Donor Only</u>
	N (%)	N (%)	N (%)
Missing	184 (1)	40 (<1)	147 (3)
ALL Disease status at transplant			
CR1	3782 (51)	2059 (61)	945 (43)
CR2	2109 (28)	838 (25)	633 (29)
CR3+	614 (8)	214 (6)	201 (9)
Advanced or active disease	860 (12)	259 (8)	277 (13)
Missing	82 (1)	24 (1)	121 (6)
MDS Disease status at transplant			
Early	1664 (21)	1027 (18)	409 (22)
Advanced	5316 (66)	4226 (74)	1091 (58)
Missing	1047 (13)	433 (8)	374 (20)
NHL Disease status at transplant			
CR1	668 (15)	426 (23)	157 (15)
CR2	865 (19)	391 (21)	169 (17)
CR3+	405 (9)	186 (10)	93 (9)
PR	446 (10)	111 (6)	99 (10)
Advanced	2031 (45)	750 (40)	466 (46)
Missing	73 (2)	18 (1)	31 (3)
Recipient age at transplant			
0-9 years	4219 (8)	1566 (6)	1752 (13)
10-17 years	3346 (6)	1209 (4)	1237 (9)
18-29 years	6115 (12)	2470 (9)	1785 (13)
30-39 years	5730 (11)	2463 (9)	1603 (12)
40-49 years	7624 (15)	3311 (12)	1951 (14)
50-59 years	10532 (20)	5263 (19)	2375 (17)
60-69 years	11535 (22)	8488 (30)	2536 (18)
70+ years	3046 (6)	3482 (12)	647 (5)
Median (Range)	49 (0-84)	57 (0-84)	43 (0-84)
Recipient race			
White	45472 (91)	24731 (91)	10192 (87)
Black or African American	2540 (5)	1147 (4)	691 (6)
Asian	1405 (3)	859 (3)	661 (6)
Native Hawaiian or other Pacific Islander	80 (<1)	39 (<1)	48 (<1)
American Indian or Alaska Native	213 (<1)	127 (<1)	70 (1)
Other	49 (<1)	27 (<1)	28 (<1)
More than one race	320 (1)	184 (1)	74 (1)
Unknown	2068 (N/A)	1138 (N/A)	2122 (N/A)
Recipient ethnicity			
Hispanic or Latino	4496 (10)	2200 (9)	1302 (11)

Variable	<u>Samples</u>		
	<u>Available for</u>	<u>Samples</u>	<u>Samples</u>
	<u>Recipient and</u>	<u>Available for</u>	<u>Available for</u>
	<u>Donor</u>	<u>Recipient Only</u>	<u>Donor Only</u>
	N (%)	N (%)	N (%)
Non Hispanic or non-Latino	39733 (88)	23054 (90)	7386 (63)
Non-resident of the U.S.	894 (2)	312 (1)	2952 (25)
Unknown	7024 (N/A)	2686 (N/A)	2246 (N/A)
Recipient sex			
Male	30213 (58)	16592 (59)	8251 (59)
Female	21934 (42)	11660 (41)	5635 (41)
Karnofsky score			
10-80	18511 (35)	11453 (41)	4433 (32)
90-100	31769 (61)	16064 (57)	8777 (63)
Missing	1867 (4)	735 (3)	676 (5)
HLA-A B DRB1 groups - low resolution			
<=3/6	33 (<1)	129 (<1)	11 (<1)
4/6	336 (1)	196 (1)	95 (1)
5/6	7308 (14)	3629 (13)	2009 (15)
6/6	43950 (85)	23052 (85)	10876 (84)
Unknown	520 (N/A)	1246 (N/A)	895 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	916 (2)	203 (1)	95 (1)
6/8	1918 (4)	342 (1)	285 (3)
7/8	9748 (19)	3950 (17)	2176 (22)
8/8	38113 (75)	19160 (81)	7403 (74)
Unknown	1452 (N/A)	4597 (N/A)	3927 (N/A)
HLA-DPB1 Match			
Double allele mismatch	12928 (28)	4490 (23)	1421 (24)
Single allele mismatch	24714 (54)	10180 (52)	3098 (53)
Full allele matched	8405 (18)	4749 (24)	1345 (23)
Unknown	6100 (N/A)	8833 (N/A)	8022 (N/A)
High resolution release score			
No	16427 (32)	28182 (>99)	13376 (96)
Yes	35720 (68)	70 (<1)	510 (4)
KIR typing available			
No	38299 (73)	28227 (>99)	13815 (99)
Yes	13848 (27)	25 (<1)	71 (1)
Graft type			
Marrow	17023 (33)	5857 (21)	5094 (37)
PBSC	34988 (67)	22130 (78)	8706 (63)
BM+PBSC	27 (<1)	34 (<1)	11 (<1)
PBSC+UCB	39 (<1)	197 (1)	11 (<1)
Others	70 (<1)	34 (<1)	64 (<1)

Variable	<u>Samples</u>		
	<u>Available for</u>	<u>Samples</u>	<u>Samples</u>
	<u>Recipient and</u>	<u>Available for</u>	<u>Available for</u>
	<u>Donor</u>	<u>Recipient Only</u>	<u>Donor Only</u>
	N (%)	N (%)	N (%)
Conditioning regimen			
Myeloablative	30866 (59)	13348 (47)	8328 (60)
RIC/Nonmyeloablative	21046 (40)	14823 (52)	5380 (39)
TBD	235 (<1)	81 (<1)	178 (1)
Donor age at donation			
To Be Determined/NA	240 (<1)	573 (2)	172 (1)
0-9 years	4 (<1)	33 (<1)	1 (<1)
10-17 years	2 (<1)	11 (<1)	2 (<1)
18-29 years	26493 (51)	16448 (58)	6223 (45)
30-39 years	14635 (28)	7186 (25)	4164 (30)
40-49 years	8272 (16)	3074 (11)	2521 (18)
50+ years	2501 (5)	927 (3)	803 (6)
Median (Range)	30 (0-69)	28 (0-89)	31 (4-77)
Donor/Recipient CMV serostatus			
+/+	13243 (25)	7832 (28)	3717 (27)
+/-	6106 (12)	3591 (13)	1693 (12)
-/+	17148 (33)	8556 (30)	4247 (31)
-/-	14974 (29)	7541 (27)	3717 (27)
CB - recipient +	35 (<1)	154 (1)	10 (<1)
CB - recipient -	4 (<1)	50 (<1)	2 (<1)
CB - recipient CMV unknown	0	1 (<1)	0
Missing	637 (1)	527 (2)	500 (4)
GvHD Prophylaxis			
No GvHD Prophylaxis	224 (<1)	192 (1)	76 (1)
TDEPLETION alone	132 (<1)	51 (<1)	67 (<1)
TDEPLETION +/- other	1147 (2)	325 (1)	391 (3)
CD34 select alone	324 (1)	191 (1)	120 (1)
CD34 select +/- other	551 (1)	312 (1)	148 (1)
Cyclophosphamide alone	235 (<1)	99 (<1)	61 (<1)
Cyclophosphamide +/- others	6203 (12)	8638 (31)	1597 (12)
FK506 + MMF +/- others	5571 (11)	2339 (8)	1028 (7)
FK506 + MTX +/- others(not MMF)	21357 (41)	10248 (36)	3724 (27)
FK506 +/- others(not MMF,MTX)	2524 (5)	1438 (5)	512 (4)
FK506 alone	1206 (2)	547 (2)	235 (2)
CSA + MMF +/- others(not FK506)	3132 (6)	1059 (4)	1096 (8)
CSA + MTX +/- others(not MMF,FK506)	7032 (13)	1975 (7)	3594 (26)
CSA +/- others(not FK506,MMF,MTX)	1091 (2)	342 (1)	468 (3)
CSA alone	468 (1)	134 (<1)	406 (3)
Other GVHD Prophylaxis	769 (1)	306 (1)	229 (2)

Variable	<u>Samples</u>		
	<u>Available for</u>	<u>Samples</u>	<u>Samples</u>
	<u>Recipient and</u>	<u>Available for</u>	<u>Available for</u>
	<u>Donor</u>	<u>Recipient Only</u>	<u>Donor Only</u>
	N (%)	N (%)	N (%)
Missing	181 (<1)	56 (<1)	134 (1)
Donor/Recipient sex match			
Male-Male	20961 (40)	11157 (39)	5327 (38)
Male-Female	12851 (25)	6690 (24)	3046 (22)
Female-Male	9136 (18)	5170 (18)	2851 (21)
Female-Female	8977 (17)	4769 (17)	2539 (18)
CB - recipient M	17 (<1)	112 (<1)	3 (<1)
CB - recipient F	22 (<1)	93 (<1)	9 (<1)
Missing	183 (<1)	261 (1)	111 (1)
Year of transplant			
1986-1990	347 (1)	47 (<1)	103 (1)
1991-1995	1838 (4)	439 (2)	745 (5)
1996-2000	3305 (6)	1184 (4)	1213 (9)
2001-2005	5347 (10)	1070 (4)	1880 (14)
2006-2010	9592 (18)	1921 (7)	1877 (14)
2011-2015	13348 (26)	3587 (13)	2650 (19)
2016-2020	10385 (20)	7194 (25)	2810 (20)
2021-2025	7985 (15)	12810 (45)	2608 (19)
Follow-up among survivors, Months			
N Eval	24194	17127	6810
Median (Range)	48 (0-384)	23 (0-362)	35 (0-385)

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

Variable	<u>Samples</u>	<u>Samples</u>	<u>Samples</u>
	<u>Available for</u> <u>Recipient and</u> <u>Donor</u> N (%)	<u>Available for</u> <u>Recipient</u> <u>Only</u> N (%)	<u>Available for</u> <u>Donor Only</u> N (%)
Number of patients	6535	1939	2412
Source of data			
CRF	4585 (70)	1190 (61)	1115 (46)
TED	1950 (30)	749 (39)	1297 (54)
Number of centers	156	145	231
Disease at transplant			
AML	2470 (38)	678 (35)	791 (33)
ALL	1345 (21)	417 (22)	530 (22)
Other leukemia	102 (2)	31 (2)	38 (2)
CML	140 (2)	38 (2)	61 (3)
MDS	594 (9)	184 (9)	193 (8)
Other acute leukemia	103 (2)	28 (1)	50 (2)
NHL	418 (6)	112 (6)	142 (6)
Hodgkin Lymphoma	104 (2)	27 (1)	35 (1)
Plasma Cell Disorders, MM	38 (1)	12 (1)	13 (1)
Other malignancies	12 (<1)	1 (<1)	3 (<1)
SAA	97 (1)	39 (2)	52 (2)
Inherited abnormalities erythrocyte diff fxn	171 (3)	51 (3)	45 (2)
Inherited bone marrow failure syndromes	10 (<1)	5 (<1)	7 (<1)
Hemoglobinopathies	3 (<1)	1 (<1)	1 (<1)
SCIDs	302 (5)	108 (6)	190 (8)
Inherited abnormalities of platelets	21 (<1)	6 (<1)	10 (<1)
Inherited disorders of metabolism	420 (6)	144 (7)	158 (7)
Histiocytic disorders	112 (2)	37 (2)	56 (2)
Autoimmune disorders	8 (<1)	0	6 (<1)
MPN	54 (1)	17 (1)	21 (1)
Others	11 (<1)	3 (<1)	10 (<1)
AML Disease status at transplant			
CR1	1311 (53)	398 (59)	410 (52)
CR2	654 (26)	164 (24)	198 (25)
CR3+	69 (3)	11 (2)	30 (4)
Advanced or active disease	428 (17)	102 (15)	147 (19)
Missing	8 (<1)	3 (<1)	6 (1)
ALL Disease status at transplant			

Variable	<u>Samples</u> <u>Available for</u> <u>Recipient and</u> <u>Donor</u>	<u>Samples</u> <u>Available for</u> <u>Recipient</u> <u>Only</u>	<u>Samples</u> <u>Available for</u> <u>Donor Only</u>
	N (%)	N (%)	N (%)
CR1	599 (45)	179 (43)	230 (43)
CR2	515 (38)	154 (37)	189 (36)
CR3+	152 (11)	59 (14)	67 (13)
Advanced or active disease	78 (6)	24 (6)	42 (8)
Missing	1 (<1)	1 (<1)	2 (<1)
MDS Disease status at transplant			
Early	179 (30)	44 (24)	76 (39)
Advanced	358 (60)	123 (67)	92 (48)
Missing	57 (10)	17 (9)	25 (13)
NHL Disease status at transplant			
CR1	66 (16)	12 (11)	28 (20)
CR2	80 (19)	28 (25)	36 (26)
CR3+	47 (11)	11 (10)	12 (9)
PR	68 (16)	12 (11)	16 (11)
Advanced	154 (37)	48 (43)	46 (33)
Missing	0	1 (1)	3 (2)
Recipient age at transplant			
0-9 years	1989 (30)	704 (36)	872 (36)
10-17 years	683 (10)	184 (9)	278 (12)
18-29 years	781 (12)	173 (9)	256 (11)
30-39 years	626 (10)	183 (9)	240 (10)
40-49 years	690 (11)	185 (10)	228 (9)
50-59 years	885 (14)	229 (12)	299 (12)
60-69 years	757 (12)	237 (12)	218 (9)
70+ years	124 (2)	44 (2)	21 (1)
Median (Range)	27 (0-83)	23 (0-84)	20 (0-85)
Recipient race			
White	4580 (74)	1334 (73)	1456 (72)
Black or African American	966 (16)	271 (15)	306 (15)
Asian	389 (6)	144 (8)	179 (9)
Native Hawaiian or other Pacific Islander	38 (1)	5 (<1)	23 (1)
American Indian or Alaska Native	63 (1)	18 (1)	25 (1)
Other	1 (<1)	1 (<1)	1 (<1)
More than one race	138 (2)	42 (2)	40 (2)
Unknown	360 (N/A)	124 (N/A)	382 (N/A)
Recipient ethnicity			
Hispanic or Latino	1378 (22)	371 (20)	412 (18)
Non Hispanic or non-Latino	4938 (78)	1460 (78)	1422 (61)
Non-resident of the U.S.	53 (1)	31 (2)	512 (22)

Variable	<u>Samples</u>	<u>Samples</u>	<u>Samples</u>
	<u>Available for</u> <u>Recipient and</u> <u>Donor</u> N (%)	<u>Available for</u> <u>Recipient</u> <u>Only</u> N (%)	<u>Available for</u> <u>Donor Only</u> N (%)
Unknown	166 (N/A)	77 (N/A)	66 (N/A)
Recipient sex			
Male	3628 (56)	1105 (57)	1375 (57)
Female	2907 (44)	834 (43)	1037 (43)
Karnofsky score			
10-80	1738 (27)	494 (25)	601 (25)
90-100	4547 (70)	1309 (68)	1588 (66)
Missing	250 (4)	136 (7)	223 (9)
HLA-A B DRB1 groups - low resolution			
<=3/6	197 (3)	124 (7)	63 (3)
4/6	2648 (41)	719 (40)	948 (41)
5/6	2736 (43)	706 (40)	953 (42)
6/6	809 (13)	236 (13)	324 (14)
Unknown	145 (N/A)	154 (N/A)	124 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	3048 (54)	765 (55)	989 (54)
6/8	1352 (24)	333 (24)	434 (24)
7/8	809 (14)	196 (14)	270 (15)
8/8	389 (7)	109 (8)	141 (8)
Unknown	937 (N/A)	536 (N/A)	578 (N/A)
HLA-DPB1 Match			
Double allele mismatch	999 (37)	193 (31)	259 (36)
Single allele mismatch	1424 (53)	368 (59)	384 (54)
Full allele matched	263 (10)	58 (9)	70 (10)
Unknown	3849 (N/A)	1320 (N/A)	1699 (N/A)
High resolution release score			
No	5006 (77)	1889 (97)	2378 (99)
Yes	1529 (23)	50 (3)	34 (1)
KIR typing available			
No	5263 (81)	1933 (>99)	2383 (99)
Yes	1272 (19)	6 (<1)	29 (1)
Graft type			
UCB	6124 (94)	1734 (89)	2265 (94)
BM+UCB	1 (<1)	0	0
PBSC+UCB	378 (6)	197 (10)	132 (5)
Others	32 (<1)	8 (<1)	15 (1)
Number of cord units			
1	5485 (84)	0	2021 (84)
2	1048 (16)	0	390 (16)

Variable	<u>Samples</u>	<u>Samples</u>	<u>Samples</u>
	<u>Available for</u> <u>Recipient and</u> <u>Donor</u>	<u>Available for</u> <u>Recipient</u> <u>Only</u>	<u>Available for</u> <u>Donor Only</u>
	N (%)	N (%)	N (%)
3	1 (<1)	0	0
Unknown	1 (N/A)	1939 (N/A)	1 (N/A)
Conditioning regimen			
Myeloablative	4267 (65)	1244 (64)	1519 (63)
RIC/Nonmyeloablative	2250 (34)	689 (36)	872 (36)
TBD	18 (<1)	6 (<1)	21 (1)
Donor age at donation			
To Be Determined/NA	5148 (79)	814 (42)	1942 (81)
0-9 years	1076 (16)	868 (45)	372 (15)
10-17 years	60 (1)	98 (5)	23 (1)
18-29 years	75 (1)	46 (2)	17 (1)
30-39 years	66 (1)	45 (2)	27 (1)
40-49 years	52 (1)	30 (2)	13 (1)
50+ years	58 (1)	38 (2)	18 (1)
Median (Range)	5 (0-72)	5 (0-73)	4 (0-67)
Donor/Recipient CMV serostatus			
+/+	0	0	1 (<1)
-/-	0	0	1 (<1)
CB - recipient +	4108 (63)	1182 (61)	1472 (61)
CB - recipient -	2324 (36)	687 (35)	860 (36)
CB - recipient CMV unknown	103 (2)	70 (4)	78 (3)
GvHD Prophylaxis			
No GvHD Prophylaxis	25 (<1)	10 (1)	17 (1)
TDEPLETION alone	1 (<1)	0	0
TDEPLETION +- other	27 (<1)	9 (<1)	9 (<1)
CD34 select alone	0	2 (<1)	1 (<1)
CD34 select +- other	308 (5)	156 (8)	86 (4)
Cyclophosphamide alone	0	0	1 (<1)
Cyclophosphamide +- others	19 (<1)	11 (1)	13 (1)
FK506 + MMF +- others	1956 (30)	633 (33)	507 (21)
FK506 + MTX +- others(not MMF)	218 (3)	58 (3)	78 (3)
FK506 +- others(not MMF,MTX)	237 (4)	69 (4)	94 (4)
FK506 alone	148 (2)	42 (2)	27 (1)
CSA + MMF +- others(not FK506)	2956 (45)	760 (39)	1157 (48)
CSA + MTX +- others(not MMF,FK506)	100 (2)	30 (2)	51 (2)
CSA +- others(not FK506,MMF,MTX)	341 (5)	116 (6)	241 (10)
CSA alone	50 (1)	19 (1)	74 (3)
Other GVHD Prophylaxis	137 (2)	21 (1)	46 (2)
Missing	12 (<1)	3 (<1)	10 (<1)

Variable	<u>Samples</u> <u>Available for</u> <u>Recipient and</u> <u>Donor</u>	<u>Samples</u> <u>Available for</u> <u>Recipient</u> <u>Only</u>	<u>Samples</u> <u>Available for</u> <u>Donor Only</u>
	N (%)	N (%)	N (%)
Donor/Recipient sex match			
Male-Female	0	0	1 (<1)
Female-Male	0	0	1 (<1)
CB - recipient M	3628 (56)	1105 (57)	1373 (57)
CB - recipient F	2907 (44)	834 (43)	1036 (43)
CB - recipient sex unknown	0	0	1 (<1)
Year of transplant			
1996-2000	1 (<1)	2 (<1)	5 (<1)
2001-2005	112 (2)	85 (4)	34 (1)
2006-2010	1847 (28)	427 (22)	623 (26)
2011-2015	2679 (41)	513 (26)	839 (35)
2016-2020	1340 (21)	528 (27)	553 (23)
2021-2025	556 (9)	384 (20)	358 (15)
Follow-up among survivors, Months			
N Eval	3247	1102	1277
Median (Range)	60 (0-196)	39 (0-213)	38 (0-240)

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

Variable	<u>Samples</u> <u>Available for</u>	<u>Samples</u> <u>Available for</u>	<u>Samples</u> <u>Available for</u>
	<u>Recipient and</u> <u>Donor</u>	<u>Recipient</u> <u>Only</u>	<u>Donor Only</u>
	N (%)	N (%)	N (%)
Number of patients	13687	2413	1156
Source of data			
CRF	4321 (32)	632 (26)	346 (30)
TED	9366 (68)	1781 (74)	810 (70)
Number of centers	97	80	69
Disease at transplant			
AML	4487 (33)	768 (32)	409 (35)
ALL	2299 (17)	490 (20)	209 (18)
Other leukemia	232 (2)	46 (2)	19 (2)
CML	396 (3)	59 (2)	28 (2)
MDS	1810 (13)	297 (12)	159 (14)
Other acute leukemia	214 (2)	39 (2)	12 (1)
NHL	1106 (8)	208 (9)	101 (9)
Hodgkin Lymphoma	238 (2)	44 (2)	29 (3)
Plasma Cell Disorders, MM	276 (2)	43 (2)	21 (2)
Other malignancies	25 (<1)	0	1 (<1)
Breast cancer	1 (<1)	0	0
SAA	679 (5)	106 (4)	45 (4)
Inherited abnormalities erythrocyte diff fxn	503 (4)	71 (3)	17 (1)
Inherited bone marrow failure syndromes	57 (<1)	7 (<1)	8 (1)
Hemoglobinopathies	319 (2)	57 (2)	20 (2)
Paroxysmal nocturnal hemoglobinuria	4 (<1)	1 (<1)	0
SCIDs	309 (2)	52 (2)	28 (2)
Inherited abnormalities of platelets	13 (<1)	0	0
Inherited disorders of metabolism	30 (<1)	8 (<1)	3 (<1)
Histiocytic disorders	79 (1)	11 (<1)	6 (1)
Autoimmune disorders	18 (<1)	0	0
MPN	577 (4)	104 (4)	41 (4)
Others	15 (<1)	2 (<1)	0
AML Disease status at transplant			
CR1	3007 (67)	529 (69)	265 (65)
CR2	673 (15)	97 (13)	50 (12)
CR3+	55 (1)	18 (2)	2 (<1)
Advanced or active disease	745 (17)	119 (15)	92 (22)

Refresh Date: Dec 2025

Variable	<u>Samples</u> <u>Available for</u> <u>Recipient and</u> <u>Donor</u>	<u>Samples</u> <u>Available for</u> <u>Recipient</u> <u>Only</u>	<u>Samples</u> <u>Available for</u> <u>Donor Only</u>
	N (%)	N (%)	N (%)
Missing	7 (<1)	5 (1)	0
ALL Disease status at transplant			
CR1	1355 (59)	298 (61)	131 (63)
CR2	697 (30)	130 (27)	56 (27)
CR3+	150 (7)	35 (7)	10 (5)
Advanced or active disease	97 (4)	27 (6)	12 (6)
MDS Disease status at transplant			
Early	312 (17)	44 (15)	27 (17)
Advanced	1425 (79)	230 (77)	123 (77)
Missing	73 (4)	23 (8)	9 (6)
NHL Disease status at transplant			
CR1	225 (20)	49 (24)	25 (25)
CR2	211 (19)	40 (19)	17 (17)
CR3+	115 (10)	26 (13)	7 (7)
PR	71 (6)	14 (7)	7 (7)
Advanced	475 (43)	78 (38)	45 (45)
Missing	5 (<1)	0	0
Recipient age at transplant			
0-9 years	1542 (11)	241 (10)	100 (9)
10-17 years	1443 (11)	199 (8)	83 (7)
18-29 years	1622 (12)	327 (14)	132 (11)
30-39 years	1042 (8)	213 (9)	122 (11)
40-49 years	1585 (12)	289 (12)	120 (10)
50-59 years	2706 (20)	506 (21)	232 (20)
60-69 years	3121 (23)	528 (22)	304 (26)
70+ years	626 (5)	110 (5)	63 (5)
Median (Range)	48 (0-82)	48 (0-81)	51 (0-83)
Recipient race			
White	10027 (78)	1626 (74)	837 (79)
Black or African American	1884 (15)	340 (15)	129 (12)
Asian	667 (5)	194 (9)	71 (7)
Native Hawaiian or other Pacific Islander	49 (<1)	9 (<1)	3 (<1)
American Indian or Alaska Native	95 (1)	16 (1)	9 (1)
More than one race	186 (1)	24 (1)	17 (2)
Unknown	779 (N/A)	204 (N/A)	90 (N/A)
Recipient ethnicity			
Hispanic or Latino	2664 (20)	594 (25)	260 (23)
Non Hispanic or non-Latino	10617 (79)	1729 (74)	841 (75)
Non-resident of the U.S.	133 (1)	28 (1)	18 (2)

Variable	<u>Samples</u>	<u>Samples</u>	<u>Samples</u>
	<u>Available for</u> <u>Recipient and</u> <u>Donor</u> N (%)	<u>Available for</u> <u>Recipient</u> <u>Only</u> N (%)	<u>Available for</u> <u>Donor Only</u> N (%)
Unknown	273 (N/A)	62 (N/A)	37 (N/A)
Recipient sex			
Male	8010 (59)	1414 (59)	680 (59)
Female	5677 (41)	999 (41)	476 (41)
Karnofsky score			
10-80	4910 (36)	955 (40)	502 (43)
90-100	8271 (60)	1384 (57)	591 (51)
Missing	506 (4)	74 (3)	63 (5)
HLA-A B DRB1 groups - low resolution			
<=3/6	3403 (26)	585 (26)	344 (34)
4/6	1015 (8)	196 (9)	105 (10)
5/6	295 (2)	56 (2)	31 (3)
6/6	8568 (65)	1444 (63)	529 (52)
Unknown	406 (N/A)	132 (N/A)	147 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	4233 (33)	722 (33)	400 (44)
6/8	191 (1)	51 (2)	14 (2)
7/8	200 (2)	37 (2)	21 (2)
8/8	8264 (64)	1357 (63)	482 (53)
Unknown	799 (N/A)	246 (N/A)	239 (N/A)
HLA-DPB1 Match			
Double allele mismatch	15 (<1)	1 (<1)	4 (1)
Single allele mismatch	3612 (40)	491 (65)	287 (67)
Full allele matched	5377 (60)	261 (35)	136 (32)
Unknown	4683 (N/A)	1660 (N/A)	729 (N/A)
High resolution release score			
No	7234 (53)	2384 (99)	1143 (99)
Yes	6453 (47)	29 (1)	13 (1)
Graft type			
Marrow	3974 (29)	528 (22)	290 (25)
PBSC	9582 (70)	1840 (76)	856 (74)
UCB	2 (<1)	15 (1)	0
BM+PBSC	22 (<1)	7 (<1)	1 (<1)
BM+UCB	52 (<1)	15 (1)	3 (<1)
PBSC+UCB	1 (<1)	2 (<1)	4 (<1)
Others	54 (<1)	6 (<1)	2 (<1)
Conditioning regimen			
Myeloablative	7617 (56)	1319 (55)	587 (51)
RIC/Nonmyeloablative	6003 (44)	1077 (45)	551 (48)

Variable	<u>Samples</u>	<u>Samples</u>	<u>Samples</u>
	<u>Available for</u> <u>Recipient and</u> <u>Donor</u>	<u>Available for</u> <u>Recipient</u> <u>Only</u>	<u>Available for</u> <u>Donor Only</u>
	N (%)	N (%)	N (%)
TBD	67 (<1)	17 (1)	18 (2)
Donor age at donation			
To Be Determined/NA	15 (<1)	9 (<1)	2 (<1)
0-9 years	970 (7)	142 (6)	39 (3)
10-17 years	1156 (8)	188 (8)	78 (7)
18-29 years	2584 (19)	460 (19)	260 (22)
30-39 years	2165 (16)	433 (18)	222 (19)
40-49 years	2160 (16)	382 (16)	177 (15)
50+ years	4637 (34)	799 (33)	378 (33)
Median (Range)	40 (0-82)	40 (0-79)	39 (0-80)
Donor/Recipient CMV serostatus			
+/+	5561 (41)	1076 (45)	477 (41)
+/-	1467 (11)	209 (9)	115 (10)
-/+	3460 (25)	584 (24)	302 (26)
-/-	2958 (22)	478 (20)	229 (20)
CB - recipient +	32 (<1)	18 (1)	6 (1)
CB - recipient -	23 (<1)	14 (1)	1 (<1)
Missing	186 (1)	34 (1)	26 (2)
GvHD Prophylaxis			
No GvHD Prophylaxis	198 (1)	26 (1)	16 (1)
TDEPLETION alone	141 (1)	44 (2)	17 (1)
TDEPLETION +- other	144 (1)	39 (2)	19 (2)
CD34 select alone	91 (1)	29 (1)	12 (1)
CD34 select +- other	106 (1)	35 (1)	10 (1)
Cyclophosphamide alone	81 (1)	11 (<1)	10 (1)
Cyclophosphamide +- others	5079 (37)	841 (35)	507 (44)
FK506 + MMF +- others	897 (7)	114 (5)	34 (3)
FK506 + MTX +- others(not MMF)	4530 (33)	682 (28)	358 (31)
FK506 +- others(not MMF,MTX)	892 (7)	368 (15)	77 (7)
FK506 alone	127 (1)	19 (1)	6 (1)
CSA + MMF +- others(not FK506)	256 (2)	44 (2)	19 (2)
CSA + MTX +- others(not MMF,FK506)	773 (6)	105 (4)	46 (4)
CSA +- others(not FK506,MMF,MTX)	83 (1)	11 (<1)	3 (<1)
CSA alone	84 (1)	11 (<1)	3 (<1)
Other GVHD Prophylaxis	193 (1)	25 (1)	19 (2)
Missing	12 (<1)	9 (<1)	0
Donor/Recipient sex match			
Male-Male	4539 (33)	848 (35)	396 (34)
Male-Female	2908 (21)	498 (21)	248 (21)

Variable	<u>Samples</u> <u>Available for</u>	<u>Samples</u> <u>Available for</u>	<u>Samples</u> <u>Available for</u>
	<u>Recipient and</u> <u>Donor</u> N (%)	<u>Recipient</u> <u>Only</u> N (%)	<u>Donor Only</u> N (%)
Female-Male	3433 (25)	546 (23)	281 (24)
Female-Female	2748 (20)	488 (20)	224 (19)
CB - recipient M	34 (<1)	19 (1)	3 (<1)
CB - recipient F	21 (<1)	13 (1)	4 (<1)
Missing	4 (<1)	1 (<1)	0
Year of transplant			
2006-2010	613 (4)	74 (3)	56 (5)
2011-2015	3719 (27)	525 (22)	215 (19)
2016-2020	5089 (37)	910 (38)	403 (35)
2021-2025	4266 (31)	904 (37)	482 (42)
Follow-up among survivors, Months			
N Eval	8910	1577	753
Median (Range)	28 (0-150)	24 (0-124)	24 (0-148)



TO: Morbidity, Recovery, and Survivorship Working Committee Members

FROM: Rachel Phelan, MD and Amy Moskop, MD, MS; Scientific Directors for the Morbidity, Recovery, and Survivorship Working Committee

RE: 2025-2026 Studies in Progress Summary

AC16-01 Pattern of use and outcomes with donor lymphocyte infusion after human leukocyte antigen haploidentical allogeneic hematopoietic stem cell transplant (E Gupta/ J Foran/ V Roy). The purpose of this study is to describe the frequency of use of DLI, CD3 cell dose, and the efficacy and toxicity of DLI after HLA haploidentical T-replete HCT. It also aims to explore the specific characteristics associated with outcomes (remission / restoration of full donor chimerism/ or GVHD). This study is currently in manuscript preparation. The goal of this study is to submit by June 2026.

Status: **Manuscript Preparation**

LE17-01 Late effects after hematopoietic stem cell transplantation for sickle cell disease (E Stenger/L Krishnamurti/S Shenoy). This study aims to describe incidence of late effects after HCT for sickle cell disease (SCD) and the relationship of transplant-related factors to organ dysfunction and SCD-related complications. This study is currently in manuscript preparation. However, some additional analysis is being included to compare the population to a non-HCT cohort. The goal of this study is to submit by June 2026.

Status: **Manuscript Preparation/Analysis**

LE18-01 Trends in late mortality amongst two year survivors of pediatric allogeneic hematopoietic cell transplantation for hematologic malignancies (PI: Prakash Satwani/ Larisa Broglie) The purpose of this study is to make comparisons among late effects and other outcomes between AML late-mortality patients transplanted between 2000-2006 and 2007-2013. These comparisons were made for pediatric and AYA patients. This study is currently in manuscript preparation and being finalized for submission. The goal of this study is to be published by June 2026.

Status: **Manuscript Preparation/Submit**

CT19-02 Prolonged cytopenia following CD-19 targeted chimeric antigen receptor T therapy for diffuse large B-cell lymphoma (M Shadman). The purpose of this study is to evaluate the incidence and severity of cytopenia and delayed count recovery after treatment with FDA approved CD19 targeted CAR-T product, Axi-cel for large cell lymphoma. It also aims to determine the rate and grade of thrombocytopenia and neutropenia CAR-T therapy, as well as pre- and post- CAR-T treatment factors that may be associated with prolonged cytopenia after CAR-T therapy. This study is currently in manuscript preparation. The goal of this study is to submit by June 2026.

Status: **Manuscript Preparation**

LE20-01 Cardiometabolic risk after total body irradiation during childhood (D Novetsky Friedman/E Chow). This study will utilize linked Childhood Cancer Survivor Study (CCSS) and Center for International Blood and Marrow Transplant Research (CIBMTR) data to enrich our understanding of the relative contributions of clinical factors to cardiometabolic risk among an aging cohort of TBI-exposed HSCT survivors. This study is currently in manuscript preparation. The goal of this study is to submit by July 2026.

Status: **Manuscript preparation**

CT20-03c Determinants of effectiveness of CAR T cells for lymphoma (H Hashmi/ R Shouval/ K Wudhikarn). The study aims to assess disease factors and their associations with response and survival outcomes. This study is currently in manuscript preparation. The goal of this study is to submit by June 2026.

Status: **Manuscript Preparation**

CT20-04 Determinants of outcomes after chimeric antigen receptor T cells for acute lymphoblastic leukemia (S Mirza/ D Ragoonanan). The goal of this study is to describe efficacy outcomes in patients with ALL following CAR T-cell therapy, as well as the impact of associated patient and disease-related factors. It also aims to describe CRS, ICANS, prolonged cytopenia, and toxicities in this population. This study is currently in data file preparation. The goal of this study is to be in analysis by June 2026.

Status: **Data File Preparation**

LE21-01 Risk of subsequent neoplasms in patients with post-transplant cyclophosphamide use for graft-versus-host disease prophylaxis (A Tomas/I Muhsen/L Yanez San Segundo/S K. Hashmi/ M-Angel Perales/A Kansagra). This study will compare the outcomes with different patients who used PTCy and who used other CNI-based prophylaxis. This study is currently in data file preparation with analysis on solid tumors complete. The goal of this study is to be in manuscript prep by June 2026.

Status: **Data File Preparation/Analysis**

RT19-01 Analysis of comorbidity-associated toxicity at a regimen-based level (R Shouval/ B Savani/A Nagler). This study aims to 1) evaluate the comorbidity-specific risk of non-relapse mortality and overall mortality within patients receiving pre-defined conditioning regimens, and 2) within patients stratified by conditioning intensity groups (myeloablative, reduced-intensity, and non-myeloablative, and 3) explore toxicities associated with specific conditioning regimen stratified by preexisting comorbidities. This study was combined with CK22-02 from the Leukemia Working Committee. This study is currently in manuscript preparation. The goal of this study is to submit by June 2026.

Status: **Manuscript Preparation**

RT19-02 Hemorrhagic cystitis (HC) as a complication of hematopoietic cell transplantation with post-transplant cyclophosphamide (PTCy)-based graft-versus-host disease prophylaxis compared to other allogeneic transplants (K Adekola/ N Ali/ O Frankfurt/ L Metheny/ J Moreira/ M de Lima). This study aims to determine the incidence and severity of HC in patients who received PTCy as part of GVHD prophylaxis, 2) to describe disease characteristics and pre-transplant regimens in patients that developed HC after receiving PTCy-based GVHD prophylaxis and 3) to evaluate survival outcomes in

PTCy patients with HC. This study is currently in protocol development with a significant amount of data file preparation complete. The goal of this study is to be in analysis by June 2026.

Status: **Protocol development/Data file preparation**

RT20-01 Toxicities of older adults receiving allogeneic hematopoietic cell transplant compared to younger patients (R Jayani/H Murff). This study aims to determine the incidence of organ toxicities in older and younger adult allo transplants for hematologic malignancies, 2) to describe comorbid conditions in this population and 3) to evaluate survival, progression-free survival, and non-relapse mortality outcome. This study is currently in analysis. The goal of this study is to be in manuscript prep by June 2026. **This study is presented as a poster at Tandem.**

Status: **Analysis**

CT22-01 CD19-CAR-T therapy failure: Impact of subsequent therapy in patients with B-cell malignancies (L Gowda/ G Murthy). The primary goal of this study is to describe clinical outcomes and real-world utilization patterns of subsequent treatment after CAR-T cell therapy for patients with CD19+ hematologic neoplasms, including the second infusion of CD19 CAR T cells. This study is currently in protocol development with a significant amount of data file preparation complete. The goal of this study is to be in analysis by June 2026.

Status: **Protocol Development/Data file preparation**

CT22-02 Machine learning for predicting toxicity and early clinical outcomes in DLBCL and B-ALL patients treated with commercial CAR T products in the real-world setting: an analysis of the CIBMTR registry (A Tomas/ L Appell/ E Bezerra/ A Mirza/ M Perales/ A Sharma/ Y Lin/ L Gowda/ G Murthy). The goal of this study is to identify predictors of early toxicities, including severe CRS, neurotoxicity, and day 30 cytopenia associated with CAR-T therapy. It also aims to identify homogeneous patient subgroups from baseline data using unsupervised machine learning tools, and correlate these with disease response and drug-specific toxicity with disease outcomes. This study is currently in analysis. The goal of this study is to be in manuscript preparation by June 2026.

Status: **Analysis**

MRS22-01 Racial/ethnic disparities and role of poverty in long-term health outcomes among survivors of allogeneic hematopoietic cell transplant performed in childhood (N Bhatt/A Sharma/L Jimenez-Kurlander/C Duncan). This study aims to compare the cumulative incidence and risks of malignant and non-malignant late effects by 1) race/ethnicity and 2) neighborhood poverty and insurance type at time of transplant in survivors of allogeneic HCT who have survived for at least 1 year. This study is currently in protocol development. The goal of this study is to be in data file preparation by June 2026.

Status: **Protocol Development**

MRS22-02 Incidence, risk factors and outcomes of acute cardiac complications after post-transplant cyclophosphamide based GVHD prophylaxis: A retrospective analysis from the CIBMTR database (K Poonsombudlert/C Strouse/H Rangarajan/P Satwani/D Modi). This study aims to evaluate the incidence of ACE after use of PT-Cy compared to non-PT-Cy based GVHD prophylaxis regimen and determine pre-transplant factors associated with the development of ACE. This study also aims to evaluate overall survival, disease free survival, and non-relapse mortality in patients who developed ACE compared to

patients who did not. This study is currently in protocol development. The goal of this study is to be in protocol development by June 2026.

Status: **Protocol Development**

MRS 23-01 Updated Analysis of Long-Term Survival and Late Deaths after Allogeneic Hematopoietic Cell Transplantation for Hematologic Malignancies and Severe Aplastic Anemia (M Battiwalla/U Rao). This study aims to determine the probability of survival at 10 years after HCT. It will further investigate risk factors of late mortality, change in late mortality over time, and comparing relative mortality after HCT with the general population. This study is currently in protocol development. The goal of this study is to be in protocol development by June 2026.

Status: **Protocol Development**

MRS24-01 Toxicity profile and survival of patients with body mass index >30 undergoing allogeneic stem cell transplantation (N Tijaro Ovalle/ A Jakubowski). The goal of this study is to compare outcomes and toxicities across BMI groups 25-29, 30-39, and 40+. The study also aims to identify incidence and mechanism of dose adjustment of any conditioning agents as well as their impact on outcomes. This study is currently in protocol development. The goal of this study is to be in protocol development by June 2026.

Status: **Protocol Development**

MRS24-02 Determinants of immune effector cell-associated hematotoxicity following CAR-T therapy across disease entities (K Rejeski/ R Shouval). The goal of this study is to describe the comparative incidence of early and late cytopenias across different lymphoma subtypes and CAR-T products. It also aims to identify determinants of severe hematotoxicity at time of leukapheresis and lymphodepletion. This study is currently in analysis. The goal of this study is to be in manuscript preparation by June 2026.

Status: **Analysis**

MRS25-01 Association of fludarabine exposure on car-t outcomes (K Sweiss/ S Ahmed). The goal of this study is to determine if there is an association between fludarabine lymphodepletion exposure and clinical outcomes after CAR-T therapy in lymphoma and multiple myeloma. This study is currently in protocol development. The goal of this study is to be in protocol development by June 2026.

Status: **Protocol Development**

MRS25-02 CIBMTR Validation of the Transplant Conditioning Intensity (TCI) Classification System in Patients with Acute Myeloid Leukemia and Myelodysplastic Syndrome receiving GVHD prophylaxis with or without Post-Transplant Cyclophosphamide (A Jimenez Jimenez/ B Shaffer/ C Jackson/ L Muffly). The goal of this study is to determine if the transplant conditioning intensity (TCI) score developed by the ALWP of EBMT be externally validated using CIBMTR data as a predictive measurement of transplant conditioning intensity. This study is currently in protocol development. The goal of this study is to be in protocol development by June 2026.

Status: **Protocol Development**

MRS25-03 Real World Experience of Immune Effector Cell Associated Hemophagocytic Lymphohistiocytosis-like Syndrome (IEC HS) in CAR T-cell Recipients (K McNerney/ T Jain/ N Vojjala/ N Ahmed). The goal of this study is to determine the incidence of IEC-HS and its contribution to morbidity

and outcomes among CAR-T patients. This study is currently in protocol development. The goal of this study is to be in protocol development by June 2026.

Status: **Protocol Development**

Field	Response
Proposal Number	2509-47-HUNZEKER
Proposal Title	Use of Anakinra for the Treatment of ICANS after Anti-CD19 Autologous CART in B-cell Lymphoma
Key Words	B-cell lymphoma, CART, ICANS, Anakinra
Principal Investigator #1: - First and last name, degree(s)	Zachary Hunzeker, MD
Principal Investigator #1: - Email address	zhunzeker@mdanderson.org
Principal Investigator #1: - Institution name	MD Anderson Cancer Center
Principal Investigator #1: - Academic rank	Resident
Junior investigator status (defined as 助、5 years from fellowship)	Yes
Do you identify as an underrepresented/minority?	No
Principal Investigator #2 (If applicable): - First and last name, degree(s):	Paolo Strati, MD
Principal Investigator #2 (If applicable): - Email address:)	PStrati@mdanderson.org
Principal Investigator #2 (If applicable): - Institution name:	MD Anderson Cancer Center
Principal Investigator #2 (If applicable): - Academic rank:	Associate Professor, Department of Lymphoma & Myeloma
Junior investigator status (defined as 助、5 years from fellowship)	No
Do you identify as an underrepresented/minority?	No
We encourage a maximum of two Principal Investigators per study. If more than one author is listed, please indicate who will be identified as the corresponding PI below:	Zachary Hunzeker, MD
Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.	None
Do any of the PI(s) within this proposal have a CIBMTR WC study in manuscript preparation >6 months?	No
PROPOSED WORKING COMMITTEE:	Lymphoma
Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.	No
RESEARCH QUESTION:	To describe the pattern of utilization and efficacy of anakinra for the management of ICANS in B-cell lymphoma patients treated with autologous anti-CD19 CAR T-cell therapy

Field	Response
RESEARCH HYPOTHESIS:	We hypothesize that off-label use of anakinra for the management of ICANS in B-cell lymphoma patients treated with autologous anti-CD19 CAR T-cell therapy is frequent and effective
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	Primary: to describe the efficacy of anakinra for the management of ICANS in B-cell lymphoma patients treated with autologous anti-CD19 CAR T-cell therapy Secondary: to describe the frequency and pattern of utilization of anakinra for the management of ICANS in B-cell lymphoma patients treated with autologous anti-CD19 CAR T-cell therapy
SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.	The off-label use of anakinra for the management of ICANS in B-cell lymphoma patients treated with autologous anti-CD19 CAR T-cell therapy is frequent, but remains off-label and based on small case series. In addition, no trials are currently planned to support its FDA-approval, limiting its use, despite clear efficacy, in many non-academic centers. This large multi-center retrospective experience, similarly to what done for tocilizumab, may favor its registration, and increase access to this potentially life-saving agent to more patients.

Field	Response
<p>SCIENTIFIC JUSTIFICATION: Provide a background summary of previous related research and their strengths and weaknesses, justification of your research and why your research is still necessary.</p>	<p>Autologous anti-CD19 chimeric antigen receptor (CAR) T-cell therapy is currently approved by the Food and Drug Administration (FDA) for the treatment of patients with relapsed and/or B-cell lymphoma. While effective, its use results in immune effector cell-associated neurotoxicity syndrome (ICANS) in up to 60% of patients based on utilized product and lymphoma subtype. While tocilizumab, a monoclonal antibody targeting the interleukin (IL)-6 receptor, is used for the treatment of cytokine release syndrome (CRS), corticosteroids represent the only current treatment option for ICANS. Although low dose of corticosteroids can be safely used to manage toxicities, higher doses and prolonged duration of treatment may hamper CAR T-cell function, potentially resulting in worse outcomes in some series. Hence, the development of corticosteroid-sparing strategies for the treatment of ICANS are needed. To this regard, the presence of myeloid-like ICANS-associated cells (IACs) expressing high levels of IL-1β within infusion products of lymphoma patients has been shown to associate with the development of high grade ICANS following treatment with CART. IL-1β has also been strongly implicated in ICANS pathophysiology in animal models. Pre-clinical studies have shown that anakinra, an IL-1 receptor antagonist, may abrogate CRS and ICANS without negatively impacting CAR T-cell function. Anakinra is currently approved by the FDA for the treatment of patients with refractory rheumatoid arthritis (RA; at a dose of 100 mg SC daily), cryopyrin-associated periodic syndromes and deficiency of IL-1 receptor antagonist (at a dose of up to 8 mg/kg SC daily). In patients with RA, the most common toxicity is injection site reaction (observed in 65% of cases), while grade 3-4 infections are reported in only 0.8% of patients. The use of anakinra for the treatment of CRS/ICANS after CAR T-cell therapy has previously been reported by multiple groups, and shown to be safe, without any increase in infections complications. However, this is based on small samples (the largest of which featured 43 patients), and no trials are currently planned to support its utilization. As such, its use remains off-label, and patients treated at few academic centers are able to access it.</p>

Field	Response
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	Male or female patients greater than 18 years of age who have been treated from January 01, 2015 to present day and received CAR-T cell therapy (tisagenlecleucel, lisocabtagene maraleucel, axicabtagene ciloleucel, or brexucabtagene) for the diagnosis of large B cell lymphoma (LBCL), follicular lymphoma, or mantle cell lymphoma
Does this study include pediatric patients?	No
If this study does not include pediatric patients, please provide justification:	This project is outlined for adult patients in an attempt to add to the literature in this population without additional confounding from marked age differences.

Field	Response
<p>DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Outline any supplementary data required.</p>	<p>Patient-related: - Age at CART infusion - Gender: male or female - Karnofsky performance status at CART infusion: <80% vs. 80% - HCT comorbidity index at CART cell infusion 0, 1, 2, and 3 - Charlston comorbidity index variables - B symptoms (yes or no) - Additional markers: - LDH - baseline inflammatory markers (IL-6, IL-2, serum ferritin, interferon gamma, C reactive protein) - thrombocytopenia - neutropenia - lymphopenia - anemia - history of CNS disease - history of neurological disorder Disease-related: - Prior autologous HCT (yes or no) - Primary refractory vs. relapsed disease - Number of prior therapy (before transplant): 2-3 vs. >3 - Dosage of the conditioning chemotherapy - Disease status at the time of CART: chemoresponsive vs. non-responsive/refractory - Bridging therapy prior to CART (yes or no) - Extra nodal involvement at the time of prior relapse or PD (yes or no) - Length of prior CR1 (<12 vs. >=12 months) - B symptoms at the time of prior relapse or PD (yes or no) - Volume of disease generally defined as bulk (>=10cm yes or no) - Ferritin at time of CART infusion Treatment-related: - Complications related to CAR-T cell therapy CRS, ICANS (ASTCT grading system) - Side effects related to conditioning chemotherapy (sepsis, any other organ dysfunction beyond expected for CART (respiratory, cardiac, hepatic,etc) - Duration of hospitalization post CAR-T cell therapy - Prolonged cytopenia - Disease status Anakinra-related: - Use of anakinra (yes or no). - Previous use of corticosteroids (yes or no) - Previous use of tocilizumab (yes or no). - Resolution of ICANS with anakinra (yes or no) - Need to continue corticosteroids with anakinra (yes or no)</p>
<p>Types of cellular therapy data this proposal includes:</p>	<p>Chimeric Antigen Receptor (CAR) T-Cell Therapy (CAR-T)</p>
<p>PATIENT REPORTED OUTCOME (PRO) REQUIREMENTS: If the study requires PRO data collected by CIBMTR, the proposal should include: 1) A detailed description of the PRO domains, timepoints, and proposed analysis of PROs; 2) A description of the hypothesis speci</p>	<p>None</p>

Field	Response
MACHINE LEARNING: Please indicate if the study requires methodology related to machine-learning and clinical predictions.	No
SAMPLE REQUIREMENTS: If the study requires biologic samples from the CIBMTR Repository, the proposal should also include: 1) A detailed description of the proposed testing methodology and sample requirements; 2) A summary of the investigator's previous e	None
NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required.	No
REFERENCES:	<p>1. Strati P, Ahmed S, Kebriaei P, et al. Clinical efficacy of anakinra to mitigate CAR T-cell therapy-associated toxicity in large B-cell lymphoma. <i>Blood Adv.</i> 2020;4(13):3123-3127. 2. Wehrli M, Gallagher K, Chen YB, et al. Single-center experience using anakinra for steroid-refractory immune effector cell-associated neurotoxicity syndrome (ICANS). <i>J Immunother Cancer.</i> 2022;10(1). 3. Dreyzin A, Jacobsohn D, Angiolillo A, et al. Intravenous anakinra for tisagenlecleucel-related toxicities in children and young adults. <i>Pediatr Hematol Oncol.</i> 2022;39(4):370-378. 4. Munugala N, Dashkevych U, Husnain M. Role of anakinra in the management of icans after CAR T-cell therapy for lymphoma. <i>Journal of Clinical Oncology.</i> 2022;40(16). 5. Gazeau N, Barba P, Iacoboni G, et al. Safety and Efficacy of Two Anakinra Dose Regimens for Refractory CRS or Icans after CAR T-Cell Therapy. <i>Blood.</i> 2021;138. 6. Gazeau N, Liang E, Wu Q, et al. Anakinra for Refractory Cytokine Release Syndrome or Immune Effector Cell-Associated Neurotoxicity Syndrome after Chimeric Antigen Receptor T Cell Therapy. <i>Transplantation and Cellular Therapy.</i> 2023;29:430-437.</p>
CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning?	No, I do not have any conflicts of interest pertinent to this proposal

Population characteristics of NHL adult patients receiving first CAR-T, 2021+

Characteristic	N (%)
No. of patients	10575
No. of centers	188
Patient Characteristics	
Age, by decades, no. (%)	
Median (range)	66 (18-91)
18-19	18 (0)
20-29	222 (2)
30-39	401 (4)
40-49	808 (8)
50-59	1917 (18)
60-69	3663 (35)
70+	3546 (34)
Recipient Sex, no. (%)	
Male	6800 (64)
Female	3773 (36)
Not reported	2 (0)
Recipient race, no. (%)	
White	7906 (75)
Black or African American	517 (5)
Asian	579 (5)
Native Hawaiian or other Pacific Islander	19 (0)
American Indian or Alaska Native	50 (0)
Other	54 (1)
More than one race	527 (5)
Missing	923 (9)
Ethnicity, no. (%)	
Hispanic or Latino	1098 (10)
Non-Hispanic or Latino	7745 (73)
Non-resident of the U.S.	1368 (13)
Not reported	364 (3)
Current CCN region of patient, no. (%)	
US	9156 (87)
Canada	816 (8)
Europe	99 (1)
Asia	96 (1)
Australia/New Zealand	144 (1)
Mideast/Africa	179 (2)
Central/South America	85 (1)

Characteristic	N (%)
Karnofsky performance score prior to CT, no. (%)	
90-100	4161 (39)
80	3085 (29)
< 80	2011 (19)
Not reported	1318 (12)
ECOG prior to CT, no. (%)	
Asymptomatic	4475 (42)
Symptomatic but completely ambulatory	4997 (47)
Symptomatic, < 50% in bed during the day	581 (5)
Symptomatic, > 50% in bed, but not bedbound	52 (0)
Bedbound	6 (0)
Not reported	464 (4)
HCT comorbidity score, no. (%)	
0	3140 (30)
1	2150 (20)
2	1510 (14)
3	1505 (14)
4	970 (9)
5+	1248 (12)
Not reported	52 (0)
Disease related	
Time from initial diagnosis to CT, months, median (range)	15 (.36-471)
Disease status prior to CT for lymphoma, no. (%)	
CR	958 (9)
PR	2370 (22)
Resistant	5972 (56)
Untreated	638 (6)
Unknown	637 (6)
Neurotoxicity related	
Maximum neurotoxicity grade (during follow-up for this CT), no. (%)	
No neurologic impairment	6060 (57)
Grade 1	1399 (13)
Grade 2	914 (9)
Grade 3	1355 (13)
Grade 4	388 (4)
Grade 5	66 (1)
Not reported	393 (4)
Therapy given for neurotoxicity: anakinra (during follow-up for this CT), no. (%)	
No neurologic impairment reported	6453 (61)
No	1989 (19)

Characteristic	N (%)
Yes	498 (5)
Not reported	1635 (15)
Infusion related	
No. of lines of prior therapies (including CT and HCT), no. (%)	
Median (range)	3.0 (1.0-16)
1-3	4280 (40)
4-6	2150 (20)
7-9	313 (3)
10+	85 (1)
No lines reported/not reported	3747 (35)
Prior HCT, no. (%)	
No	8825 (83)
Yes	1736 (16)
Not reported	14 (0)
Lymphodepleting regimen, no. (%)	
Fludarabine + Cyclophosphamide	6464 (61)
Bendamustine only	817 (8)
Others	3290 (31)
Not reported	4 (0)
Product, no. (%)	
Kymriah	1131 (11)
Yescarta	5886 (56)
Tecartus	1054 (10)
Breyanzi	2071 (20)
Other	433 (4)
Commercial vs. noncommercial CAR-T product, no. (%)	
Commercial	10142 (96)
Noncommercial	433 (4)
Is the recipient participating in a cellular therapy clinical trial?, no. (%)	
No	9902 (94)
Yes	673 (6)
2-year product embargo, no. (%)	
No	9870 (93)
Yes	705 (7)
Year of infusion, no. (%)	
2021	1738 (16)
2022	2464 (23)
2023	2904 (27)
2024	2915 (28)
2025	554 (5)

Characteristic	N (%)
Follow-up of survivors, months, median (range), months	13 (<1-53)

Epidemiology and predictors of non-infectious pulmonary toxicities of contemporary allogeneic transplantation, 2017-2024

Consolidated From: 2509-159-BAO, 2509-133-VANGALEN, 2509-75-TIJAROOVALL

Authors: Ailcia Bao, Usama Gergis, Craig Sauter, Natalia Tijaro Ovalle, Joseph Van Galen*

*Designated PI/Presenter

KEY WORDS: Noninfectious pulmonary toxicities, idiopathic pneumonia syndrome, bronchiolitis obliterans syndrome, diffuse alveolar hemorrhage, cryptogenic organizing pneumonia, graft-versus-host disease prophylaxis, post-transplant cyclophosphamide, reduced-intensity conditioning, total body irradiation, lung shielding, intravenous busulfan, therapeutic drug monitoring, non-relapse mortality

SCIENTIFIC IMPACT

Noninfectious pulmonary toxicities (NPT) of allogeneic hematopoietic cell transplantation (allo-HCT)- including idiopathic pneumonia syndrome (IPS), bronchiolitis obliterans syndrome (BOS), chronic pulmonary GvHD (cpGVHD) diffuse alveolar hemorrhage (DAH), and cryptogenic organizing pneumonia (COP)- drive early morbidity, intensive care unit (ICU) admission, and non-relapse mortality (NRM)^{1,2,3}. Epidemiologic risks and biological mediators for individual pathologies are not well understood, and limited data are available to support specific treatment strategies. Most recently, a 2022 CIBMTR report provided valuable insight into NPT epidemiology, based on data collected from patients treated with allo-HCT between 2008 and 2017.⁴ Changing patterns in donor selection, recipient conditioning, and graft versus host disease prophylaxis are expected to have influenced NPT incidence in the interim.

Perhaps most importantly among such changes, wider adoption of post-transplant cyclophosphamide (PTCy) has reduced the risk of severe acute and chronic graft-versus-host disease (GVHD) in the last two decades, presumably affecting the incidence of cpGVHD,

¹ Panoskaltis-Mortari A, Griese M, Madtes DK, Belperio JA, Haddad IY, Folz RJ, et al. An Official American Thoracic Society Research Statement: Noninfectious Lung Injury after Hematopoietic Stem Cell Transplantation: Idiopathic Pneumonia Syndrome. *Am J Respir Crit Care Med.* 2011 May 1;183(9):1262–79.

² Klein O, Cooke K. Idiopathic pneumonia syndrome following hematopoietic stem cell transplantation. *J Pediatr Intensive Care.* 2015 July 28;03(03):147–57.

³ Verde M, Mota A, Costa W, Sampaio J, Vasconcelos J, Araujo B, et al. IDIOPATHIC PNEUMONIA SYNDROME AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION. *Hematol Transfus Cell Ther.* 2024 Oct;46:S1131.

⁴ Patel SS, Ahn KW, Khanal M, et al. Noninfectious Pulmonary Toxicity after Allogeneic Hematopoietic Cell Transplantation. *Transplant Cell Ther.* 2022;28(6):310-320.

including prototypical BOS.⁵⁶⁷ Increasing use of intravenous (IV) busulfan dosed using pharmacokinetic monitoring in the same period might have also affected the incidence of NPT⁸. Other overlapping developments that must be considered in isolating such risk effects include changes in total body irradiation (TBI) techniques, including dose rate and fractionation and the use of lung shielding.⁹

Complicating any analysis of recent NPT trends is, of course, the advent of the COVID-19 pandemic and associated population shifts in viral and immunogen exposures. Early data suggest that COVID-19 exposure might modulate NPT risk.¹⁰ The study that we propose would leverage the scale of CIBMTR database in order to: 1) provide an update on the epidemiology of NPT risk, and 2) perform a controlled analysis of how donor selection, baseline lung function, and choice of conditioning and GVHD prophylaxis strategies affect NPT rates and associated patient-important outcomes. Comparison of data collected before versus after March 2020 may provide novel insight into the relationship between viral infections and the development of lung-damaging allo-immunity.

SCIENTIFIC JUSTIFICATION

Idiopathic pneumonia syndrome and other NPT entities overlap in clinical presentation and pathophysiology, involving epithelial damage due to conditioning, adoptive cell allo-reactivity, and innate immune activation.¹¹ It is not well known how the recent widescale adoptions of PTCy and precision busulfan dosing modulate the significance of classical NPT risk factors such as conditioning intensity, TBI dose, and recipient age.¹²

⁵ Curtis DJ, Patil SS, Reynolds J, Purtill D, Lewis C, Ritchie DS, et al. Graft-versus-Host Disease Prophylaxis with Cyclophosphamide and Cyclosporin. *N Engl J Med*. 2025 July 17;393(3):243–54.

⁶ Seo S, Yu J, Jenkins IC, Leisenring WM, Steven-Ayers T, Kuypers JM, et al. Diagnostic and Prognostic Plasma Biomarkers for Idiopathic Pneumonia Syndrome after Hematopoietic Cell Transplantation. *Biol Blood Marrow Transplant*. 2018 Apr;24(4):678–86.

⁷ Vande Vusse LK, Wurfel MM, Madtes DM, Schoch HG, Harju-Baker S, Hill JA, et al. Alveolar levels of immunoinflammatory mediators in diffuse alveolar hemorrhage after allogeneic transplant. *Bone Marrow Transplant*. 2018 Sept;53(9):1206–9.

⁸ Seydoux C, Bategay R, Halter J, Heim D, Rentsch KM, Passweg JR, et al. Impact of busulfan pharmacokinetics on outcome in adult patients receiving an allogeneic hematopoietic cell transplantation. *Bone Marrow Transplant*. 2022 June;57(6):903–10.

⁹ Vogel J, Hui S, Hua CH, Dusenbery K, Rassiah P, Kalapurakal J, et al. Pulmonary Toxicity After Total Body Irradiation – Critical Review of the Literature and Recommendations for Toxicity Reporting. *Front Oncol*. 2021 Aug 26; 11:708906.

¹⁰ Mushtaq MU, Shahzad M, Chaudhary SG, Luder M, Ahmed N, Abdelhakim H, et al. Impact of SARS-CoV-2 in Hematopoietic Stem Cell Transplantation and Chimeric Antigen Receptor T Cell Therapy Recipients. *Transplant Cell Ther*. 2021 Sept 1;27(9):796.e1-796.e7.

¹¹ Wenger DS, Triplette M, Crothers K, Cheng GS, Hill JA, Milano F, et al. Incidence, Risk Factors, and Outcomes of Idiopathic Pneumonia Syndrome after Allogeneic Hematopoietic Cell Transplantation. *Biol Blood Marrow Transplant*. 2020 Feb;26(2):413–20.

¹² Liu MA, Lee CC, Phung Q, Dao QL, Tehrani B, Yao M, et al. Incidence and predictors of idiopathic pneumonia syndrome in hematopoietic stem cell transplant patients: a nationwide registry study. *Int J Hematol*. 2022 Nov;116(5):770–7.

PTCy dosing on days +3 and +4 after allo-HCT selectively depletes rapidly proliferating alloreactive T cells, preserves regulatory T-cell populations, and reshapes the early inflammatory milieu.¹³ Clinically, PTCy use reduces the incidence and severity of aGVHD and cGVHD across matched and alternative donors techniques mitigating a major driver of NPT risk.⁴⁵ Still, further exploration is needed to better understand how the choice of agents adjunct to PTCy and immunosuppression taper techniques might affect lung inflammation, susceptibility to infection, and treatment responsiveness in cases where clinical NPT develops.¹⁴

The adoption of intravenous administration busulfan with pharmacokinetic monitoring and time-exposure dosing narrows inter-patient variability and reduces rates of overexposure.⁸ Although reductions in sinusoidal obstruction syndrome rates are best documented, we hypothesize that avoidance of supra-therapeutic alkylator exposure also mitigates pulmonary epithelial damage and NPT risk.¹⁵¹⁶ Modern TBI planning might also personalization dosing in a manner that reduces NPT risk. Total dose, fractionation scheme, instantaneous and average dose rate, and the use of lung shielding together shape the magnitude and kinetics of pulmonary radiation injury.¹⁷¹⁸ An understanding of how these strategies affect the pathogenesis and progression of lung damage after allo-HCT is most likely to be achieved through large-data modeling as the CIBMTR registry uniquely enables.

In modelling recent pulmonary complication data, investigators must consider the changes in patient exposure that have been associated with the COVID-19 pandemic.¹⁹ Institutional series describe increased presentations of late-onset, severe lung syndromes after transplantation during the pandemic years, but these reports are limited by size, heterogeneity, and varying

¹³ Fletcher RE, Nunes NS, Patterson MT, Vinod N, Khan SM, Mendu SK, et al. Posttransplantation cyclophosphamide expands functional myeloid-derived suppressor cells and indirectly influences Tregs. *Blood Adv.* 2023 Apr 11;7(7):1117–29.

¹⁴ Seo S, Renaud C, Kuypers JM, Chiu CY, Huang ML, Samayoa E, et al. Idiopathic pneumonia syndrome after hematopoietic cell transplantation: evidence of occult infectious etiologies. *Blood.* 2015 June 11;125(24):3789–97.

¹⁵ Bilgrami SF, Metersky ML, McNally D, Naqvi BH, Kapur D, Raible D, et al. Idiopathic pneumonia syndrome following myeloablative chemotherapy and autologous transplantation. *Ann Pharmacother.* 2001 Feb;35(2):196–201.

¹⁶ Fukuda T, Hackman RC, Guthrie KA, Sandmaier BM, Boeckh M, Maris MB, et al. Risks and outcomes of idiopathic pneumonia syndrome after nonmyeloablative and conventional conditioning regimens for allogeneic hematopoietic stem cell transplantation. *Blood.* 2003 Oct 15;102(8):2777–85.

¹⁷ Shankar G, Cohen DA. Idiopathic pneumonia syndrome after bone marrow transplantation: the role of pre-transplant radiation conditioning and local cytokine dysregulation in promoting lung inflammation and fibrosis. *Int J Exp Pathol.* 2001 Apr; 82(2):101-13.

¹⁸ Vogel J, Hui S, Hua CH, Dusenbery K, Rassiah P, Kalapurakal J, et al. Pulmonary Toxicity After Total Body Irradiation – Critical Review of the Literature and Recommendations for Toxicity Reporting. *Front Oncol.* 2021 Aug 26;11:708906.

¹⁹ Wen Q, Guo Z, Zhang XH, Xu LP, Wang Y, Yan CH, et al. COVID-19 was associated with the complications after allogeneic hematopoietic stem cell transplantation. *Sci Rep.* 2024 May 23;14(1):11778.

definitions.²⁰²¹²² The current proposal is motivated in part by a desire to further investigate our own clinical experience of the same phenomenon. A registry-scale comparison anchored to a pre-pandemic baseline may be able to establish whether a true epidemiologic inflection occurred, quantify its magnitude, and test whether effects were moderated or mediated by donor source, conditioning intensity, busulfan exposure, TBI parameters, or chronic GVHD diagnosis.

The primary goal of our proposed study is to leverage large data for a controlled analysis of associations that might prompt further observational or interventional studies of allo-HCT pulmonary complications. Subanalysis would leverage CRF-level data to explore how pre-transplantation pulmonary function data are best operationalized to predict NPT risk, how precision busulfan dosing affects NPT risk, and how different patterns of bronchoscopy and pathogen assessment might drive outcomes for patients with lung injury after allo-SCT.

To maximize the power our primary analysis, we propose that mixed effects first be modelled as predictors of overall NPT incidence (IPT+DAH+COP+BOS+cpGVHD). Secondary analyses would apply the same model specifications as derived above in order to model two subclasses whose patterns may overlap or diverge (IPT+DAH+COP vs. BOS+cpGVHD). Whether associated patient-important NPT outcomes are formulated rate of mechanical ventilation (MV) versus days free of MV, etc. would depend on volume and distribution of outcomes data.

We propose that data be included for outcomes recorded between D30 and D365, subject to competing risk, so as to capture a more homogenous set of outcomes than would be the case if very early and very late post-transplant events were included.

RESEARCH QUESTION

In adults undergoing first allo-SCT between 2017 and 2024, were the incidence and outcomes of NPTs independently associated with choice of conditioning regimen (especially in reference to busulfan and TBI exposure) and GVHD prophylaxis regimen (especially in reference to PTCy)? How did the global spread of COVID-19 impact such associations for patients treated with allo-SCT in March 2020 and beyond? Do the same clinical associations exist when NPT diagnoses are subclassified to include or exclude BOS/cpGVHD?

²⁰ Astashchanka A, Ryan J, Lin E, Nokes B, Jamieson C, Kligerman S, et al. Pulmonary Complications in Hematopoietic Stem Cell Transplant Recipients-A Clinician Primer. *J Clin Med.* 2021 July 22;10(15):3227.

²¹ O'Brien H, Murray J, Orfali N, Fahy RJ. Pulmonary complications of bone marrow transplantation. *Breathe Sheff Engl.* 2024 Oct;20(3):240043.

²² Traunero A, Peri F, Badina L, Amaddeo A, Zuliani E, Maschio M, et al. Hematopoietic Stem Cells Transplant (HSCT)-Related Chronic Pulmonary Diseases: An Overview. *Child Basel Switz.* 2023 Sept 11;10(9):1535.

RESEARCH HYPOTHESES

1. Early (\leq Day +120) NPT incidence differs by GVHD prophylaxis strategy, with a lower incidence among patients treated with PTCy-based strategies.
2. The use of busulfan dosing based on pharmacokinetics and lower overall dose exposure (AUC) is associated with lower early and late (Day 120-360) NPT diagnosis rate. The use of fractionation, as well as lower total lung dose of TBI is associated with lower NPT diagnosis rates.
3. Higher rates of late NPT and related 1-year mortality were seen among allo-SCT recipients treated in March 2020-2024, as compared to those treated 2017- February 2020.

PRIMARY OBJECTIVE

1. Estimate the early, late, and total 1-year incidence rates of overall NPT (IPT+DAH+COP+BOS+cpGVHD) and subcategorized NPT (IPT+DAH+COP vs. BOS+cpGVHD) in the period 2017-2024.

SECONDARY OBJECTIVES

1. Measure associations of key clinical predictors with NPT incidence and related patient-important outcomes: conditioning intensity and regimen, use of PTCy-based GvHD prophylaxis, incidence and treatment of aGVHD and cGVHD, use of busulfan dosing based on pharmacokinetics, overall busulfan dose exposure (AUC), and use, dose, and fractionation and TBI.
2. Compare NPT outcomes for allo-HCT patients treated in 2017-February 2020, versus in March 2020-2024, controlling for key clinical and transplant-related factors.

EXPLORATORY OBJECTIVES

1. Describe NPT/IPS clinical trajectory with respect to mechanical ventilation and mortality.
2. Compare clinical trajectories among patients diagnosed with NPT and treated with corticosteroids alone versus those treated with adjunctive agents (etanercept, ruxolitinib)
3. Compare clinical trajectories among patients for whom NPT diagnostic evaluation did versus did not include bronchoscopy and respiratory viral testing.
4. Compare the predictive power of pre-transplant FEV1 and DLCO measurements for NPT incidence and related patient-important outcomes when values are considered continuously versus as categorized in HCT-CI.

INCLUSION CRITERIA

1. Adults \geq 18 years at the time of first allogeneic HCT for malignant or nonmalignant indications performed in 2017–2024.
2. Availability of follow-up to at least Day +365 or documentation of earlier competing events.

EXCLUSION CRITERIA

1. Prior allo-SCT
2. Non-malignant transplant indication
3. Cord blood allo-SCT
4. Insufficient baseline or follow-up data after imputation to adjudicate NPT or key covariates

REASONS TO EXCLUDE PEDIATRIC PATIENTS

Mechanism and management of lung injury is significantly different pediatric versus adult patients due to both biologic and iatrogenic factors including: differences in exposure pattern and host response to respiratory viral exposures, differences in GVHD prophylaxis approaches, and different age-specific thresholds for supportive care, mechanical ventilation, and intensive care transfer. Because the quantitative effects of these factors are not well studied, inclusion of pediatric patients might confound results in a way that is not readily measured or controlled.

PATIENT VARIABLES

Age, sex, race/ethnicity, body mass index, smoking history, HCT-Comorbidity Index (HCT-CI), Karnofsky Performance Index, baseline pulmonary function (FEV1, DLCO), pre-HCT oxygen requirement, history of COVID-19 vaccination/infection, pre-HCT irradiation (regionality, lung dose), history of mechanical ventilation, baseline moderate or severe co-existing pulmonary impairment

DISEASE VARIABLE

Underlying diagnosis/indication (AML, MDS, ALL, lymphoma, etc.), disease risk index/stage, remission status at HCT, prior therapy lines of therapy, cytogenetic/molecular high-risk features (when available).

INFUSION VARIABLES

Donor type (MRD/MUD/MMUD/Haplo/Cord), HLA match, graft source (PBSC/BM/Cord), ABO compatibility, CD34+ cell dose, conditioning regimen and intensity, TBI use yes/no, TBI total dose/fractionation/lung average dose, busulfan use/total prescribed dose/administration/measurement with AUC and dose adjustment, treosulfan use/dose, melphalan use/dose, ATG use/dose, alemtuzumab use/dose, GVHD prophylaxis regimen (PTCy/cyclosporin/tacrolimus/sirolimus/mycophenolate mofetil/methotrexate/abatacept).

POST-TRANSPLANTATION VARIABLES

Last known alive, engraftment day, relapse y/n/date, acute GVHD yes/no/date, acute GVHD grade at diagnosis/max grade, acute GVHD organ stage, acute GVHD treatment, acute GVHD persistence, chronic GVHD yes/no/date, chronic GVHD onset, chronic GVHD severity, chronic GVHD treatment, chronic GVHD NIH organ site scores, chronic GVHD treatment persistence, antibacterial prophylaxis, antiviral prophylaxis, antifungal prophylaxis, PJP prophylaxis, clinically significant infection of lung, mechanical ventilation yes/no/date, successful extubation

yes/no/date, IPS/ARDS/other non-infectious pulmonary abnormality yes/no/date/diagnostic method/resolution.

RELEVANT FORMS

2000, 2006, 2100, 2400, 2402, 2450, 2900

Population characteristics of first alloHCT adult patients (CRF only)

Characteristic	N (%)
No. of patients	34591
No. of centers	299
Patient-Related Characteristics	
Age, by decades, no. (%)	
Median (range)	56 (18-88)
18-19	907 (3)
20-29	4027 (12)
30-39	3564 (10)
40-49	4757 (14)
50-59	7870 (23)
60-69	10573 (31)
70+	2893 (8)
Sex, no. (%)	
Male	20349 (59)
Female	14242 (41)
Race, no. (%)	
White	26775 (77)
Black or African American	2955 (9)
Asian	2259 (7)
Native Hawaiian or other Pacific Islander	170 (0)
American Indian or Alaska Native	157 (0)
More than one race	401 (1)
Not reported	1874 (5)
Ethnicity, no. (%)	
Hispanic or Latino	3087 (9)
Non-Hispanic or Latino	27565 (80)
Non-resident of the U.S.	3368 (10)
Not reported	571 (2)
CCN region at transplant, no. (%)	

Characteristic	N (%)
U.S	30125 (87)
Non U.S	4466 (13)
Karnofsky score prior to HCT, no. (%)	
90-100%	19973 (58)
< 90%	14092 (41)
Not reported	526 (2)
ECOG prior to HCT, no. (%)	
Asymptomatic	19973 (58)
Symptomatic but completely ambulatory	13410 (39)
Symptomatic, < 50% in bed during the day	640 (2)
Symptomatic, > 50% in bed, but not bedbound	28 (0)
Bedbound	14 (0)
Not reported	526 (2)
HCT-Cl, no. (%)	
0	9222 (27)
1	4896 (14)
2	4863 (14)
3	5908 (17)
4	3785 (11)
5+	5229 (15)
Not reported	688 (2)
Has the patient been infected with COVID-19 (SARS-CoV-2) based on a positive test result at any time prior to the start of the preparative regimen / infusion?, no. (%)	
No	4787 (14)
Yes	1189 (3)
Not reported	28615 (83)
Was a vaccine for COVID-19 (SARS-CoV-2) received?, no. (%)	
No	865 (3)
Yes	2470 (7)

Characteristic	N (%)
Not reported	31256 (90)
Moderate Pulmonary, no. (%)	
No	24706 (71)
Yes	8817 (25)
Not reported	1068 (3)
Severe Pulmonary, no. (%)	
No	28443 (82)
Yes	5079 (15)
Not reported	1069 (3)
Disease-Related Characteristics	
Primary disease, no. (%)	
AML	11034 (32)
ALL	3471 (10)
Other leukemia	124 (0)
CLL	755 (2)
CML	915 (3)
MDS	7048 (20)
Other acute leukemia	297 (1)
NHL	2411 (7)
HD	1148 (3)
MM	485 (1)
Other PCD	76 (0)
Solid tumor	15 (0)
Aplastic anemia	2179 (6)
Inherited bone marrow failure syndromes	123 (0)
Hemoglobinopathies	566 (2)
Paroxysmal nocturnal hemoglobinuria (PNH)	96 (0)
Disorders of the immune system	96 (0)
Inherited abnormalities of platelets	4 (0)
Inherited disorders of metabolism	17 (0)
Histiocytic disorders	32 (0)
Autoimmune diseases	11 (0)
Other disease	15 (0)
Tolerance induction associated with solid organ transplant	2 (0)

Characteristic	N (%)
MPN	3671 (11)
Interval from diagnosis to HCT, months, median (range)	9 (0-673)
Transplant-Related Characteristics	
Conditioning regimen, no. (%)	
TBI/Cy	2713 (8)
TBI/Cy/Flu	5653 (16)
TBI/Cy/Flu/TT	325 (1)
TBI/Cy/TT	61 (0)
TBI/Cy/VP	116 (0)
TBI/VP	417 (1)
TBI/Mel	1026 (3)
TBI/Flu	2727 (8)
TBI/other(s)	319 (1)
Bu/Cy/Mel	4 (0)
Bu/Cy	3246 (9)
Bu/Mel	125 (0)
Flu/Bu/TT	404 (1)
Flu/Bu	8424 (24)
Flu/Mel/TT	298 (1)
Flu/Mel	5706 (16)
FCR	149 (0)
Cy/Flu	851 (2)
Cy alone	375 (1)
CBV	25 (0)
BEAM	137 (0)
BEAM like	3 (0)
Mel alone	89 (0)
Mel/other(s)	61 (0)
Treosulfan	265 (1)
Carb/Etop	3 (0)
TLI	211 (1)
Other(s)	445 (1)
None	9 (0)
Missing	404 (1)
Donor type, no. (%)	
HLA identical sibling	8118 (23)

Characteristic	N (%)
Twin	238 (1)
Haploidentical donor	4975 (14)
Other related	848 (2)
Well-matched unrelated (8/8)	12886 (37)
Partially-matched unrelated (7/8)	2987 (9)
Mismatched unrelated (<= 6/8)	241 (1)
Multi-donor	267 (1)
Unrelated (matching cannot be determined)	1050 (3)
Cord blood	2981 (9)
Donor/recipient sex match, no. (%)	
M-M	12163 (35)
M-F	7287 (21)
F-M	6413 (19)
F-F	5452 (16)
CB - recipient M	1700 (5)
CB - recipient F	1458 (4)
Not reported	118 (0)
GVHD prophylaxis, no. (%)	
Ex-vivo T-cell depletion	210 (1)
CD34 selection	567 (2)
PtCy + other(s)	7822 (23)
PtCy alone	128 (0)
TAC + MMF +- other(s) (except PtCy)	4718 (14)
TAC + MTX +- other(s) (except MMF, PtCy)	11619 (34)
TAC + other(s) (except MMF, MTX, PtCy)	1694 (5)
TAC alone	785 (2)
CSA + MMF +- other(s) (except PtCy,TAC)	2754 (8)
CSA + MTX +- other(s) (except PtCy,TAC,MMF)	2480 (7)
CSA + other(s) (except PtCy,TAC,MMF,MTX)	117 (0)
CSA alone	419 (1)
Other(s)	504 (1)
Missing	774 (2)
Use of PTCy, no. (%)	

Characteristic	N (%)
No	25888 (75)
Yes	8703 (25)
Donor age, by decades, no. (%)	
Median (range)	33 (0-85)
0-9	853 (2)
10-19	1505 (4)
20-29	11556 (33)
30-39	6879 (20)
40-49	4823 (14)
50-59	3979 (12)
60-69	2205 (6)
70+	278 (1)
Not reported	2513 (7)
Year of current transplant, no. (%)	
2008	2615 (8)
2009	2329 (7)
2010	1506 (4)
2011	1130 (3)
2012	1147 (3)
2013	2206 (6)
2014	2809 (8)
2015	2685 (8)
2016	2556 (7)
2017	2558 (7)
2018	2455 (7)
2019	2340 (7)
2020	1528 (4)
2021	1549 (4)
2022	1473 (4)
2023	1629 (5)
2024	1814 (5)
2025	262 (1)
Follow-up of survivors, median (range), months	72 (<1-205)

Field	Response
Proposal Number	2509-79-LAMBLE
Proposal Title	Incidence and Causes of Non-Relapse Mortality Following CAR T-cell Therapy in Pediatric and Young Adult B-ALL
Key Words	CAR T-cell therapy, Immunotherapy, Toxicity, Mortality, Infection, Organ Failure, B-acute lymphoblastic leukemia (B-ALL)
Principal Investigator #1: - First and last name, degree(s)	Adam Lamble, MD
Principal Investigator #1: - Email address	adam.lamble@seattlechildrens.org
Principal Investigator #1: - Institution name	Seattle Children's Hospital
Principal Investigator #1: - Academic rank	Associate Professor
Junior investigator status (defined as 笭、5 years from fellowship)	No
Do you identify as an underrepresented/minority?	No
Principal Investigator #2 (If applicable): - First and last name, degree(s):	Nirali Shah
Principal Investigator #2 (If applicable): - Email address:)	nirali.shah@nih.gov
Principal Investigator #2 (If applicable): - Institution name:	NIH
Principal Investigator #2 (If applicable): - Academic rank:	Senior Investigator
Junior investigator status (defined as 笭、5 years from fellowship)	No
Do you identify as an underrepresented/minority?	No
We encourage a maximum of two Principal Investigators per study. If more than one author is listed, please indicate who will be identified as the corresponding PI below:	Adam Lamble
Do any of the PI(s) within this proposal have a CIBMTR WC study in manuscript preparation >6 months?	No
PROPOSED WORKING COMMITTEE:	Pediatric Cancer
Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.	Yes
If you have already spoken with a scientific director or working committee chair regarding this study, then please specify who:	Jeff Auletta

Field	Response
RESEARCH QUESTION:	<p>While CAR T-cell therapy has transformed outcomes for relapsed/refractory B-cell acute lymphoblastic leukemia (B-ALL) and is increasingly used in other hematologic malignancies, non-relapse mortality (NRM) remains an important but poorly understood endpoint. Unlike in hematopoietic stem cell transplantation (HSCT), where NRM has been rigorously studied and integrated into both trial endpoints and clinical practice, systematic evaluation of NRM after CAR T for pediatric, adolescents, and young adults (AYA) is lacking. A recent meta-analysis of >7,600 adult patients treated with CD19- and BCMA-directed CAR T-cell therapies reported a pooled NRM incidence of 6.8% (95% CI 5.8–8.0%) at ~1 year. While informative, these findings are limited to adults with lymphomas and myeloma and cannot be extrapolated to pediatrics, where the only approved indication remains B-ALL. Importantly, adults often present with greater comorbidity burden, extensive prior therapy, and different disease biology, all of which may shape NRM risk. This proposal will directly address the gap in knowledge regarding NRM in pediatric and AYA CAR T recipients, with specific focus on age-related contrasts and treatment-era effects. Given the overall rarity of NRM, it is critical to use a larger data repository, such as the CIBMTR, to collect a sufficient sample size for meaningful analysis.</p> <p>This proposal seeks to:</p> <ol style="list-style-type: none"> 1. Define the incidence, timing, and causes of NRM in pediatric and AYA CAR T recipients with B-ALL. 2. Assess patient-, disease-, and treatment-related factors that influence NRM risk. 3. Compare patterns of NRM by age group (children vs. AYAs vs. adults), CAR construct, disease indication, and treatment era.

Field	Response
RESEARCH HYPOTHESIS:	<p>(1) Age effect: When controlling for diagnosis, we hypothesize that pediatric patients will experience lower NRM compared with adults, due to fewer comorbidities, greater organ reserve, and reduced vulnerability to infectious complications. (2)</p> <p>Cause of NRM differs by age group: We hypothesize that the predominant causes of NRM differ by age group. In adults, infections, secondary malignancies, and organ failure are expected to account for the majority of NRM, whereas in pediatric patients, non-infectious mechanisms such as inflammatory toxicities are proportionally more frequent. (3)</p> <p>Treatment era effect: We hypothesize that NRM has declined over time as clinicians have become more adept at managing CAR T-associated toxicities, supportive care practices have become standardized, and CAR T is being offered earlier in the treatment course (leading to less cumulative toxicity and lower disease burden at infusion). (4)</p> <p>Construct and product effect: We hypothesize that NRM rates differ across CAR constructs and disease indications, reflecting varying toxicity profiles.</p>

Field	Response
<p>SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):</p>	<p>I. Part 1: Descriptive Analyses of NRM A. Primary objective: Determine the incidence and causes of NRM in pediatric patients at 30 days, 100 days, 6 months, and 1 year post CAR T. B. Secondary objectives:</p> <p>(1) Characterize the timing and primary causes of NRM (e.g., infection, organ failure, bleeding, CRS, ICANS, IEC-HS, secondary malignancy, etc.). (2) Compare causes of NRM between pediatric patients and adults. (3) Assess whether NRM incidence has decreased in recent treatment eras.</p> <p>II. Part 2: Multivariable: Identify risk factors predictive of NRM. A. Primary Objective: Identify risk factors predictive of NRM in pediatric CAR T recipients. B. Secondary objectives: (1) Test whether younger age independently predicts lower NRM, controlling for diagnosis, disease burden, HSCT, and CAR construct. (2) Evaluate treatment era as a covariate to assess whether outcomes improve with evolving supportive care and earlier CAR T use. (3) Explore disparities in NRM across demographic groups (e.g., age strata, ethnicity, comorbidity status). (4) Develop a predictive model for NRM risk in pediatric CAR T recipients.</p>

Field	Response
<p>SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.</p>	<p>NRM has historically shaped decision-making in HSCT, but it remains far less defined in the setting of CAR T-cell therapy. This gap is particularly striking in pediatrics, where causes of NRM may differ from adults due to distinct disease biology, prior treatment exposures, and age-related immune and organ reserve differences. This is highlighted in the setting of HSCT, where adults have a higher incidence of NRM compared to pediatrics, driven largely by infection-related mortality. Adult data suggest NRM is relatively low after CAR T but predominantly driven by infection, organ dysfunction, and secondary malignancy (Table 1). In pediatrics, the incidence and distribution of NRM are likely distinct, due to different disease indications, CAR constructs, and co-morbidities. In contrast, pediatric reports, primarily from single centers and clinical trials such as ELIANA, have suggested a low incidence of NRM (Table 2). Surprisingly, a recent CIBMTR real-world data of 768 pediatric and young adult tisagenlecleucel recipients (median age 13.8 years) reported a 13.1% NRM rate, which is far higher than anticipated based on institutional and multicenter investigational experiences. While efficacy outcomes paralleled prior reports (CR/CRi 86%, 12-month OS 79%), the unexpectedly elevated NRM requires further exploration. Potential contributors include inclusion of higher-risk patients typically excluded from clinical trials (e.g., poor performance status, CNS disease, prior CAR-T, out-of-specification products), heterogeneous reporting of cause of death, and confounding by transplant-related toxicities. These findings underscore both the importance and the challenge of systematically characterizing NRM in pediatrics. This proposal directly addresses that unmet need. By systematically characterizing the incidence, causes, and risk factors for NRM across age groups, treatment eras, and CAR constructs, the study will complement existing work on relapse, durability, and CAR persistence. These insights will inform clinical trial design, patient counseling, and supportive care strategies to improve long-term outcomes for pediatric and AYA CAR T recipients.</p>

Field	Response
<p>SCIENTIFIC JUSTIFICATION: Provide a background summary of previous related research and their strengths and weaknesses, justification of your research and why your research is still necessary.</p>	<p>The rationale for this proposal rests on several biologic and clinical considerations. First, age is likely to influence both the incidence and causes of NRM. Children typically have fewer baseline comorbidities, greater organ reserve, and lower susceptibility to severe infections compared with adults. As a result, pediatric patients may be relatively protected from infection-driven NRM, the predominant cause in adults, yet remain vulnerable to other mechanisms such as inflammatory toxicities. Older AYAs, particularly those closer to the adult age range, may share more of the comorbidity burden and infectious vulnerability observed in adults. Second, NRM is dynamic and may evolve across treatment eras. Over the past decade, clinicians have become more skilled at recognizing and managing acute CAR T toxicities such as CRS and ICANS, while supportive care practices have become more standardized. In parallel, the patient population eligible for CAR T has shifted, with therapy increasingly offered earlier in the treatment course. This trend means patients are now infused with fewer cumulative toxicities, less disease burden, and fewer comorbidities, all factors that plausibly lower the risk of NRM. Finally, heterogeneity across diagnoses and products adds an additional layer of complexity. Different co-stimulatory domains, manufacturing platforms, and disease indications may influence toxicity profiles and supportive care practices, leading to variation in NRM risk. Together, these considerations strongly support the need for a comprehensive analysis of NRM across pediatric and adult CAR T recipients.</p>
<p>SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF) - Id</p>	<p>F_1nOvHM6qBQMnWJn</p>
<p>SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF) - Name</p>	<p>Screenshot 2025-09-20 at 11.29.58 AM.png</p>
<p>SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF) - Size</p>	<p>165587</p>
<p>SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF) - Type</p>	<p>image/png</p>
<p>PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.</p>	<p>(1) Patients receiving commercially available or investigational CAR T for hematologic malignancies, reported to CIBMTR. (2) Exclude patients with relapse/progression as primary cause of death to isolate NRM events.</p>
<p>Does this study include pediatric patients?</p>	<p>Yes</p>

Field	Response
Types of cellular therapy data this proposal includes:	Chimeric Antigen Receptor (CAR) T-Cell Therapy (CAR-T)

<p>SAMPLE REQUIREMENTS: If the study requires biologic samples from the CIBMTR Repository, the proposal should also include: 1) A detailed description of the proposed testing methodology and sample requirements; 2) A summary of the investigator's previous e</p>	<p>Patient and disease details: Variable Form/ #Question Age 4000R10/ # 47-48 Sex 4000R10/ # 49 Ethnicity/Race 4000R10/ # 1-2 CAR T indication 4000R10/ #18, 73, / 2402R9/ #2,104, 393, 411 Disease status at CAR T 2402R9/ #166,167, 169-178, 402-408, 454-456; 2011R5 #64-83; 2018R6/ # 234-286; 2016R5/ #188-245 Lines therapy pre-CAR T 2402R9/# 168, #409 Prior stem cell transplant details 4000R10/ #26-32 Comorbidities 4000R10/ #81-97 Functional Status 4000R10/ #77-80 Pre-infusion WBC, Hgb, Plt, ANC 4000R9/#88-98; 4001R1/ #15-25 Pre-infusion LDH, CRP, Ferritin 4000R10:#74-76; 4000R9 #99-107; 4001R1/ #26-31 CAR T details: Variable Form/ #Question Product Name, dose, details 4000R10/ #8,51,52; 4006R6/ #2-31; 40003R5 #2 Concomitant therapy 4006R6/ #32-35 Lymphodepletion used 4001R1/ #5-10 CRS/ICANS prophylaxis used 4001R1/ #11-14 Toxicities Variable Form/ #Question CRS/ICANS prophylaxis used 4001R1/ #11-14 Admitted to hospital post-infusion 4101R1/ #2 CRS details (therapy, timing, severity, resolution) 4101R9/ #47-67 MAS/HLH and details (timing, therapy, splenomegaly, hemophagocytosis, fibrinogen, TG, resolution)4101R1/ #69-80 Neurotoxicity/ICANS, details 4101R1/ #81-136 Cytopenias; growth factor use 4101R1/ #15-23; 2100R9/ #21 Tumor lysis syndrome 4101R1/ #142-147 Other toxicity 4101R1/ #148-153 Grade 3 & 4 organ toxicities 4101R1/ #154-167 Infections 4101R1/ #178-189 Hospitalization duration 2100R9/ #384-387 Outcomes Variable Form/ #Question Date of last contact and patient status 4100R9/ #2-3 Subsequent infusion of CAR T/HSCT 4100R9/ #4-11/ 2100R9/ #409-412 Best response to cell therapy 4100R9/ #12-14; 2118R4; 2116R5; 2111R4 Disease relapse/progression 4100R9/ #24-25; 2118R4; 2116R5; 2111R4 Additional therapy given 2111R4/ #35; 2118R4; 2116R5 Evidence of antigen escape 4101R1/ #5-8 Most recent hematologic findings 4101R1/ #10-20 Persistence of cells 4101R1/ #21-45 Cause of death 4900/ #1-7 -product name -was the product a clinical trial product (4000 R10 #8) -Any prior engineered T-cell therapy -lymphodepletion chemotherapy -time from</p>
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Field	Response
	diagnosis -bridging therapy (yes/no) -type of bridging therapy -disease status at the time of CAR (active disease or CR) -Therapy given for the prevention of CRS, if any -Therapy given for prevention of neurotoxicity (ICANS) if any Outcomes details: -duration of hospitalization -ICU transfer (yes/no) -duration of ICU stay -infections complications post CAR T -type of infection(s) -bleeding complications -severity of bleeding complication -best disease response -disease response day 30 -day 100 outcomes (alive y/n, in remission y/n) -1-year outcomes (alive y/n, in remission y/n) -relapse/progression -death/survival/last follow up -cause of death -Duration of hospitalization requirement (Form 4100 R8.0 #204-205) -Persistence of CAR T-cells, if available (Form 4100 R8.0 #44-68)

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doi:10.1001/jamaoncol.2021.3676 3. Czyzewski K, Styczynski J, Giebel S, et al. Age-dependent determinants of infectious complications profile in children and adults after hematopoietic cell transplantation: lesson from the nationwide study. *Ann Hematol.* Sep 2019;98(9):2197-2211.
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doi:10.3389/fimmu.2023.1219289 7. Curran KJ, Margossian SP, Kernan NA, et al. Toxicity and response after CD19-specific CAR T-cell therapy in pediatric/young adult relapsed/refractory B-ALL. *Blood.* Dec 26 2019;134(26):2361-2368.
doi:10.1182/blood.2019001641 8. Laetsch TW, Maude SL, Rives S, et al. Three-Year Update of Tisagenlecleucel in Pediatric and Young Adult Patients With Relapsed/Refractory Acute Lymphoblastic Leukemia in the ELIANA Trial. *J Clin Oncol.* Mar 20 2023;41(9):1664-1669.
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Field	Response
	relapsed B-cell acute lymphocytic leukaemia: a single-arm, phase 2 study. <i>Lancet Oncol.</i> Nov 2023;24(11):1229-1241. doi:10.1016/S1470-2045(23)00436-9 10. John S, Curran KJ, Hall EM, et al. Real-world data for tisagenlecleucel in patients with R/R B-ALL: subgroup analyses from the CIBMTR registry. <i>Blood Adv.</i> Jun 24 2025;doi:10.1182/bloodadvances.2025015881
CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning?	No, I do not have any conflicts of interest pertinent to this proposal

Table 1: Publications reporting NRM in Adults

Study/Trial	Population/Indication	CAR T Product(s)	NRM (%) / Events	NRM Causes
Dos Santos et al. (2024) ¹	Lymphoma, myeloma (adults)	Multiple	5.7–10.6% (entity-specific)	Infections (50.9%), CV/respiratory (7.3%), CAR T toxicities (11.5%)
Mahmood et al. (2023) ⁵	Adult anti-CD19 CAR T recipients	Anti-CD19 CAR T	3.5% (100d), 6.7% (1yr)	Cardiovascular events, infections
Benjamin et al. (2020) ⁴	Pediatric & adult R/R B-ALL	UCART19 (allogeneic)	9.5% (1/14 adults)	Pulmonary hemorrhage

Table 2: Publications reporting NRM in Pediatrics

Study/Trial	Population/Indication	CAR T Product(s)	NRM (%) / Events	NRM Causes
ELIANA (Phase II) ⁸	Pediatric/young adult R/R B-ALL	Tisagenlecleucel	0–3% (2/79)	Infection
CART-PICU Study ⁶	Pediatric B-ALL, PICU admissions	4-1BB CAR constructs	8.3% (2/24)	carHLH
Pan et al. (2023) ⁹	Pediatric R/R B-ALL	CD19 & CD22 CAR T	0%	No treatment-related deaths
Benjamin et al. (2020) ⁴	Pediatric & adult R/R B-ALL	UCART19 (allogeneic)	14% (1/7 children)	Neutropenic sepsis
Curran et al. (2019) ⁷	Pediatric/young adult R/R B-ALL	19-28z CAR T	0%	No NRM reported

Characteristics of patients with B-ALL who underwent CAR-T during 2014-2025

Characteristic	N(%)
No. of patients	2452
No. of centers	195
Patient-Related Characteristics	
Age by decades, no. (%), years	
Median (range)	18.2 (0.0-84.3)
0-9	612 (25)
10-19	748 (31)
20-29	485 (20)
30-39	174 (7)
40-49	120 (5)
50-59	137 (6)
60-69	122 (5)
70+	54 (2)
Age, new grouping, no. (%), years	
0-26	1774 (72)
>26	678 (28)
Recipient Sex, no. (%)	
Male	1479 (60)
Female	973 (40)
Recipient race, no. (%)	
White	1643 (67)
Black or African American	150 (6)
Asian	112 (5)
Native Hawaiian or other Pacific Islander	9 (0)
American Indian or Alaska Native	22 (1)
Other	51 (2)
More than one race	272 (11)
Not reported	193 (8)
Ethnicity, no. (%)	
Hispanic or Latino	900 (37)
Non-Hispanic or Latino	1210 (49)
Non-resident of the U.S.	278 (11)
Not reported	64 (3)
Current CCN region of patient, no. (%)	
US	2198 (90)
Non-US	254 (10)
Karnofsky performance score prior to CT, no. (%)	
90-100	1384 (56)

Characteristic	N(%)
80	489 (20)
< 80	339 (14)
Not reported	240 (10)
ECOG prior to CT, no. (%)	
Asymptomatic	1419 (58)
Symptomatic but completely ambulatory	763 (31)
Symptomatic, < 50% in bed during the day	113 (5)
Symptomatic, > 50% in bed, but not bedbound	9 (0)
Bedbound	1 (0)
Not reported	147 (6)
HCT comorbidity score, no. (%)	
0	872 (36)
1	545 (22)
2	294 (12)
3	341 (14)
4	187 (8)
5+	163 (7)
Not reported	50 (2)
Disease-Related Characteristics	
Time from initial diagnosis to CT, median (range), months	24 (0-387)
Disease status prior to CT for leukemia, no. (%)	
CR1	309 (13)
CR2	481 (20)
CR3+	286 (12)
Relapse, 1st	606 (25)
Relapse, other	532 (22)
PIF/Untreated	223 (9)
Not reported	15 (1)
Infusion-Related Characteristics	
No. of lines of prior therapies (including CT and HCT), no. (%)	
1-3	817 (33)
>3	1068 (44)
No lines reported/not reported	567 (23)
Prior HCT, no. (%)	
No	1738 (71)
Yes	681 (28)
Not reported	33 (1)
Lymphodepleting regimen, no. (%)	
Fludarabine + Cyclophosphamide	2065 (84)
Bendamustine only	11 (0)

Characteristic	N(%)
Others	365 (15)
Not reported	11 (0)
Product, no. (%)	
Tisagenlecleucel	1391 (57)
Brexucabtagene autoleucel	683 (28)
Other	378 (15)
Commercial vs. noncommercial CAR-T product, no. (%)	
Commercial	2074 (85)
Noncommercial	378 (15)
Is the recipient participating in a cellular therapy clinical trial? no. (%)	
No	2061 (84)
Yes	391 (16)
2-year product embargo, no. (%)	
No	2261 (92)
Yes	191 (8)
Year of infusion, no. (%)	
Before 2017	32 (1)
2017	55 (2)
2018	173 (7)
2019	245 (10)
2020	223 (9)
2021	238 (10)
2022	428 (17)
2023	457 (19)
2024	506 (21)
2025	95 (4)
Follow-up of survivors, median (range), months	25.0 (0.5-120.7)

Field	Response
Proposal Number	2509-81-DREYZIN
Proposal Title	Delayed engraftment and graft rejection in pediatric patients after CAR T-cell therapy
Key Words	stem cell transplant, engraftment, CAR T-cells, cell therapy, rejection, leukemia, lymphoma
Principal Investigator #1: - First and last name, degree(s)	Alexandra Dreyzin, MD MS
Principal Investigator #1: - Email address	alexandra.dreyzin@nih.gov
Principal Investigator #1: - Institution name	National Institutes of Health
Principal Investigator #1: - Academic rank	Assistant Research Physician
Junior investigator status (defined as 助、5 years from fellowship)	Yes
Do you identify as an underrepresented/minority?	No
Principal Investigator #2 (If applicable): - First and last name, degree(s):	Amy Keating
Principal Investigator #2 (If applicable): - Email address:)	amy_keating@dfci.harvard.edu
Principal Investigator #2 (If applicable): - Institution name:	Boston Children's Hospital/Dana-Farber Cancer Institute
Principal Investigator #2 (If applicable): - Academic rank:	Full Professor
Junior investigator status (defined as 助、5 years from fellowship)	No
Do you identify as an underrepresented/minority?	No
We encourage a maximum of two Principal Investigators per study. If more than one author is listed, please indicate who will be identified as the corresponding PI below:	Alexandra Dreyzin
Do any of the PI(s) within this proposal have a CIBMTR WC study in manuscript preparation >6 months?	No
PROPOSED WORKING COMMITTEE:	Pediatric Cancer
Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.	No
RESEARCH QUESTION:	Do patients who undergo HSCT after chimeric antigen receptor (CAR) T-cell therapy have higher rates of graft rejection or delayed engraftment compared to those who have not had CAR T-cells?

Field	Response
RESEARCH HYPOTHESIS:	<p>1. Among pediatric patients with hematologic malignancies who undergo transplant after relapsed disease, those who are treated with CAR T-cells prior to transplant will have higher rates of rejection compared to those have not been exposed to CAR T-cells. 2. Patients undergoing HSCT after CAR T-cell therapy will have longer time to engraftment compared to those who have not had CAR T-cells.</p>
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	<p>Primary objective: To determine the impact of prior CAR T-cell exposure on: A. Graft Failure B. Time to engraftment Exploratory/Secondary objectives: 1. To examine whether time from prior CAR T-cell therapy impacts engraftment time or rates of graft failure. 2. To examine whether response to prior CAR T-cell therapy impacts engraftment time or rates of graft failure. 3. To describe the overall incidence of graft rejection among patients with hematologic malignancies. 4. To compare rates of GVHD among patients with and without CAR T-cell exposure prior to transplant.</p>
SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.	<p>Use of CAR T-cells and other cellular therapies are increasing, and HSCT is often used as a consolidative therapy post-CAR. Cell therapies can cause long-term changes to the immune system, which are not well-studied. Specifically, the effect of prior CAR exposure on HSCT engraftment is not known. If differences in rejection rates are observed among patients with prior CAR, this could help optimize pre-transplant conditioning regimens and immune suppression post-transplant for this growing population.</p>

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

Graft failure is a rare but potentially devastating complication after HSCT, reported in 2-4% of patients who undergo transplant for hematologic malignancies.[1-4] A larger proportion of patients, around 20%, experience delayed engraftment, defined as engraftment later than 30 days.[5] Risk factors for graft failure or delayed engraftment may include HLA-mismatched grafts, inadequate CD34+ cell dose in the infused product, or insufficient conditioning. Some patients may be sensitized by prior exposures such as blood transfusions, although this is more common in non-malignant conditions like aplastic anemia.[6] An increasing number of patients are undergoing CAR T-cell therapy for relapsed B-ALL, and consolidative HSCT is an important part of post-CAR therapy, especially for patients with poor CAR T-cell persistence.[7] It is not known whether approach to transplant after CAR T-cells should differ from standard HSCT in patients with B-ALL. CAR T-cells can lead to increased immunogenicity, triggering both humoral and cellular responses.[8-10] Although the majority of CAR-associated toxicities are short term, long-term cytopenias and immune deficiencies have been reported.[11] The impact of prior CAR on consolidative transplant outcomes has not been well established. Given the risk of increased immunogenicity, it is possible that prior exposure to CAR T-cell therapy increases risk of non-engraftment or delayed engraftment. In one recent study of HSCT patients in China, those who had prior CAR T-cell therapy had a higher risk of platelet non-engraftment and chronic GVHD compared to those who had previously received only chemotherapy.[12] In adult patients with DLBCL who received HSCT after failure to respond to CD19-targeted CAR T-cells, 4 of 39 patients failed to achieve engraftment [13], although it is not clear whether this was due to rejection or early death from relapsed disease. Real world outcomes from a European cohort of adult and children with B-ALL who had HSCT after CAR T-cell therapy have reported survival outcomes, but rates of non-engraftment or delayed engraftment were not specifically reported from this cohort. [14] Engraftment after HSCT performed post-CAR has not been characterized in the US population, or specifically in the pediatric population. An understanding of these outcomes may help guide decision-making regarding transplant conditioning and post-transplant immune suppression.

Field	Response
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	Inclusion: Patients aged 0-26 yrs, with B-cell malignancies (leukemia or lymphoma) receiving hematopoietic stem cell transplant Exclusion: -Autologous transplant
Does this study include pediatric patients?	Yes

<p>DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Outline any supplementary data required.</p>	<p>Pre-Transplant Essential Data: 2400 R10 Date of Transplant 1. DOB 2. 2. Sex 3. Ethnicity 4. Race 31. Reason for current HCT 36. Prior Cell therapy 38. Date of cell therapy 44. Donor information (auto vs allo related or unrelated) 45. Product type (BM, PBCS, cord blood) 48. Related donor type (HLA matched vs mismatched) 51. Degree of mismatch 52. Unrelated Donor type 68. Donor blood type 69. Donor Rh factor 84. Recipient blood type 85. Recipient Rh factor 122. Was a pre-HCT regimen prescribed? 123. Classify preparative regimen (myeloablative, non-meyloablative, RIC) 124. Was irradiation planned? 125. What was the prescribed radiation field? (TBI, IMRT, lymphoid/nodal regions, thoracoabdominal region) 130. Report each drug given as preparative regimen. 132. Total prescribed dose 135. Specify drugs given: ATG, alemtuzumab 140. Was GVHF prophylaxis planned? 141. Specify drugs/intervention. Post Transplant Essential Data (2450-R8) 1. Survival date of follow-up 2. Survival status 4. Was there evidence of initial hematopoietic recovery? Yes/no 5. Date ANC &gt; 500 6. Did late graft failure occur? 7. Date platelets &gt; 20 8. Did acute GVHD develop? 19. Maximum overall grade of acute GVHD 27. Did chronic GVHD develop? 30. Maximum grade of chronic GVHD 66. Compared to disease status prior to the preparative regimen, what was the best response to infusion? (CCR, CR, not in CR) Acute Lymphoblastic Leukemia Pre-Infusion (2011R5) Laboratory studies at Last Evaluation prior to the Start of Preparative Regimen: 27. Was therapy given? For those with cell therapy history, include any therapies given after cell therapy IF cell therapy, 52. Was recipient MRD negative following this line of therapy? 53. Did the recipient relapse following this line of therapy? 67. Blasts in blood 70. Blasts in bone marrow 73. Was flow cytometry performed? if yes, was disease detected? Hodgkin and Non-Hodgkin Lymphoma Pre-Infusion Data (2018R6) 166. Was therapy given? 216. Cellular therapy Yes/no IF Cell therapy was given, include any therapies given after cell therapy. IF cell therapy was given, 168. Date therapy started. 217. Best response to line of therapy by CT criteria 219. Best response to line of therapy by PET criteria 222. Did</p>
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Field	Response
	disease relapse/progression occur following this line of therapy?
Types of cellular therapy data this proposal includes:	Hematopoietic Cell Transplantation (HCT)

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2. Olsson R, Remberger M, Schaffer M, Berggren DM, Svahn B-M, Mattsson J et al. Graft failure in the modern era of allogeneic hematopoietic SCT. *Bone Marrow Transplant* 2013; 48: 537–543.
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Field	Response
	<p>outcomes following CAR T cell therapy: what we know so far. Nat Rev Clin Oncol 2023; 20: 359–371. 12. Yang L, Lai X, Liu L, Shi J, Zhao Y, Yu J et al. Higher risk of platelet engraftment failure and chronic graft-versus-host disease after allogeneic haematopoietic stem cell transplantation following chimeric antigen receptor T-cell therapy compared to chemotherapy: A propensity score-matched analysis. Br J Haematol 2025; 207: 162–170. 13. Fried S, Shouval R, Walji M, Flynn JR, Yerushalmi R, Shem-Tov N et al. Allogeneic Hematopoietic Cell Transplantation after Chimeric Antigen Receptor T Cell Therapy in Large B Cell Lymphoma. Transplantation and Cellular Therapy 2023; 29: 99–107. 14. Ottaviano G, Alonso-Saladrigues A, Ortiz-Maldonado V, Galimard J-E, Farhan SY, Vuyyala S et al. “Real World” Outcome of Hematopoietic Stem Cell Transplantation after CAR19 T Cell Therapy in Children and Adults with B-ALL: A Gocart Coalition Study on Behalf of the PDWP, ALWP, and Ctiwp of the EBMT. Blood 2024; 144: 112–112.</p>
<p>CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning?</p>	<p>No, I do not have any conflicts of interest pertinent to this proposal</p>

Population characteristics of ALL and NHL patients age 0-26 that had a CAR-T infusion prior to first alloHCT

Characteristic	ALL	NHL	Total
No. of patients	753	29	782
No. of centers	118	24	127
Patient-Related Characteristics			
Age, by decades, no. (%)			
Median (range)	14 (1-26)	24 (18-26)	14 (1-26)
0-9	246 (33)	0 (0)	246 (31)
10-19	325 (43)	3 (10)	328 (42)
20-26	182 (24)	26 (90)	208 (27)
Sex, no. (%)			
Male	485 (64)	20 (69)	505 (65)
Female	268 (36)	9 (31)	277 (35)
Race, no. (%)			
White	520 (69)	18 (62)	538 (69)
Black or African American	29 (4)	4 (14)	33 (4)
Asian	36 (5)	5 (17)	41 (5)
Native Hawaiian or other Pacific Islander	4 (1)	0 (0)	4 (1)
American Indian or Alaska Native	5 (1)	0 (0)	5 (1)
More than one race	20 (3)	0 (0)	20 (3)
Not reported	139 (18)	2 (7)	141 (18)
Ethnicity, no. (%)			
Hispanic or Latino	330 (44)	8 (28)	338 (43)
Non-Hispanic or Latino	327 (43)	18 (62)	345 (44)
Non-resident of the U.S.	81 (11)	2 (7)	83 (11)
Not reported	15 (2)	1 (3)	16 (2)
Current CCN region of patient, no. (%)			
US	688 (91)	28 (97)	716 (92)
Canada	46 (6)	0 (0)	46 (6)
Europe	1 (0)	0 (0)	1 (0)
Asia	1 (0)	0 (0)	1 (0)
Australia/New Zealand	9 (1)	1 (3)	10 (1)
Mideast/Africa	4 (1)	0 (0)	4 (1)
Central/South America	4 (1)	0 (0)	4 (1)
Karnofsky score prior to HCT, no. (%)			
90-100%	587 (78)	21 (72)	608 (78)
< 90%	142 (19)	6 (21)	148 (19)
Not reported	24 (3)	2 (7)	26 (3)
ECOG prior to HCT, no. (%)			

Characteristic	ALL	NHL	Total
Asymptomatic	587 (78)	21 (72)	608 (78)
Symptomatic but completely ambulatory	133 (18)	4 (14)	137 (18)
Symptomatic, < 50% in bed during the day	7 (1)	2 (7)	9 (1)
Symptomatic, > 50% in bed, but not bedbound	1 (0)	0 (0)	1 (0)
Bedbound	1 (0)	0 (0)	1 (0)
Not reported	24 (3)	2 (7)	26 (3)
HCT-CI, no. (%)			
0	320 (42)	8 (28)	328 (42)
1	158 (21)	1 (3)	159 (20)
2	97 (13)	8 (28)	105 (13)
3	82 (11)	8 (28)	90 (12)
4	51 (7)	2 (7)	53 (7)
5+	42 (6)	2 (7)	44 (6)
Not reported	3 (0)	0 (0)	3 (0)
Disease-Related Characteristics			
ALL pre-HCT disease stage, no. (%)			
Disease is not ALL	0 (0)	29 (100)	29 (4)
CR1	136 (18)	0 (0)	136 (17)
CR2	257 (34)	0 (0)	257 (33)
CR3+	331 (44)	0 (0)	331 (42)
Advanced or active disease	29 (4)	0 (0)	29 (4)
NHL pre-HCT disease stage, no. (%)			
Disease is not NHL	753 (100)	0 (0)	753 (96)
CR1	0 (0)	6 (21)	6 (1)
CR2	0 (0)	6 (21)	6 (1)
CR3+	0 (0)	4 (14)	4 (1)
Advanced	0 (0)	13 (45)	13 (2)
Interval from diagnosis to HCT, months, median (range)	34 (1-253)	22 (6-59)	33 (1-253)
Transplant-Related Characteristics			
Conditioning regimen intensity (F2400 pre-TED data), no. (%)			
MAC	638 (85)	13 (45)	651 (83)
RIC	46 (6)	11 (38)	57 (7)
NMA	25 (3)	2 (7)	27 (3)
Not reported	44 (6)	3 (10)	47 (6)
Conditioning regimen, no. (%)			
TBI/Cy	182 (24)	2 (7)	184 (24)
TBI/Cy/Flu	65 (9)	2 (7)	67 (9)
TBI/Cy/Flu/TT	2 (0)	0 (0)	2 (0)
TBI/Cy/TT	100 (13)	0 (0)	100 (13)
TBI/Cy/VP	21 (3)	0 (0)	21 (3)

Characteristic	ALL	NHL	Total
TBI/VP	38 (5)	0 (0)	38 (5)
TBI/Mel	17 (2)	3 (10)	20 (3)
TBI/Flu	111 (15)	4 (14)	115 (15)
TBI/other(s)	16 (2)	0 (0)	16 (2)
Bu/Cy	11 (1)	0 (0)	11 (1)
Bu/Mel	7 (1)	1 (3)	8 (1)
Flu/Bu/TT	44 (6)	1 (3)	45 (6)
Flu/Bu	28 (4)	4 (14)	32 (4)
Flu/Mel/TT	55 (7)	1 (3)	56 (7)
Flu/Mel	16 (2)	5 (17)	21 (3)
Cy/Flu	3 (0)	0 (0)	3 (0)
Cy alone	1 (0)	0 (0)	1 (0)
CBV	0 (0)	1 (3)	1 (0)
BEAM	0 (0)	2 (7)	2 (0)
Mel alone	2 (0)	0 (0)	2 (0)
Mel/other(s)	12 (2)	0 (0)	12 (2)
Treosulfan	3 (0)	0 (0)	3 (0)
Other(s)	3 (0)	3 (10)	6 (1)
Not reported	16 (2)	0 (0)	16 (2)
Donor type, no. (%)			
HLA identical sibling	151 (20)	10 (34)	161 (21)
Haploidentical donor	262 (35)	10 (34)	272 (35)
Other related	17 (2)	1 (3)	18 (2)
Well-matched unrelated (8/8)	182 (24)	5 (17)	187 (24)
Partially-matched unrelated (7/8)	56 (7)	2 (7)	58 (7)
Mismatched unrelated (<= 6/8)	4 (1)	0 (0)	4 (1)
Multi-donor	1 (0)	0 (0)	1 (0)
Unrelated (matching cannot be determined)	15 (2)	1 (3)	16 (2)
Cord blood	65 (9)	0 (0)	65 (8)
Donor/recipient sex match, no. (%)			
M-M	234 (31)	11 (38)	245 (31)
M-F	120 (16)	3 (10)	123 (16)
F-M	206 (27)	9 (31)	215 (27)
F-F	117 (16)	6 (21)	123 (16)
CB - recipient M	41 (5)	0 (0)	41 (5)
CB - recipient F	25 (3)	0 (0)	25 (3)
Not reported	10 (1)	0 (0)	10 (1)
GVHD prophylaxis, no. (%)			
Ex-vivo T-cell depletion	90 (12)	0 (0)	90 (12)
CD34 selection	17 (2)	0 (0)	17 (2)

Characteristic	ALL	NHL	Total
PtCy + other(s)	221 (29)	19 (66)	240 (31)
PtCy alone	3 (0)	0 (0)	3 (0)
TAC + MMF +- other(s) (except PtCy)	62 (8)	0 (0)	62 (8)
TAC + MTX +- other(s) (except MMF, PtCy)	205 (27)	5 (17)	210 (27)
TAC + other(s) (except MMF, MTX, PtCy)	11 (1)	1 (3)	12 (2)
TAC alone	5 (1)	2 (7)	7 (1)
CSA + MMF +- other(s) (except PtCy,TAC)	47 (6)	1 (3)	48 (6)
CSA + MTX +- other(s) (except PtCy,TAC,MMF)	65 (9)	1 (3)	66 (8)
CSA alone	3 (0)	0 (0)	3 (0)
Other(s)	5 (1)	0 (0)	5 (1)
Missing	19 (3)	0 (0)	19 (2)
Donor age, by decades, no. (%)			
Median (range)	26 (0-55)	27 (14-59)	26 (0-59)
0-9	60 (8)	0 (0)	60 (8)
10-19	137 (18)	4 (14)	141 (18)
20-29	265 (35)	17 (59)	282 (36)
30-39	142 (19)	5 (17)	147 (19)
40-49	73 (10)	1 (3)	74 (9)
50-59	17 (2)	2 (7)	19 (2)
Not reported	59 (8)	0 (0)	59 (8)
Year of current transplant, no. (%)			
2016	6 (1)	0 (0)	6 (1)
2017	13 (2)	0 (0)	13 (2)
2018	31 (4)	0 (0)	31 (4)
2019	89 (12)	3 (10)	92 (12)
2020	90 (12)	5 (17)	95 (12)
2021	105 (14)	3 (10)	108 (14)
2022	133 (18)	4 (14)	137 (18)
2023	136 (18)	9 (31)	145 (19)
2024	131 (17)	5 (17)	136 (17)
2025	19 (3)	0 (0)	19 (2)
CAR-T Related Characteristics			
Time from first CAR-T to subsequent alloHCT, months, median (range)	6 (1-64)	9 (2-22)	6 (1-64)
Product, no. (%)			
Kymriah	586 (78)	4 (14)	590 (75)
Yescarta	0 (0)	19 (66)	19 (2)
Tecartus	23 (3)	0 (0)	23 (3)
Breyanzi	0 (0)	1 (3)	1 (0)
Other	144 (19)	5 (17)	149 (19)
Commercial vs. noncommercial CAR-T product, no. (%)			

Characteristic	ALL	NHL	Total
Commercial	609 (81)	24 (83)	633 (81)
Noncommercial	144 (19)	5 (17)	149 (19)
Is the recipient participating in a cellular therapy clinical trial?, no. (%)			
No	605 (80)	24 (83)	629 (80)
Yes	148 (20)	5 (17)	153 (20)
2-year product embargo, no. (%)			
No	745 (99)	28 (97)	773 (99)
Yes	8 (1)	1 (3)	9 (1)
Follow-up of survivors, median (range), months	25 (3-100)	24 (4-60)	25 (3-100)

Field	Response
Proposal Number	2509-120-HURWITZ
Proposal Title	Machine Learning Predictive Modeling of Autologous Mobilization Success and Transplant Outcomes
Key Words	Autologous HCT; Stem cell mobilization; Donor; Recipient Outcomes
Principal Investigator #1: - First and last name, degree(s)	Stephanie N. Hurwitz, MD, PhD
Principal Investigator #1: - Email address	sthurw@iu.edu
Principal Investigator #1: - Institution name	Indiana University Indianapolis
Principal Investigator #1: - Academic rank	Assistant Professor
Junior investigator status (defined as 3-5 years from fellowship)	Yes
Do you identify as an underrepresented/minority?	No
Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.	Not applicable
Do any of the PI(s) within this proposal have a CIBMTR WC study in manuscript preparation >6 months?	No
PROPOSED WORKING COMMITTEE:	Donor and Recipient Health Services
Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.	No
RESEARCH QUESTION:	Among patients undergoing autologous HCT, can machine learning approaches be used to model and accurately predict (A) donor mobilization success and (B) post-transplantation engraftment, progression-free survival, and overall survival?
RESEARCH HYPOTHESIS:	Through the collection and analysis of demographic and laboratory data from healthy allogeneic donors, we have recently developed a deep learning-based predictive model for mobilization failure, offering opportunities for cost- and resource-saving early interventions. We hypothesize that a similar approach could be used to develop a data-driven model for optimizing mobilization strategies and timing for autologous patients, a population at much greater risk for cell collection failure. We further hypothesize that routine clinical and laboratory variables may be used to predict post-transplant outcomes in autologous patients, and that model explanations will identify reproducible risk factors to guide clinical decision making.

Field	Response
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	Primary Aim: Develop machine learning models (including deep neural networks) to evaluate patient baseline, post-mobilization, and post-transplantation variables to predict individual A) probability of mobilization success and B) post-transplant engraftment outcomes, progression-free survival, and overall survival. Secondary Aims: 1) Evaluate the performance of predictive models by various metrics including area under the curve, receiver operating characteristic (AUC-ROC), accuracy, sensitivity, and specificity. 2) Use model explainability techniques to systematically evaluate and rank model features, identifying the patient factors that are critical for accurate prediction of mobilization success and post-transplant outcomes.

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

Hematopoietic stem and progenitor cell (HSPC) transplantation remains a powerful curative therapy for a variety of hematologic malignancies and inherited blood disorders. However, despite decades of clinical use, patient outcomes vary widely. Among autologous transplant patients, recent 3-year probabilities of overall survival are approximately 80%; mortality rates are significantly lower in allogeneic transplant patient populations[1]. In part, therapeutic success may be limited by poor or suboptimal mobilization, defined by requirement of more than 1 consecutive apheresis collection day or failure to meet the total CD34+ cell/kg goal. Consequences of suboptimal cell collection include delayed transplantation, risk of disease progression, multiple apheresis sessions that add patient discomfort and healthcare cost, and poorer transplant outcomes. Poor mobilization may also limit patient access to emerging gene therapy treatments that are coupled with autologous transplantation[2, 3]. Up to 40% of autologous donors may experience suboptimal mobilization, and although baseline risk factors are recognized[4, 5], they are inconsistently applied prior to apheresis and lack predictive precision. While poor mobilization outcomes may both confer and predict worse post-transplant outcomes, additional patient-specific variables also significantly impact engraftment kinetics, graft durability, and relapse risk. However, interactions of these variables are not well modeled. In the studies outlined in this proposal, we will build upon our prior work to refine two complementary strategies to advance patient outcome modeling in autologous HCT: (1) Develop a pre-emptive mobilization risk assessment that identifies poor mobilizers before apheresis; and (2) Establish a data-driven model to predict and explain post-transplant outcomes. These aims will have several scientific and clinical impacts. Early identification of poor mobilizers will facilitate preemptive changes to drug regimens, including GCSF dose intensification, preemptive addition of the CXCR4 inhibitor plerixafor, or incorporation of novel short-acting agents[6, 7] to reduce failed collections, shorten mobilization courses, and curb unnecessary apheresis sessions. Furthermore, large data-driven approaches to model and predict transplant outcomes in autologous donors will contribute to clinical decision making of transplant timing, hospitalization course, surveillance, risk counseling, and supportive-care planning. Finally, explainable deep learning (e.g.,

Field	Response
	feature attributions) will identify generalizable, biologically plausible risk factors of patients that may guide the development of simpler prognostic algorithms, future therapeutics, and clinical trial management.

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

Early identification of donors who face challenges with mobilization offers opportunities to intervene, and will likely lead to better overall transplantation outcomes and reduced healthcare costs. However, identifying poor mobilizers in advance remains challenging, with a recent scoping review concluding that there is “poor consensus” on the best predictors of CD34 yield, reflecting the fact that most clinical studies report small or contradictory effects of individual covariates[8]. Despite attempts to standardize what “poor mobilizer” means, endpoints and cut-offs still vary across centers, and criteria haven’t seen broad prospective validation[9, 10]. In addition, the most reliable single signal, pre-apheresis peripheral blood CD34 count, is measured after G-CSF administration, and is therefore inherently reactive. The resulting gap is clear: the field lacks a robust biomarker or model that can identify poor mobilizers before mobilization regimens are chosen and administered. In addition, outcomes after autologous HCT vary, with overall recent 100-day mortality rates of 1.5-2% and 3-year mortality rates of 17% across adult and pediatric populations[1]. However, these rates vary significantly across disease types; for example, pediatric patients receiving autologous HCT for the treatment of Wilms’ tumor have 5-year overall survival estimates of 45%. Across all patients, early mortality is driven by organ failure, infections, and primary disease, while late mortality is dominated by relapse. In a cohort of myeloma patients, only 50% achieved a 5-year progression-free survival[11]. Despite improving outcomes over the past decades, standard prognostic tools and risk indices are limited in their capture of complex, interacting variables in patients that drive variable outcomes and facilitate tailored clinical decision making. Through its large, diverse, multi-center registry composed of standardized patient data, the CIBMTR offers a unique resource to support the development and validation of data-driven models, with overall goals of addressing large-scale, current gaps in clinical predictions of patient outcomes. We recently collaborated with the DiPersio and Sica groups to evaluate the performance of transformer-based and attention-aware deep learning models for HSPC mobilization outcomes in allogeneic healthy donors[12]. Leveraging demographic data and complete blood counts (CBCs), we developed a model that accepts donor data either before or after G-CSF mobilization, offering the dual advantage of early prediction and refined risk

assessment once G-CSF exposure has begun (Fig. 1A). This model was validated on a cohort of multi-institutional donor data (n=21,956) compiled by the CIBMTR[13]. We achieved a receiver operating characteristic (ROC) of the area under the curve (AUC) of 0.87 with an overall predictive accuracy of nearly 80% and a specificity of 92% (Fig. 1B-C). Applying TabPFN, a novel supervised tabular learning method to separated pre- and post- mobilization data further improved accuracies to 89% and 95%, respectively (Fig. 1D)[14]. Furthermore, we demonstrated that key patient variables explaining mobilization success vary before and after G-CSF exposure (Fig. 1E-F). Here we aim to fill a key gap in our understanding of autologous donor mobilization variability. We hypothesize that a similar approach could be used to develop data-driven predictive models for autologous donors, a population at much greater risk for cell collection failure, with application toward guiding transplantation-related clinical decision making in these patients. Our approach aligns with prior CIBMTR committee work that applies machine learning to routine registry data to build clinical decision-support (GV20-01), but addresses distinct gaps in prospective identification of high-risk autologous transplant patients.

Aim 1. Predict pre-apheresis mobilization success in autologous transplant patients using advanced deep learning. In collaboration with the CIBMTR Donor and Recipient Health Services working committee, we will collect demographic and clinical data captured on CIBMTR's Transplant Essential Data (TED), forms, as well as baseline (pre-mobilization) and post-mobilization complete blood counts (CBCs). Product analysis data, including total mononuclear cells and total CD34+ cells collected prior to thawing (Form 2006R6) will serve as mobilization outcome metrics. Data will be collected from patients who underwent transplantation between 2018-2020. Based on our prior analyses, we will collect data from a minimum of 20,000 patients to achieve acceptable analytical power. We will utilize both the high-performing TabPFN model and our more complex attention-aware neural network (Fig. 1A). In both, we will maintain an 80:20 train:test split of autologous donor data. Given the lack of consensus of optimal CD34+ cell dose across variable patient populations, we will use several cutoffs to define good versus poor mobilizers ($2, 2.5, 4, 5, 6 \times 10^6$ CD34+ cells/kg collected on apheresis day 1) to test whether model accuracy is maintained across arbitrary clinical cutoffs.

This will allow for flexibility in the future, as growing knowledge in the field shapes updated disease-type or patient-specific clinical guidelines for optimal cell dose. We will also test a non-binary outcome prediction of day 1 apheresis collection (poor vs suboptimal vs good), as well as prediction of donors who will require >1 day of apheresis collection. In our prior studies examining healthy allogeneic donors, frequencies of good mobilizers were much higher than poor mobilizers. To account for this class imbalance, we applied the Synthetic Minority Oversampling Technique (SMOTE) training data to balance class frequencies[15]. By achieving an approximately 1:1 class ratio in the training set, we aimed to prevent biased model learning and improve generalization to both mobilization outcomes. In the current proposed study, autologous donor mobilization success is more evenly distributed (our internal data suggests only 55% of our patients achieve adequate collections on day 1 of apheresis). However, as we test variable cutoffs and non-binary predictors, class balances may shift; in these cases, we will similarly apply SMOTE to the training dataset. Performance metrics of test set predictions will be evaluated, including AUC-ROC, overall accuracy, precision, recall, and F1-score. A key barrier to the clinical adoption of machine learning models is their "black box" nature. To interpret how model predictions were made, we will employ a SHapley Additive Explanations (SHAP) analysis[16]. SHAP assigns each feature an importance value for individual predictions, enabling a game-theoretic understanding of the contribution of each predictor to the model's output. These data will allow us to identify which donor features most strongly influenced the mobilization outcome predictions, shedding light on possible single or few variable metrics that may be used empirically to guide clinical decision making, including choice of mobilization regimen.

Aim 2. Utilize machine learning to predict and explain post-transplant outcomes across diverse patient populations. As mentioned, there are contradictory reports on the impact of CD34+ cell dose in autologous patient survival; controversy is in part reflective of the fact that many clinical studies report relatively small populations, and are limited to specific disease types, single institutions, and univariate or limited variable analyses. It is likely that CD34+ dose serves as an interacting variable with other complex patient factors, including age, disease type, socioeconomic factors, co-morbidities, and conditioning strategies to

Field	Response
	<p>impact transplant outcomes. In this aim, with the support of the working committee, we will assemble baseline, infusion-related, and post-transplant follow-up patient data from the same population identified in Aim 1. Using this dataset, we will establish binary metrics of transplantation outcome, including 100-day survival, 3- and 5-year overall survival (OS), delayed neutrophil engraftment (> 20 days to neutrophil recovery), delayed platelet recovery (> 60 days until platelet count >20,000/μL), and progression-free survival (PFS). TabPFN models will be trained with CIBMTR patient data (Fig. 1G), and model performance will be evaluated as described in Aim 1. Initial (static) models will use pre-transplant data (demographic information, disease, organ function, functional status, baseline laboratory values, total CD34+ collected) and transplant parameters (CD34+/kg dose, conditioning strategy) to predict engraftment and survival outcomes. Subsequent (dynamic) models will take into account early post-transplant laboratory values, including CBC and engraftment metrics, to update risk stratification of PFS and 3- and 5-year OS. Finally, to identify key donor features influencing the predictions of transplant outcomes, we will perform SHAP analysis on each model. If disease type is a major influencer, we will train and test an attention-aware model (as in Fig. 1A) with a disease type flag to uncover additional variables driving outcomes both dependent on and independent of primary disease. These findings will offer a relatively unbiased, large-scale picture of which donor features strongly influence the prediction of autologous transplant outcomes across a broad spectrum of patients.</p>
<p>SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF) - Id</p>	<p>F_ueMkybSbgGemUIH</p>
<p>SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF) - Name</p>	<p>figure_1_proposal_submitted.png</p>
<p>SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF) - Size</p>	<p>727265</p>
<p>SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF) - Type</p>	<p>image/png</p>

Field	Response
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	Inclusion: All patients who underwent first autologous HCT mobilization and PBSC transplantation between 2018-2020. Exclusion: Allogeneic donors Subsequent (other than first time) autologous mobilization/HCT Autologous patients missing key demographic, laboratory, or primary outcome data
Does this study include pediatric patients?	Yes
DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Outline any supplementary data required.	Data will be obtained from existing CIBMTR collection forms: Recipient Baseline Data (2000R6), Pre Transplant Essential Data (TED) (2400), Hematopoietic Cellular Transplant Infusion (2006R6), Laboratory Studies (3502), and contextual outcomes from Post TED (2450), Recipient Death (2900R5) and Infusion Follow Up (2100). If pre-mobilization data is not available for autologous patients in the registry, we request to collaborate with the working committee to obtain a cohort of patients with these data for Aim 1. Variables needed: The study will gather variables from multiple collection forms. The major variables include: patient demographics (e.g. age, sex, race, BMI, weight, height), clinical status (Karnofsky score, Lansky score), socioeconomic factors (work status, education, annual income), comorbid conditions (e.g. prior malignancy, co-existing disease, tobacco use, CMV status), organ function prior to the preparative regimen (AST, ALT, DLCO, LDH, serum creatinine), baseline laboratory data (pre-mobilization CBC, post-mobilization CBC, pre-preparative regimen CBC), mobilization agents used, preparative regimen, and additional drugs given in the peri-transplantation period. Outcome data will include mobilized product analyses (TNC, TMC, total CD34+ cells), initial ANC and platelet recovery, and recipient vital status (patient survival status, progression-free survival, date of death, primary cause of death).
Types of cellular therapy data this proposal includes:	Hematopoietic Cell Transplantation (HCT)
PATIENT REPORTED OUTCOME (PRO) REQUIREMENTS: If the study requires PRO data collected by CIBMTR, the proposal should include: 1) A detailed description of the PRO domains, timepoints, and proposed analysis of PROs; 2) A description of the hypothesis speci	Not applicable.
MACHINE LEARNING: Please indicate if the study requires methodology related to machine-learning and clinical predictions.	The proposal will develop and utilize multiple machine learning algorithms.

Field	Response
SAMPLE REQUIREMENTS: If the study requires biologic samples from the CIBMTR Repository, the proposal should also include: 1) A detailed description of the proposed testing methodology and sample requirements; 2) A summary of the investigator's previous e	No biologic specimens are requested.
NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required.	Not applicable.

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Field	Response
	<p>“Poor mobilizer: A retrospective study on proven and predicted incidence according to GITMO criteria,” <i>Transfus. Apher. Sci.</i>, vol. 47, no. 2, pp. 217–221, Oct. 2012, doi: 10.1016/j.transci.2012.06.008. [11] O. Pasvolsky et al., “Trends in Outcomes After Upfront Autologous Transplant for Multiple Myeloma Over Three Decades,” <i>Transplant. Cell. Ther.</i>, vol. 30, no. 8, p. 772.e1-772.e11, Aug. 2024, doi: 10.1016/j.jtct.2024.06.001. [12] A. Adil et al., “Advanced Deep Learning Enables Prediction of Allogeneic Stem Cell Mobilization Success,” Sep. 20, 2025, bioRxiv. doi: 10.1101/2025.09.17.676674. [13] J. W. Hsu et al., “Collection of Peripheral Blood Progenitor Cells in 1 Day Is Associated with Decreased Donor Toxicity Compared to 2 Days in Unrelated Donors,” <i>Biol. Blood Marrow Transplant.</i>, vol. 26, no. 6, pp. 1210–1217, Jun. 2020, doi: 10.1016/j.bbmt.2020.02.011. [14] N. Hollmann et al., “Accurate predictions on small data with a tabular foundation model,” <i>Nature</i>, vol. 637, no. 8045, pp. 319–326, Jan. 2025, doi: 10.1038/s41586-024-08328-6. [15] N. V. Chawla, K. W. Bowyer, L. O. Hall, and W. P. Kegelmeyer, “SMOTE: Synthetic Minority Over-sampling Technique,” <i>J. Artif. Intell. Res.</i>, vol. 16, pp. 321–357, Jun. 2002, doi: 10.1613/jair.953. [16] S. M. Lundberg and S.-I. Lee, “A Unified Approach to Interpreting Model Predictions,” in <i>Advances in Neural Information Processing Systems</i>, Curran Associates, Inc., 2017. Accessed: May 21, 2025. [Online]. Available: https://papers.nips.cc/paper_files/paper/2017/hash/8a20a8621978632d76c43dfd28b67767-Abstract.html</p>
<p>CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning?</p>	<p>No, I do not have any conflicts of interest pertinent to this proposal</p>

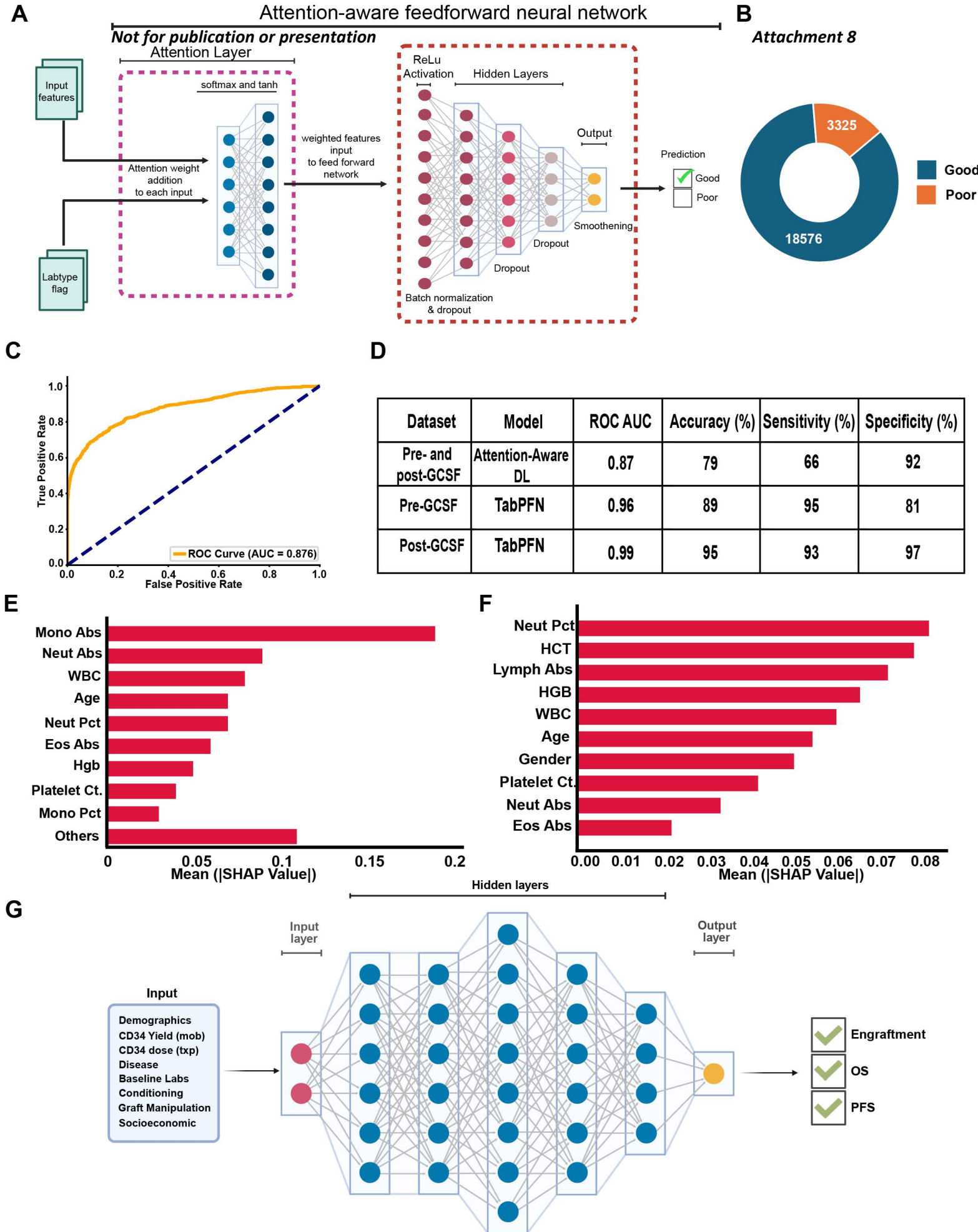


Figure 1. Advanced deep learning enables prediction of healthy donor mobilization success. A) Attention-aware feed forward neural network for donor mobilization prediction. B) Frequency of good and poor mobilizers in CIBMTR dataset (poor=CD34/uL <40 on day of collection). C) ROC curve showing accuracy of CIBMTR donor prediction. D) Metrics across optimized models. SHAP summary plots depicting the contribution of each input variable to models output, for E) pre-GCSF and F) post-GCSF. G) Deep learning model to predict CIBMTR patient transplant outcomes.

Population characteristics of first autoHCT patients, 2018-2024

Characteristic	TED	CRF (RES)	Total
No. of patients	81052	5473	86525
No. of centers	338	209	338
Patient-Related Characteristics			
Age, by decades, no. (%)			
Median (range)	60 (<1-86)	59 (<1-83)	60 (<1-86)
0-9	2853 (4)	186 (3)	3039 (4)
10-19	1177 (1)	134 (2)	1311 (2)
20-29	3427 (4)	307 (6)	3734 (4)
30-39	4481 (6)	319 (6)	4800 (6)
40-49	8327 (10)	619 (11)	8946 (10)
50-59	19577 (24)	1302 (24)	20879 (24)
60-69	29978 (37)	1994 (36)	31972 (37)
70+	11232 (14)	612 (11)	11844 (14)
Sex, no. (%)			
Male	47778 (59)	3197 (58)	50975 (59)
Female	33274 (41)	2276 (42)	35550 (41)
Race, no. (%)			
White	54239 (67)	3315 (61)	57554 (67)
Black or African American	9869 (12)	1367 (25)	11236 (13)
Asian	3478 (4)	310 (6)	3788 (4)
Native Hawaiian or other Pacific Islander	153 (0)	17 (0)	170 (0)
American Indian or Alaska Native	418 (1)	54 (1)	472 (1)
More than one race	927 (1)	100 (2)	1027 (1)
Not reported	11968 (15)	310 (6)	12278 (14)
Ethnicity, no. (%)			

Characteristic	TED	CRF (RES)	Total
Hispanic or Latino	9133 (11)	595 (11)	9728 (11)
Non-Hispanic or Latino	55160 (68)	4324 (79)	59484 (69)
Non-resident of the U.S.	14445 (18)	419 (8)	14864 (17)
Not reported	2314 (3)	135 (2)	2449 (3)
CCN region at transplant, no. (%)			
U.S	64552 (80)	4937 (90)	69489 (80)
Non U.S	16500 (20)	536 (10)	17036 (20)
Karnofsky score prior to HCT, no. (%)			
90-100%	45900 (57)	2840 (52)	48740 (56)
< 90%	33473 (41)	2473 (45)	35946 (42)
Not reported	1679 (2)	160 (3)	1839 (2)
ECOG prior to HCT, no. (%)			
Asymptomatic	45900 (57)	2840 (52)	48740 (56)
Symptomatic but completely ambulatory	31530 (39)	2364 (43)	33894 (39)
Symptomatic, < 50% in bed during the day	1852 (2)	108 (2)	1960 (2)
Symptomatic, > 50% in bed, but not bedbound	85 (0)	1 (0)	86 (0)
Bedbound	6 (0)	0 (0)	6 (0)
Not reported	1679 (2)	160 (3)	1839 (2)
HCT-Cl, no. (%)			
0	25051 (31)	1488 (27)	26539 (31)
1	12350 (15)	771 (14)	13121 (15)
2	12561 (15)	919 (17)	13480 (16)
3	13106 (16)	936 (17)	14042 (16)
4	7946 (10)	617 (11)	8563 (10)
5+	9782 (12)	716 (13)	10498 (12)
Not reported	256 (0)	26 (0)	282 (0)

Characteristic	TED	CRF (RES)	Total
Disease-Related Characteristics			
Primary disease, no. (%)			
AML	207 (0)	8 (0)	215 (0)
ALL	59 (0)	2 (0)	61 (0)
Other leukemia	28 (0)	4 (0)	32 (0)
CLL	8 (0)	0 (0)	8 (0)
CML	1 (0)	0 (0)	1 (0)
MDS	2 (0)	0 (0)	2 (0)
Other acute leukemia	12 (0)	0 (0)	12 (0)
NHL	16752 (21)	1024 (19)	17776 (21)
HD	6438 (8)	532 (10)	6970 (8)
MM	48431 (60)	3031 (55)	51462 (59)
Other PCD	2896 (4)	456 (8)	3352 (4)
Solid tumor	4729 (6)	214 (4)	4943 (6)
Inherited bone marrow failure syndromes	5 (0)	1 (0)	6 (0)
Hemoglobinopathies	33 (0)	120 (2)	153 (0)
Disorders of the immune system	11 (0)	22 (0)	33 (0)
Inherited disorders of metabolism	29 (0)	22 (0)	51 (0)
Histiocytic disorders	4 (0)	1 (0)	5 (0)
Autoimmune diseases	1394 (2)	35 (1)	1429 (2)
Other disease	11 (0)	1 (0)	12 (0)
Tolerance induction associated with solid organ transplant	1 (0)	0 (0)	1 (0)
MPN	1 (0)	0 (0)	1 (0)
Interval from diagnosis to HCT, months, median (range)	8.26 (<1-657)	8.03 (<1-504)	8.22 (<1-657)
Transplant-Related Characteristics			
Year of current transplant, no. (%)			

Characteristic	TED	CRF (RES)	Total
2018	9708 (12)	1922 (35)	11630 (13)
2019	11056 (14)	1188 (22)	12244 (14)
2020	11170 (14)	311 (6)	11481 (13)
2021	12002 (15)	254 (5)	12256 (14)
2022	12386 (15)	579 (11)	12965 (15)
2023	12690 (16)	573 (10)	13263 (15)
2024	12040 (15)	646 (12)	12686 (15)
Follow-up of survivors, median (range), months	33.4 (<1-91)	57.6 (<1-89)	34.8 (<1-91)

Field	Response
Proposal Number	2509-153-RAMAN
Proposal Title	Developing a Novel Composite Mortality Prediction Score Incorporating Hemoglobinopathy Specific Clinical Biomarkers with the HCT-CI in Allogeneic Transplant Recipients with Sickle Cell Disease
Key Words	Hematopoietic Cell Transplantation Comorbidity Index; Sickle Cell Disease; Allogeneic HCT; Mortality Prediction; Composite Risk Score; Biomarkers; Risk Stratification
Principal Investigator #1: - First and last name, degree(s)	Ganesh Raman, MD
Principal Investigator #1: - Email address	graman@fredhutch.org
Principal Investigator #1: - Institution name	Fred Hutchinson Cancer Center
Principal Investigator #1: - Academic rank	Fellow Physician
Junior investigator status (defined as 5 years from fellowship)	Yes
Do you identify as an underrepresented/minority?	No
Principal Investigator #2 (If applicable): - First and last name, degree(s):	Monica Thakar, MD
Principal Investigator #2 (If applicable): - Email address:)	msthakar@fredhutch.org
Principal Investigator #2 (If applicable): - Institution name:	Fred Hutchinson Cancer Center
Principal Investigator #2 (If applicable): - Academic rank:	Professor
Junior investigator status (defined as 5 years from fellowship)	No
Do you identify as an underrepresented/minority?	No
We encourage a maximum of two Principal Investigators per study. If more than one author is listed, please indicate who will be identified as the corresponding PI below:	Ganesh Raman
Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.	None
Do any of the PI(s) within this proposal have a CIBMTR WC study in manuscript preparation >6 months?	No
PROPOSED WORKING COMMITTEE:	Non-Malignant Diseases
Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.	Yes

Field	Response
If you have already spoken with a scientific director or working committee chair regarding this study, then please specify who:	Larisa Broglie
RESEARCH QUESTION:	Can a novel, disease-specific risk score, combining the Hematopoietic Cell Transplantation Comorbidity Index (HCT-CI) and/or youth non-malignant (ynm) HCT-CI with hemoglobinopathy-relevant variables, improve prediction of overall survival (OS) and non-relapse mortality (NRM) in patients with sickle cell disease (SCD) undergoing allogeneic hematopoietic cell transplantation?
RESEARCH HYPOTHESIS:	Addition of SCD specific markers, into an augmented HCT-CI can significantly improve prediction of post-transplant mortality (both OS and NRM) in patients with SCD undergoing allogeneic hematopoietic cell transplantation, compared to standard HCT-CI +/- ynmHCT-CI alone.
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	<p>a. Primary Objective: i. Identify which SCD specific variables correlate most strongly with prediction of OS and NRM</p> <p>b. Secondary Objectives: i. Generate and validate novel HCT-CI score for the prediction of 1-year and 2-year OS and NRM in patients with SCD</p> <p>ii. Re-test/validate original HCT-CI in a larger group of patients with SCD</p>

Field	Response
<p>SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.</p>	<p>While the HCT-CI is a validated tool for predicting OS and NRM in patients of all ages undergoing allogeneic and autologous transplants for all malignant and nearly all non-malignant indications, wherein a score of 3 portends worse OS and NRM, it has not been shown to do so for patients with hemoglobinopathies. In 20 years of using HCT-CI for the assessment of comorbidities in transplant candidates, hemoglobinopathies remain the only indication where the score has not been predictive, though this has only been assessed in two studies [1, 2]. This raises the question of which variables of prognostic value specific to SCD the HCT-CI does not capture. Re-validating the original HCT-CI in a larger cohort of SCD patients and potentially developing a novel, augmented, disease-specific HCT-CI could transform pre-transplant counseling and management by allowing for better risk stratification tailored to SCD patients. This could further inform shared decision-making, particularly when balancing risks of NRM against potential curative benefit, guiding pre-transplant optimization strategies based on individualized clinical or biomarker-based risk profiles.</p>

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

Hemoglobinopathies are a heterogenous group of disorders characterized by mutations in genes encoding alpha and beta globin chains. Excluding rare unstable hemoglobin disorders, these conditions can broadly be categorized into sickle cell disease (SCD) and thalassemia, both representing chronic hematologic conditions associated with significant morbidity and mortality. It is estimated that over 100,000 individuals in the United States live with SCD [3]. Hematopoietic cell transplantation (HCT) has the potential to cure patients with hemoglobinopathies but has significant risks associated with conditioning regimen related toxicity, peri-engraftment infectious complications, as well as acute and chronic graft versus host disease (GVHD). The Hematopoietic Cell Transplantation Comorbidity Index (HCT-CI), transformed comorbidity-based risk assessment for patients undergoing HCT. It provided an accurate predictive model for estimation of non-relapse mortality (NRM) and overall survival (OS), thereby enhancing data-driven counseling and shared decision making in the pre-transplant period [4]. Subsequent studies have validated the HCT-CI's superior predictive value compared to general indices like the Charlson Comorbidity Index (CCI) and ACE 27 [5]. By incorporating laboratory data, the HCT CI improved detection of key organ specific comorbidities [5, 6]. The score was further validated in pediatric cohorts [7]. Moreover, pre-transplant comorbidity burden, as captured by HCT CI, was demonstrated to predict severity of acute GVHD (aGVHD) and GVHD associated mortality; patients with higher HCT CI scores faced significantly higher risks of severe aGVHD and poorer survival [8]. In 2019, a large CIBMTR-based study found that higher HCT-CI scores predicted decreased post-transplant survival in a wide variety of non-malignant conditions [1]. However, the HCT-CI failed to discriminate outcomes in patients with hemoglobinopathies; survival rates were similar regardless of HCT-CI score [1]. This finding was replicated in an ad hoc analysis of a cohort of pediatric patients with hemoglobinopathies who underwent allogeneic transplant [2]. It is theorized that this discrepancy is a result of unique disease-specific comorbidities or improvement in disease related organ dysfunction due to transplant that the HCT-CI does not capture as well [2]. Few studies have looked at identifying variables of prognostic value in SCD patients undergoing HCT. In one study four independent predictors of all-cause mortality were

identified including BUN, LDH, RDW, and absolute reticulocyte count [9]. Additionally, an abstract published in 2025 showed that pre-transplant liver fibrosis is an independent predictor of poorer OS in these patients [10]. Another study found that SCD patients who suffered their first disease-related chronic condition before age 30 developed multiple chronic conditions at a rate 19 times faster than those at a later age [11]. Therefore, age may also be an SCD specific prognostic variable. This is noteworthy, as age has not been included in widely implemented comorbidity indices including HCT-CI and CHARM [4,12]. Late effects investigations looking at causes of post-HCT morbidity and mortality in SCD patients are scarce. In one cohort, the most common causes of mortality two or more years out from transplant included cGVHD and graft failure, accounting for 45% and 22% of deaths respectively [13]. It is however unknown if the cGVHD identified in these patients was specific to organs that had pre-existing dysfunction prior to transplant. It is possible that factors like chronic liver disease secondary to transfusion related iron overload, or chronic lung disease prior to transplant increase the risk of cGVHD developing in these vital organs, which ultimately tend to have poorer prognosis [14]. Recognizing the overall need for more tailored, age, and disease-specific comorbidity indices, researchers developed an expanded HCT CI (ynmHCT-CI) for pediatric and young adult patients with non-malignant indications for transplant. This score included broadened definitions, such as using percentiles to evaluate weight, incorporating underweight status, mechanical ventilation history instead of PFT abnormalities alone, and eGFR based characterization of renal disease, leading to improved capture of comorbidities [15,16]. In a cohort with non-malignant diseases (including hemoglobinopathies), the expanded score re-classified 39% of patients with higher scores and modestly improved performance of the scoring tool [15,16]. Further, a 2025 pediatric study from the Netherlands confirmed the ynmHCT-CI as the most reliable predictor of long-term survival and GVHD free outcomes in non-malignant pediatric transplant recipients [17]. Traditionally, the lack of matched unrelated donors, as well as disease specific organ toxicities, meant the majority of patients with SCD, were not transplant candidates. However, with recent promising outcomes seen with haploidentical transplantation using reduced intensity conditioning

Field	Response
	<p>and post-transplant cyclophosphamide, HCT appears to be an increasingly safe, accessible, and potential curative approach for SCD patients [18]. Therefore, the development of a novel, expanded HCT-CI score validated for SCD is of urgency and would not only enable more accurate data driven peri-transplant risk stratification in these patients, but also help with shared decision-making regarding proceeding with this potentially curative therapy versus continued conservative disease management.</p>
<p>PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.</p>	<p>a. Inclusion Criteria i. Patients of all ages who received allo-HCT for SCD between January 1st, 2008-December 31st, 2023 b. Exclusion Criteria i. Patients with less than 2 years of follow-up data ii. Patients with incomplete data (defined as missing >20% of variables desired below).</p>
<p>Does this study include pediatric patients?</p>	<p>Yes</p>

DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Outline any supplementary data required.

Due to revisions of CRF and TED forms, we understand that some variables may only be available for a given number of years depending on the form that was in use at the time. We have attempted to label variables that are affected by this below, to be as specific as possible. If a variable is unlabeled, based on our review of the documents, it is available for the entire enrollment period defined as January 1st 2008-December 31st 2023.

a. Patient Specific Variables-

i. Original HCT-CI variables [19], collected as per TED forms

ii. Additional variables in expanded ynmHCT-CI:

1. Pulmonary:

a. History of mechanical ventilation

2. GI/Nutrition:

a. BMI

i. Will be used to calculate weight percentiles for obesity determination for patients ≤ 18 years old.

ii. Used to define underweight category as ≤ 5 th percentile BMI in children ≤ 18 years or $\leq 18 \text{ kg/m}^2$ in patients 18 or older.

3. Renal/GU:

a. Serum Creatinine

i. Creatinine will be used to calculate eGFR using:

1. Bedside Schwartz Equation for patients age ≤ 18 years old

2. CKD-EPI equation for patients greater than or equal to 18 years old

ii. Use eGFR to define renal function:

1. normal ($\text{eGFR} \geq 90 \text{ ml/min/1.73m}^2$), mild CKD ($\text{eGFR} 60\text{-}89 \text{ ml/min/1.73m}^2$), or moderate/severe CKD ($\text{eGFR} \leq 60 \text{ ml/min/1.73m}^2$)

iii. Additional SCD specific variables:

a. Age

i. Age at time of HCT

b. Neuro:

i. History of stroke (Yes/No/Unknown), (2008-2020)

1. From 2020 onwards, the following will be collected including history of overt stroke, ischemic stroke, hemorrhagic stroke, CVT, Moya Moya, Silent Stroke, and TIA

ii. Was brain MRI/MRA performed prior to preparative regimen (Yes/No/Unknown)

1. Normal, (2008-2020)

2. Abnormal, (2008-2020)

3. Unknown, (2008-2020)

a. From 2020 onwards, Yes answers will be counted as "Abnormal" given the scan was by definition diagnostic the way the question is worded in the form

iii. History of seizures (Yes/No/Unknown)

c. Ophtho:

i. History of Retinopathy, (2020-2023)

d. Cardiovascular:

i. Was ECHO performed prior to preparative regimen (Yes/No/Unknown)

1. Normal (2008-2020)

a.

	<p>From 2020 onwards, manually define normal as EF>50% or LV Shortening Fraction greater than or equal to 28% and TRJV <2.5m/sec 2. Abnormal (2008-2020) a. From 2020 onwards manually define abnormal as EF less than or equal to 50% or LV Shortening Fraction less than 28% and/or TRJV greater than or equal to 2.5m/sec 3. Unknown e. Pulmonary: i. Acute Chest Syndrome: 1. History of acute chest syndrome (Yes/No/Unknown), (2008-2020) 2. Has acute chest syndrome occurred in the last two years (Yes/No/Unknown), (2020-2023) 3. Total number of episodes within 2 years prior to HCT (Known/Unknown & Number if known) 4. Total number of episodes within recipient’s lifetime, (2008-2020) 5. Did recipient require exchange transfusion (Yes/No/Unknown) ii. Were Pulmonary Function Tests Performed (Yes/No/Unknown) 1. Results: Normal, Stage I, Stage 2, Stage 3, Stage 4, unknown a. Data from 2020 onwards due to revision of form 2030, will have to be manually classified based on attached PFT reports iii. History of asthma or reactive airway disease (Yes/No/Unknown), (2020-2023) f. Hepatic: i. Was a liver biopsy performed at any time prior to the preparative regimen (Yes/No/Unknown) 1. Hepatitis (Yes/No/Unknown), (2008-2020) a. Mild, moderate, severe, unknown, (2008-2020) 2. Fibrosis (Yes/No/Unknown) a. Mild, moderate, severe, unknown, (2008-2020) 3. Hepatic Iron Concentration (Known/Unknown), (2008-2020) a. Specify HIC in mg/g, (2008-2020) 4. Evidence of Cirrhosis (Yes/No), (2020-2023) ii. Liver MRI (Yes/No/Unknown), (2020-2023) 1. What was LIC (Known/Unknown), (2020-2023) a. LIC in mg Fe/g, g Fe/kg, or umol Fe/g, (2020-2023) iii. Was iron chelation therapy performed at any time prior to the preparative regimen (Yes/No) g. Renal/GU: i. Sickle cell nephropathy (Yes/No/Unknown) (2008-2020) 1. From 2020-2023, due to revision of Form 2030, we will collect the urine albumin level. “Yes” may be defined as urine albumin greater than or equal to 30mg/g, 30,000 µg/mL, 30,000 mg/L, or 3,000 mg/mmol ii. History of Priapism (Yes/No/Unknown) 1. Number of episodes experienced in the 2 years prior to HCT,</p>
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	<p>(2008-2020) h. Hem/Onc: i. Recipient’s SCD Genotype (HbSS, HbSC, HbS Beta 0 thalassemia, HbS B+ Thalassemia, etc.) ii. Number of pRBC units transfused in lifetime,</p> <p>(2008-2020) 1. <5 2. 5-10 3. >10 iii. Number of RBC transfusion events in the last 12 months,</p> <p>(2020-2023) iv. Presence of alloantibodies 1. No 2. Yes a. 1 b. 2 or more c. Unknown 3. Unknown v. Absolute Reticulocyte Count, (2020-2023) vi. LDH (Normal/Abnormal), wherein abnormal is manually defined as greater than ULN, must be obtained within 30 days of preparative regimen vii. Ferritin (Known/Unknown), (2008-2020) 1. If known: a. <1000 ng/mL or ug/L, (2008-2020) b. Greater than or equal to 1000 ng/mL or ug/L, (2008-2020) i. From 2020 onwards actual serum level is reported and can be manually recategorized into the above stratifications viii. Vaso-occlusive Crises requiring hospitalization within 2 years prior to HCT (Yes/No/Unknown) 1. < 3 instances per year, (2008-2020) 2. Greater than or equal to 3 instances per year, (2008-2020) a. From 2020 onwards can obtain the number of episodes and manually recategorize them into these predefined stratifications from the earlier form 3. Unknown ix. History of VTE/PE (Yes/No/Unknown), (2020-2023) 1. Was it associated with indwelling catheter (Yes/No), (2020-2023) x. Did the patient receive hydroxyurea anytime prior to HCT (Yes/No/Unknown) 1. Date Started 2. Date Stopped i. Endocrine: i. History of gonadal dysfunction (Yes/No/Unknown), (2008-2020) j. Infectious Disease: i. Recipient CMV Status (Reactive, Non-reactive, Unknown, Not Done) ii. History of proven invasive fungal infection k. MSK: i. History of Osteo/Avascular Necrosis (Yes/No/Unknown) iv. Additional recipient variables, not specific to SCD: i. Sex (Male/Female) ii. Height at time of pre-HCT preparative regimen (inches or centimeters) iii. Weight at initiation of pre-HCT preparative regimen (pounds or kilograms) iv. Race v. Karnofsky/Lansky Score b. Transplant</p>
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Field	Response
	<p>Related Variables: i. Chronological number of this HCT, if >1, most recent previous HCT date and type ii. Specify Donor 1. Allogeneic, related a. HLA-identical sibling b. HLA-mismatched other relative c. HLA-mismatched relative 2. Allogeneic, unrelated a. HLA-matched unrelated b. HLA-mismatched unrelated iii. Specify Donor Product 1. Bone marrow 2. PBSC 3. Single cord blood unit 4. Other iv. Donor Sex (Male/Female) v. Conditioning Regimen (Myeloablative/Non-Myeloablative/Reduced Intensity) vi. Type of GVHD Prophylaxis c. Post-Transplant Variables: i. Survival status as of date of actual contact per post-infusion follow-up (Alive/Dead) a. Primary cause of death a. Will be used to calculate OS and NRM</p>
Types of cellular therapy data this proposal includes:	Hematopoietic Cell Transplantation (HCT)
<p>PATIENT REPORTED OUTCOME (PRO) REQUIREMENTS: If the study requires PRO data collected by CIBMTR, the proposal should include: 1) A detailed description of the PRO domains, timepoints, and proposed analysis of PROs; 2) A description of the hypothesis speci</p>	<p>This study does not require PRO data collected by CIBMTR</p>

Field	Response
<p>MACHINE LEARNING: Please indicate if the study requires methodology related to machine-learning and clinical predictions.</p>	<p>a. The study will require methodology related to machine learning (ML). ML offers significant advantages in generating predictive scoring tools by facilitating the analysis of complex and multivariate data, helping capture relationships that traditional statistical models may miss. In a recent study, researchers looked at SCD patients who underwent HCT at NIH from 2004-2020, ML was used to analyze over 73 variables. A two-step method using random forest (RF) and Stepwise Cox Proportional Hazard model (SCPH) was then used to select the variables most strongly influencing post-HCT mortality. These variables were then used to generate a risk prediction workflow which outperformed the HCT-CI in predicting outcomes for their cohort [9]. Similarly, a two-step method using ML was employed in the generation of a phenotypic risk score using over 70 variables for mortality prediction in a cohort of over 600 SCD patients enrolled at the NHBLI from 2006-2017 [20]. ML may be advantageous compared to traditional methods when used to predict outcomes in deeply phenotyped patients as they can detect more complex, non-linear relationships in the data [21].</p>
<p>SAMPLE REQUIREMENTS: If the study requires biologic samples from the CIBMTR Repository, the proposal should also include: 1) A detailed description of the proposed testing methodology and sample requirements; 2) A summary of the investigator's previous e</p>	<p>This study does not require biologic samples from the CIBMTR repository.</p>
<p>NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required.</p>	<p>This study does not require non-CIBMTR data.</p>

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Field	Response
	<p>2024;143(25):2654-2665. doi:10.1182/blood.2023023301 19. Sorrow ML. How I assess comorbidities before hematopoietic cell transplantation. Blood. 2013;121(15):2854-2863. doi:10.1182/blood-2012-09-455063 20. Li H, Sachdev V, Tian X, et al. A machine learning-based workflow for predicting transplant outcomes in patients with sickle cell disease. Br J Haematol. 2025;206(3):919-923. doi:10.1111/bjh.19842 21. Sachdev V, Tian X, Gu Y, et al. A phenotypic risk score for predicting mortality in sickle cell disease. Br J Haematol. 2021;192(5):932-941. doi:10.1111/bjh.17342</p>
<p>CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning?</p>	<p>No, I do not have any conflicts of interest pertinent to this proposal</p>

Characteristics of patients with sickle cell disease who underwent allogeneic HCT and with at least 2 years of follow-up reported to the CIBMTR during 2008-2023

Characteristic	N(%)
No. of patients	1987
No. of centers	149
Patient-Related Characteristics	
TED or RES (RF) track determined for this event, no. (%)	
TED	1011 (51)
CRF (RES)	976 (49)
Completion of forms relevant for this proposal, no. (%)	
TED	
Only Form 2030 (sickle cell disease pre-infusion form) is complete	1 (0)
Both Form 2030 and Form 2130 are complete	55 (3)
Neither Form 2030 nor Form 2130 is complete	955 (48)
CRF (RES)	
Only Form 2030 (sickle cell disease pre-infusion form) is complete	3 (0)
Only Form 2130 (sickle cell disease post-infusion form) is complete	17 (1)
Both Form 2030 and Form 2130 are complete	950 (48)
Neither Form 2030 nor Form 2130 is complete	6 (0)
Age by decades, no. (%), years	
Median (range)	13 (1-56)
0-9	729 (37)
10-19	774 (39)
20-29	312 (16)
30-39	135 (7)
40-49	30 (2)
50-59	7 (0)
Sex, no. (%)	
Male	1072 (54)
Female	915 (46)
Race, no. (%)	
White	425 (21)
Black or African American	1271 (64)
Asian	8 (0)
American Indian or Alaska Native	5 (0)
More than one race	19 (1)
Not reported	259 (13)
Ethnicity, no. (%)	
Hispanic or Latino	114 (6)
Non-Hispanic or Latino	1269 (64)

Characteristic	N(%)
Non-resident of the U.S.	568 (29)
Not reported	36 (2)
Current CCN region of patient, no. (%)	
US	1374 (69)
Non-US	613 (31)
Karnofsky score prior to HCT, no. (%)	
90-100%	1673 (84)
< 90%	280 (14)
Not reported	34 (2)
HCT-CI, no. (%)	
0	878 (44)
1	366 (18)
2	163 (8)
3	278 (14)
4	121 (6)
5+	172 (9)
Not reported	9 (0)
Is there a history of mechanical ventilation? no. (%)	
No	1795 (90)
Yes	140 (7)
Not reported	52 (3)
Disease-Related Characteristics	
Interval from diagnosis to HCT, median (range), months	142 (0-673)
Transplant-Related Characteristics	
Classify the recipient's prescribed preparative regimen, no. (%)	
Myeloablative	980 (49)
Non-myeloablative (NST)	417 (21)
Reduced intensity (RIC)	443 (22)
Not myeloablative, either NST or RIC (02Core)	144 (7)
Not reported	3 (0)
Conditioning regimen, no. (%)	
TBI/Cy	2 (0)
TBI/Cy/Flu	109 (5)
TBI/Cy/Flu/TT	198 (10)
TBI/Mel	4 (0)
TBI/Flu	8 (0)
TBI/other(s)	331 (17)
Bu/Cy	509 (26)
Flu/Bu/TT	73 (4)
Flu/Bu	309 (16)

Characteristic	N(%)
Flu/Mel/TT	127 (6)
Flu/Mel	260 (13)
Cy/Flu	7 (0)
Mel/other(s)	1 (0)
Treosulfan	36 (2)
TLI	1 (0)
Other(s)	9 (0)
Not reported	3 (0)
Donor type, no. (%)	
HLA identical sibling	1190 (60)
Twin	6 (0)
Haploidentical donor	339 (17)
Other related	91 (5)
Well-matched unrelated (8/8)	146 (7)
Partially-matched unrelated (7/8)	50 (3)
Mismatched unrelated (<= 6/8)	2 (0)
Multi-donor	11 (1)
Unrelated (matching cannot be determined)	18 (1)
Cord blood	134 (7)
Donor age by decades, no. (%), years	
Median (range)	19 (0-65)
0-9	449 (23)
10-19	470 (24)
20-29	361 (18)
30-39	256 (13)
40-49	161 (8)
50-59	73 (4)
60-69	7 (0)
Not reported	210 (11)
Donor/recipient sex match, no. (%)	
M-M	523 (26)
M-F	418 (21)
F-M	470 (24)
F-F	440 (22)
CB - recipient M	77 (4)
CB - recipient F	57 (3)
Not reported	2 (0)
Product type, no. (%)	
BM	1318 (66)
PBSC	535 (27)

Characteristic	N(%)
UCB	133 (7)
Not reported	1 (0)
GVHD prophylaxis, no. (%)	
Ex-vivo T-cell depletion	23 (1)
CD34 selection	55 (3)
PtCy + other(s)	349 (18)
PtCy alone	2 (0)
TAC + MMF +- other(s) (except PtCy)	177 (9)
TAC + MTX +- other(s) (except MMF, PtCy)	359 (18)
TAC + other(s) (except MMF, MTX, PtCy)	35 (2)
TAC alone	19 (1)
CSA + MMF +- other(s) (except PtCy,TAC)	121 (6)
CSA + MTX +- other(s) (except PtCy,TAC,MMF)	421 (21)
CSA + other(s) (except PtCy,TAC,MMF,MTX)	10 (1)
CSA alone	22 (1)
Other(s)	352 (18)
Not reported	42 (2)
Year of HCT, no. (%)	
2008-2011	237 (12)
2012-2015	392 (20)
2016-2019	692 (35)
2020-2023	666 (34)
Follow-up of survivors, median (range), months	59.3 (24.0-202.2)

Field	Response
Proposal Number	2509-209-USMAN
Proposal Title	Comparing patient reported outcomes in allogeneic stem cell transplant recipients who receive myeloablative (MAC) versus reduced intensity conditioning (RIC)
Key Words	allogeneic hematopoietic stem cell transplant, acute myeloid leukemia (AML), myelodysplastic syndrome (MDS), conditioning intensity, patient reported outcomes
Principal Investigator #1: - First and last name, degree(s)	Shireen Usman, MD
Principal Investigator #1: - Email address	usmans@mskcc.org
Principal Investigator #1: - Institution name	Memorial Sloan Kettering Cancer Center
Principal Investigator #1: - Academic rank	Adult Bone Marrow Transplant Fellow
Junior investigator status (defined as 5 years from fellowship)	Yes
Do you identify as an underrepresented/minority?	No
Principal Investigator #2 (If applicable): - First and last name, degree(s):	Gunjan Shah, MD
Principal Investigator #2 (If applicable): - Email address:)	shahg@mskcc.org
Principal Investigator #2 (If applicable): - Institution name:	Memorial Sloan Kettering Cancer Center
Principal Investigator #2 (If applicable): - Academic rank:	Associate Member, Adult BMT Service
Junior investigator status (defined as 5 years from fellowship)	No
Do you identify as an underrepresented/minority?	No
Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.	Usman: None Shah: None
Do any of the PI(s) within this proposal have a CIBMTR WC study in manuscript preparation >6 months?	No
PROPOSED WORKING COMMITTEE:	Morbidity, Recovery and Survivorship
Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.	No
RESEARCH QUESTION:	Among patients with AML/MDS who undergo hematopoietic allogeneic stem cell transplant (HSCT), how do patient reported outcomes (PROs) vary over time and differ between those who receive MAC versus RIC conditioning?

Field	Response
RESEARCH HYPOTHESIS:	<p>We hypothesize that physical, mental, and social health PROs as characterized by PROMIS-29 measures will differ in patients who receive myeloablative (MAC) versus reduced intensity conditioning (RIC). Further, we predict that the trajectory of PROs will change over time and vary between conditioning regimens in the short-term (180 days post-transplant) and long-term (1-year post-transplant). We suspect that short-term PROs in those receiving MAC may be worse, however, long-term outcomes may be similar or better as compared to RIC given adequate time for recovery and lower disease relapse rates.</p>
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	<p>Primary objective: 1. To compare short (180 days post-transplant) and long-term (1-year post-transplant) PROs in allogeneic stem cell transplant recipients who receive MAC versus RIC.</p> <p>Secondary objectives: 1. To describe how other patient and disease-related factors including gender, age, race/ethnicity, performance status, socioeconomic/employment status, development of GVHD, and disease relapse impact PROs in those receiving MAC versus RIC. 2. To compare comprehensive score for financial toxicity (COST) in allogeneic transplant recipients who receive MAC versus RIC. 3. To compare occupational functioning and sociodemographic domains in allogeneic transplant recipients who receive MAC versus RIC.</p>

Field	Response
<p>SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.</p>	<p>Several retrospective and randomized control trials have evaluated the impact of conditioning intensity on outcomes in patients with AML/MDS with variable results. Long-term follow-up from BMT CTN 0901 showed a higher rate of transplant related mortality with MAC compared to RIC in adult patients (ages 18-65) who underwent HSCT for AML or MDS. However, this was offset by a higher rate of relapse with RIC leading to superior overall survival in patients who received MAC [1]. Morbidity or patient reported quality of life measures were not included in the analysis from BMT CTN 0901 and have not been thoroughly evaluated in this patient population. The decision to pursue MAC vs RIC remains highly personalized and requires a risk-benefit discussion tailored to each individual patient. A deeper understanding of patient reported outcomes in this setting can help better frame this discussion. Further, baseline pre-transplant PROs have been shown to independently predict survival after adjustment for patient, disease, and transplant related factors [2, 3]. A comprehensive analysis of available CIBMTR PRO data in this setting can help us better understand both quality and length of survival in allogeneic stem cell transplant recipients receiving MAC versus RIC, in addition to informing potential for appropriate interventions.</p>

Field	Response
<p>SCIENTIFIC JUSTIFICATION: Provide a background summary of previous related research and their strengths and weaknesses, justification of your research and why your research is still necessary.</p>	<p>Improvements in HSCT implementation and supportive care have increased survival in transplant recipients making quality of life increasingly relevant. However, patient reported quality of life assessments have not been thoroughly evaluated and compared in HSCT recipients receiving MAC versus RIC which is a population of patients whose treatment decisions involve a highly personalized approach. Prior work which has examined PROs in this population includes a cross-sectional study of patients treated with HSCT in Germany in 2023 who completed EORTC QLQ-C30 and FACT-BMT surveys. In this study, RIC was associated with better quality of life outcomes, however, a direct comparison with MAC was not made [4]. Older studies including a single-center retrospective study completed in France between 1998-2008 used the same measures to evaluate a cohort of patients receiving RIC and found an acceptable level of functioning two years post-HSCT and good average quality of life scores [5]. Other studies comparing quality of life with RIC versus MAC have primarily been based outside of the United States and completed over 15 years ago [6-8]. Patient reported quality of life measures are considered an index of effectiveness of cancer treatment because they provide a multidimensional understanding of survival [2, 9-10]. The evolution of PROs over time in patients treated with RIC versus MAC HSCT in the United States during the current era of hematopoietic transplantation has not yet been established. Further investigation can help inform effectiveness of transplant, improve patient-provider communication, and identify areas for advancement.</p>
<p>PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.</p>	<p>Inclusion Criteria: 1. Adult recipients (18 years and older) 2. Diagnosis of acute myeloid leukemia (AML) or myelodysplastic syndrome (MDS) as the indication for transplant. 3. Received either myeloablative or reduced intensity conditioning 4. Received any type of GVHD prophylaxis with any level of HLA donor match 5. United States is country of primary residence Exclusion Criteria: 1. Pediatric recipients (younger than 18 years) 2. Received non-myeloablative conditioning</p>
<p>Does this study include pediatric patients?</p>	<p>No</p>

Field	Response
<p>If this study does not include pediatric patients, please provide justification:</p>	<p>The framework of this study is based on a population of patients receiving MAC versus RIC prior to hematopoietic stem cell transplant which is typically a decision relevant in adult or frail patients. AML/MDS may be less represented in pediatric patients and prognosis/outcomes are expected to be different as compared to adult patients which would introduce increased variability to this study. Further, PROs in pediatric patients may have greater variability in terms of type of responses and potential caregiver influence which may introduce bias.</p>
<p>DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Outline any supplementary data required.</p>	<p>The study does not require collection of additional data beyond that contained in existing CIBMTR forms.</p> <p>1. Patient Related - Age - Gender - Height and weight at initiation of pre-HCT preparative regimen - HCT-CI, specify co-existing diseases or organ impairment - Karnofsky performance status - Recipient race - Recipient ethnicity - Country of primary residence - Most recent work status - Current occupation category - Highest educational grade completed - Combined household gross income - Zip/postal code for place of primary residence</p> <p>2. Disease Related - Disease: AML, MDS - Disease status: CR1, CR2, relapse/active disease - Revised disease risk index</p> <p>3. Transplant/Infusion Specific - Year of transplant - Donor/recipient HLA-matching status: 8/8, 7/8, 5-6/8, haploidentical, matched related donor - Donor age - Conditioning regimen: myeloablative vs. reduced intensity - Date of acute GVHD diagnosis - Organ involvement of acute GVHD - Highest grade of acute GVHD - Date of chronic GVHD diagnosis - Highest grade of chronic GVHD - Date of relapse - Date of death - Follow up time</p>
<p>Types of cellular therapy data this proposal includes:</p>	<p>Hematopoietic Cell Transplantation (HCT)</p>

Field	Response
<p>PATIENT REPORTED OUTCOME (PRO) REQUIREMENTS: If the study requires PRO data collected by CIBMTR, the proposal should include: 1) A detailed description of the PRO domains, timepoints, and proposed analysis of PROs; 2) A description of the hypothesis speci</p>	<p>1) A. We plan to collect PRO data from patients who underwent allogeneic stem cell transplant for AML or MDS and received either RIC or MAC. Based on publicly available information on CIBMTR PRO protocol enrollment (as of May 20, 2025), there are 637 total participating adult patients (aged 18 and older) who underwent allogeneic hematopoietic cell transplantation between 2019-2025. Of these patients, 62 with AML completed a baseline survey with 33-196 patients completing a follow up survey between day 100 and 4 years (769 total surveys completed). There are 36 patients with MDS who completed a baseline survey with 6-103 patients completing a follow up survey between day 100 and 4 years (418 total surveys completed). B. We plan to collect data across all PROMIS-29 domains including global, physical function, fatigue, sleep disturbance, pain interference, anxiety, depression, cognitive function, ability to participate in social roles/activities, and sexual function. For our secondary aims, we also plan to collect data from additional domains including comprehensive score for financial toxicity, occupational functioning, and social determinants of health. C. We plan to collect data from all available time points including pre-infusion, day 100, day 180, year 1, year 2, year 3, and year 4. Data will be grouped based on short term (180 days post-transplant) and long-term (1-year post-transplant) PROs. D. We plan to compare T-scores from patients who received RIC versus MAC and create an AUC to see changes over time while adjusting for baseline sociodemographic factors and co-morbidities. 2) We hypothesize that short-term PROs are worse in patients who receive MAC compared RIC conditioning at day 100 and day 180 assessments. Specifically, we expect that PROs within physical and social health domains may be worse with MAC while mental health domains may be similar between two conditioning regimens. We expect long-term PROs (between 1-4 years) are similar between patients who receive MAC and RIC given adequate time for recovery. We also expect disease relapse to be correlated with worse PROs which may be more prevalent in RIC group. Pre-infusion PROs may be worse in the RIC group given likelihood of increased co-morbidities and frailty.</p>
<p>MACHINE LEARNING: Please indicate if the study requires methodology related to machine-learning and clinical predictions.</p>	<p>N/A</p>

Field	Response
SAMPLE REQUIREMENTS: If the study requires biologic samples from the CIBMTR Repository, the proposal should also include: 1) A detailed description of the proposed testing methodology and sample requirements; 2) A summary of the investigator's previous e	Biologic samples will not be required for this study.
NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required.	No external data sources will be used.

REFERENCES:

- [1] Scott BL, Pasquini MC, Fei M, Fraser R, Wu J, Devine SM, Porter DL, Maziarz RT, Warlick E, Fernandez HF, Soiffer RJ. Myeloablative versus reduced-intensity conditioning for hematopoietic cell transplantation in acute myelogenous leukemia and myelodysplastic syndromes long-term follow-up of the BMT CTN 0901 clinical trial. *Transplantation and cellular therapy*. 2021 Jun 1;27(6):483-e1. [2] Shaw BE, Brazauskas R, Millard HR, Fonstad R, Flynn KE, Abernethy A, Vogel J, Petroske C, Mattila D, Drexler R, Lee SJ. Centralized patient-reported outcome data collection in transplantation is feasible and clinically meaningful. *Cancer*. 2017 Dec 1;123(23):4687-700. [3] Wood WA, Le-Rademacher J, Syrjala KL, Jim H, Jacobsen PB, Knight JM, Abidi MH, Wingard JR, Majhail NS, Geller NL, Rizzo JD. Patient-reported physical functioning predicts the success of hematopoietic cell transplantation (BMT CTN 0902). *Cancer*. 2016 Jan 1;122(1):91-8. [4] Beer SA, Blatt J, Reu K, Maier CP, Faul C, Vogel W, Bethge W, Lengerke C. Long-term patient-reported outcomes following allogeneic hematopoietic cell transplantation. *Bone Marrow Transplantation*. 2025 Feb 26:1-8. [5] Clavert A, Peric Z, Brissot E, Malard F, Guillaume T, Delaunay J, Dubruille V, Le Guill S, Mahe B, Gastinne T, Blin N. Late complications and quality of life after reduced-intensity conditioning allogeneic stem cell transplantation. *Biology of blood and marrow transplantation*. 2017 Jan 1;23(1):140-6. [6] Gupta V, Panzarella T, Li L, Khan J, Sharma A, Lipton JH, Kuruvilla J, Messner H, Alibhai SM. A prospective study comparing the outcomes and health-related quality of life in adult patients with myeloid malignancies undergoing allogeneic transplantation using myeloablative or reduced-intensity conditioning. *Biology of Blood and Marrow Transplantation*. 2012 Jan 1;18(1):113-24. [7] Andersson I, Ahlberg K, Stockelberg D, Brune M, Persson LO. Health-related quality of life in patients undergoing allogeneic stem cell transplantation after reduced intensity conditioning versus myeloablative conditioning. *Cancer nursing*. 2009 Jul 1;32(4):325-34. [8] Bevans MF, Marden S, Leidy NK, Soeken K, Cusack G, Rivera P, Mayberry H, Bishop MR, Childs R, Barrett AJ. Health-related quality of life in patients receiving reduced-intensity conditioning allogeneic hematopoietic stem cell transplantation. *Bone marrow transplantation*. 2006 Jul;38(2):101-9. [9] Shaw BE, Flynn KE, He N, Cusatis R, D'Souza A, Hamilton BK, Horowitz MM, Mattila D, Phelan R, Lee SJ, Brazauskas

Field	Response
	<p>R. Incorporating patient-reported outcome data into a predictive calculator for allogeneic hematopoietic cell transplantation recipients. <i>Cancer</i>. 2024 May 15;130(10):1826-35. [10] Gu Z, Wu L, Li J, Zheng S, Huang M. A Visual Analysis of Patient-Reported Outcomes in Lung Cancer From 2013 to 2023. <i>Cancer Control</i>. 2024 Jun 22;31:10732748241266490.</p>
<p>CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning?</p>	<p>Yes, I have conflicts of interest pertinent to this proposal</p>
<p>If yes, provide detail on the nature of employment, name of organization, role, entity, ownership, type of financial transaction or legal proceeding and whether renumeration is >\$5000 annually.</p>	<p>Shireen Usman No conflicts of interest Gunjan Shah - Research funding to the instituion from Janssen, Amgen, BMS, Beyond Spring, GPCR, and Recordati, and is on the DSMB for ArcellX.</p>

Population characteristics of first alloHCT AML/MDS adult patients in the U.S. with any level of PRO data

Characteristic	MAC	RIC	Total
No. of patients	171	193	364
No. of centers	34	33	43
Patient-Related Characteristics			
Age, by decades, no. (%)			
Median (range)	54 (21-78)	67 (31-76)	64 (21-78)
20-29	13 (8)	0 (0)	13 (4)
30-39	29 (17)	3 (2)	32 (9)
40-49	27 (16)	3 (2)	30 (8)
50-59	51 (30)	20 (10)	71 (20)
60-69	40 (23)	116 (60)	156 (43)
70+	11 (6)	51 (26)	62 (17)
Sex, no. (%)			
Male	88 (51)	116 (60)	204 (56)
Female	83 (49)	77 (40)	160 (44)
Race, no. (%)			
White	137 (80)	163 (84)	300 (82)
Black or African American	6 (4)	6 (3)	12 (3)
Asian	14 (8)	14 (7)	28 (8)
Native Hawaiian or other Pacific Islander	2 (1)	0 (0)	2 (1)
American Indian or Alaska Native	0 (0)	1 (1)	1 (0)
More than one race	0 (0)	2 (1)	2 (1)
Not reported	12 (7)	7 (4)	19 (5)
Ethnicity, no. (%)			
Hispanic or Latino	19 (11)	17 (9)	36 (10)
Non-Hispanic or Latino	150 (88)	173 (90)	323 (89)
Not reported	2 (1)	3 (2)	5 (1)
Current CCN region of patient, no. (%)			
US	171 (100)	193 (100)	364
Karnofsky score prior to HCT, no. (%)			
90-100%	115 (67)	109 (56)	224 (62)
< 90%	56 (33)	84 (44)	140 (38)
ECOG prior to HCT, no. (%)			
Asymptomatic	115 (67)	109 (56)	224 (62)
Symptomatic but completely ambulatory	56 (33)	80 (41)	136 (37)
Symptomatic, < 50% in bed during the day	0 (0)	4 (2)	4 (1)
HCT-CI, no. (%)			
0	43 (25)	32 (17)	75 (21)

Characteristic	MAC	RIC	Total
1	36 (21)	32 (17)	68 (19)
2	25 (15)	31 (16)	56 (15)
3	34 (20)	37 (19)	71 (20)
4	16 (9)	23 (12)	39 (11)
5+	13 (8)	33 (17)	46 (13)
Not reported	4 (2)	5 (3)	9 (2)
Disease-Related Characteristics			
Primary disease, no. (%)			
AML	130 (76)	118 (61)	248 (68)
MDS	41 (24)	75 (39)	116 (32)
Interval from diagnosis to HCT, months, median (range)	5 (2-319)	6 (1-183)	6 (1-319)
Transplant-Related Characteristics			
Conditioning regimen, no. (%)			
TBI/Cy	3 (2)	0 (0)	3 (1)
TBI/Cy/Flu	2 (1)	10 (5)	12 (3)
TBI/Cy/Flu/TT	2 (1)	0 (0)	2 (1)
TBI/Mel	0 (0)	20 (10)	20 (5)
TBI/Flu	15 (9)	12 (6)	27 (7)
TBI/other(s)	4 (2)	1 (1)	5 (1)
Bu/Cy	39 (23)	0 (0)	39 (11)
Flu/Bu/TT	15 (9)	0 (0)	15 (4)
Flu/Bu	91 (53)	34 (18)	125 (34)
Flu/Mel	0 (0)	116 (60)	116 (32)
Donor type, no. (%)			
HLA identical sibling	33 (19)	22 (11)	55 (15)
Twin	0 (0)	1 (1)	1 (0)
Haploidentical donor	14 (8)	21 (11)	35 (10)
Other related	2 (1)	1 (1)	3 (1)
Well-matched unrelated (8/8)	91 (53)	120 (62)	211 (58)
Partially-matched unrelated (7/8)	15 (9)	20 (10)	35 (10)
Mismatched unrelated (<= 6/8)	1 (1)	1 (1)	2 (1)
Multi-donor	0 (0)	1 (1)	1 (0)
Unrelated (matching cannot be determined)	11 (6)	6 (3)	17 (5)
Cord blood	4 (2)	0 (0)	4 (1)
Donor/recipient sex match, no. (%)			
M-M	51 (30)	72 (37)	123 (34)
M-F	41 (24)	37 (19)	78 (21)
F-M	31 (18)	40 (21)	71 (20)
F-F	37 (22)	39 (20)	76 (21)
CB - recipient M	3 (2)	0 (0)	3 (1)

Characteristic	MAC	RIC	Total
CB - recipient F	1 (1)	0 (0)	1 (0)
Not reported	7 (4)	5 (3)	12 (3)
GVHD prophylaxis, no. (%)			
CD34 selection	5 (3)	4 (2)	9 (2)
PtCy + other(s)	86 (50)	104 (54)	190 (52)
TAC + MMF +- other(s) (except PtCy)	16 (9)	7 (4)	23 (6)
TAC + MTX +- other(s) (except MMF, PtCy)	50 (29)	59 (31)	109 (30)
TAC + other(s) (except MMF, MTX, PtCy)	0 (0)	4 (2)	4 (1)
TAC alone	8 (5)	3 (2)	11 (3)
CSA + MMF +- other(s) (except PtCy,TAC)	1 (1)	3 (2)	4 (1)
CSA + MTX +- other(s) (except PtCy,TAC,MMF)	2 (1)	1 (1)	3 (1)
Other(s)	2 (1)	1 (1)	3 (1)
Missing	1 (1)	7 (4)	8 (2)
Donor age, by decades, no. (%)			
Median (range)	30 (0-65)	29 (19-73)	30 (0-73)
0-9	1 (1)	0 (0)	1 (0)
10-19	9 (5)	7 (4)	16 (4)
20-29	69 (40)	94 (49)	163 (45)
30-39	39 (23)	46 (24)	85 (23)
40-49	20 (12)	18 (9)	38 (10)
50-59	17 (10)	10 (5)	27 (7)
60-69	6 (4)	11 (6)	17 (5)
70+	0 (0)	2 (1)	2 (1)
Not reported	10 (6)	5 (3)	15 (4)
Year of current transplant, no. (%)			
2019	1 (1)	0 (0)	1 (0)
2020	14 (8)	10 (5)	24 (7)
2021	36 (21)	37 (19)	73 (20)
2022	60 (35)	71 (37)	131 (36)
2023	20 (12)	34 (18)	54 (15)
2024	37 (22)	38 (20)	75 (21)
2025	3 (2)	3 (2)	6 (2)
Follow-up of survivors, median (range), months	25 (3-61)	24 (3-50)	24 (3-61)
PRO data availability			
PRO follow-up, no. (%)			
Baseline + at least 1 follow-up form	32 (19)	30 (16)	62 (17)
Only baseline	3 (2)	14 (7)	17 (5)
At least 1 follow-up form	136 (80)	149 (77)	285 (78)

Field	Response
Proposal Number	2509-214-SAINVIL
Proposal Title	Comparative Prognostic Value of Clinical (HCT-CI, Performance Status) and Structural (Area Deprivation Index, Rurality, Distance to Center) Risk for 1-Year Patient-Reported Recovery After Hematopoietic Cell Transplantation
Key Words	HCT; disparities; health equity; patient-reported outcomes; PROMIS; performance status; HCT-CI; neighborhood deprivation; rurality; distance-to-center
Principal Investigator #1: - First and last name, degree(s)	Marie-Michele Sainvil
Principal Investigator #1: - Email address	michele.sainvil@duke.edu
Principal Investigator #1: - Institution name	Duke Medical Center
Principal Investigator #1: - Academic rank	Post Fellowship Research Fellow
Junior investigator status (defined as 5 years from fellowship)	Yes
Do you identify as an underrepresented/minority?	Yes
Principal Investigator #2 (If applicable): - First and last name, degree(s):	Sanghee Hong
Principal Investigator #2 (If applicable): - Email address:)	sanghee.hong@duke.edu
Principal Investigator #2 (If applicable): - Institution name:	Duke medical Center
Principal Investigator #2 (If applicable): - Academic rank:	Associate Professor
Junior investigator status (defined as 5 years from fellowship)	Yes
Do you identify as an underrepresented/minority?	No
We encourage a maximum of two Principal Investigators per study. If more than one author is listed, please indicate who will be identified as the corresponding PI below:	Marie-Mich le Sainvil
If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:	Yes, I am a junior investigator and would like assistance identifying a senior mentor for my project
Do any of the PI(s) within this proposal have a CIBMTR WC study in manuscript preparation >6 months?	No
PROPOSED WORKING COMMITTEE:	Donor and Recipient Health Services
Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.	No

Field	Response
RESEARCH QUESTION:	Among patients undergoing HCT in the United States, do structural measures of disadvantage (neighborhood deprivation, rurality, distance to transplant center) predict patient-reported functional recovery as well as or better than established clinical risk scores (HCT-CI, Karnofsky/Lansky performance status)?
RESEARCH HYPOTHESIS:	Primary: Baseline performance status and HCT-CI will be strong predictors of 1-year PROMIS Physical Function recovery, but structural disadvantage (ADI quintile, rural residence, distance >100 miles) will provide incremental predictive value. Secondary: The prognostic value of structural factors will be greatest among older adults, racial/ethnic minority groups, and rural patients.
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	Compare the prognostic value of clinical vs structural risk measures for 1-year PROMIS Physical Function recovery. Examine PROMIS Fatigue, Emotional Distress, and Social Roles domains at day +100 and 1 year. Evaluate whether recovery trajectories differ by ADI quintile, RUCA classification, and distance-to-center. Explore interaction effects by age group, race/ethnicity, and donor type. Primary Outcome Definition Recovery = PROMIS Physical Function T-score at 1 year that is either: within 5 points of baseline if baseline < 45, or > 45 if baseline > 45. Secondary Outcomes Recovery in Fatigue, Emotional Distress, and Social Roles domains at day +100 and 1 year. Trajectory class membership (e.g., rapid, delayed, persistent impairment) using latent class growth analysis (LCGA). Healthcare utilization by day +100 (readmissions, inpatient days).
SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.	This study will clarify the relative and combined prognostic value of clinical risk (HCT-CI, performance status) and structural disadvantage (neighborhood deprivation, rurality, distance) for patient-reported recovery after HCT. Findings will: Inform risk stratification that integrates social context. Provide benchmarks for survivorship planning that extend beyond survival. Support health equity interventions by identifying high-risk groups for targeted rehabilitation and psychosocial support. By focusing on functional recovery, this proposal aligns with national recommendations for integrating PROs into routine transplant care.

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

Hematopoietic cell transplantation (HCT) is a curative therapy for hematologic diseases, but survivors face persistent risks of morbidity, mortality, and impaired quality of life. Prognostic indices such as the HCT-Comorbidity Index (HCT-CI) and performance status are validated predictors of non-relapse mortality and survival and are widely used for pre-transplant risk stratification [1,2]. However, these clinical models explain only part of the variability in outcomes and are not designed to capture recovery in patient-reported outcomes (PROs) such as physical function, fatigue, and social role participation [3-7]. There is growing evidence that structural and social determinants of health (SDOH) including the Area Deprivation Index (ADI), neighborhood poverty, rurality, and distance to transplant centers are independently associated with inferior survival, higher non-relapse mortality, and impaired recovery after HCT [8-13]. For example, analyses from CIBMTR and other cohorts have demonstrated that patients from disadvantaged communities have higher rates of non-relapse mortality and worse long-term health outcomes even after adjusting for HCT-CI and performance status [9-12]. These effects appear especially pronounced among racial/ethnic minority patients and those with high comorbidity burden [8,10,13]. Emerging biological data provide mechanistic plausibility: patients from socially disadvantaged backgrounds exhibit stress-related gene expression profiles, immune dysregulation, and transcriptomic signatures associated with adverse clinical outcomes [14,15]. These findings highlight that structural disadvantage is biologically embedded and likely interacts with transplant-related risks to shape recovery. At the same time, PROs are increasingly recognized as independent predictors of survival, complications, and quality of life after HCT [3-7]. Centralized, longitudinal PRO collection has been shown to be feasible and meaningful within CIBMTR [6], and national recommendations now endorse routine PRO assessment as part of survivorship care [16]. Yet, no registry-scale study has directly compared the prognostic performance of clinical vs structural risk measures for predicting PRO-defined recovery after HCT. In summary, integrating clinical and structural risk measures into predictive models for PRO recovery is scientifically justified because: 1. Both are independently associated with survival and quality-of-life outcomes. 2. Biological mechanisms support the adverse impact of structural

Field	Response
	disadvantage. 3. A clear knowledge gap remains regarding how these domains jointly inform patient-reported recovery, beyond survival. This approach has the potential to enhance risk stratification, improve survivorship planning, and facilitate targeted interventions, thereby advancing both precision medicine and health equity in transplant care.
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	Inclusion: Autologous or allogeneic HCT recipients reported by U.S. centers, 2010–2023. Baseline PRO and 1 follow-up PRO (+100 or 1 year). Exclusion: Non-U.S. centers. Missing baseline HCT-CI or Karnofsky/Lansky PS. Second HCT within 1 year. Missing ZIP code.
Does this study include pediatric patients?	Yes
DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Outline any supplementary data required.	Predictors (Clinical): HCT-CI Form 2400 (TED baseline) & Appendix J. Performance Status Appendix L, recorded on Form 2400. Predictors (Structural): Patient ZIP code Form 2400 Q9 → linked to ADI quintile and RUCA classification. Distance to center derived from Form 2400 Q9 (patient ZIP) and CIBMTR center database (center ZIP). Covariates: Demographics Form 2400 Q6–Q7 (age, sex); Q12–Q15 (race/ethnicity). Disease indication Form 2000 / Disease Classification. Donor type & graft source Form 2000/2100 (donor HLA, stem cell source). Conditioning regimen intensity Form 2000 Q87–92. GVHD Form 2100 Q270–299 (acute), Form 2450 Q95–118 (chronic). Center variables CIBMTR database (annualized transplant volume; region). Outcomes (PRO): PROMIS Physical Function, Fatigue, Emotional Distress, Social Roles collected via the CIBMTR PRO Protocol, linked to TED baseline and follow-up at +100 and 1 year. Healthcare utilization: Form 2100 Q384–389 (unplanned readmissions, inpatient days by day +100).
Types of cellular therapy data this proposal includes:	Hematopoietic Cell Transplantation (HCT)

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

Domains: - This study will analyze the following PRO domains collected through the CIBMTR PRO Protocol: - Physical Function (PROMIS-PF) primary outcome. - Fatigue (PROMIS-Fatigue) secondary. - Emotional Distress (PROMIS Emotional Distress Anxiety/Depression short forms) secondary. - Ability to Participate in Social Roles/Activities (PROMIS-Social Roles) secondary. Timepoints: - Baseline (pre-HCT assessment). - Day +100 (early recovery). - 1-year post-HCT (primary endpoint for functional recovery). - Where available, PROs captured beyond 1 year will be used in exploratory analyses of long-term survivorship trajectories. Proposed Analysis: - Primary PRO analysis: PROMIS-PF score at 1 year. Recovery will be defined as: - Within 5 points of baseline if baseline <45, or - Achieving >45 if baseline <45. Secondary analyses: - Changes in Fatigue, Emotional Distress, and Social Roles at day +100 and 1 year. - Trajectory analysis of PROMIS-PF, Fatigue, and Emotional Distress across baseline, day +100, 1 year using latent class growth analysis (2-5 classes). Handling of missingness: Linear mixed-effects models (for continuous PROs) and logistic regression (for binary recovery), accounting for repeated measures; multiple imputation for covariates; sensitivity analyses for informative dropout (joint modeling). Multiplicity: False Discovery Rate (FDR) control across secondary PRO domains. PRO-Specific Hypotheses: - Patients with higher comorbidity (HCT-CI) and worse baseline performance status will have lower rates of PROMIS-PF recovery at 1 year. - Independent of clinical risk, patients residing in disadvantaged neighborhoods (highest ADI quintile), rural areas (RUCA non-metro), or >100 miles from center will have lower probability of PROMIS-PF recovery and more frequently follow “delayed” or “persistent impairment” trajectories. - Structural disadvantage will be most strongly associated with Fatigue and Emotional Distress trajectories, reflecting the compounding effects of social stressors on psychological and physical recovery. - The prognostic value of structural factors will be greatest among older adults, racial/ethnic minority groups, and rural patients. Feasibility: CIBMTR has systematically collected PROs since 2020 using the centralized PRO protocol, with more than 5,000 patients already evaluable at baseline and at one or more follow-ups (Cusatis et al., Transplant Cell Ther, 2024). This

Field	Response
	provides a sufficient sample size to evaluate domain-specific recovery and subgroup effects.
<p>MACHINE LEARNING: Please indicate if the study requires methodology related to machine-learning and clinical predictions.</p>	<p>This study will not primarily rely on advanced machine-learning (ML) methods. However, we will conduct exploratory analyses to assess whether ML-based prediction adds incremental value to standard regression models. Exploratory ML application: Random forest and gradient boosting models will be tested to evaluate variable importance among clinical (HCT-CI, performance status) and structural predictors (ADI, RUCA, distance). Clinical prediction context: Outputs will be compared against traditional multivariable regression and mixed-effects models to assess concordance and interpretability. Rationale: These exploratory ML models will help identify non-linear interactions between structural disadvantage and clinical factors, but the primary inference and reporting will rely on interpretable regression models to ensure clinical relevance and feasibility. Bioinformatics alignment: This approach aligns with CIBMTR's Bioinformatics Research Program, though no specialized algorithms beyond supervised learning for prediction will be required. Conclusion: Machine learning is not required for the primary aims of this study, but limited exploratory use will provide added insight into variable importance and model performance.</p>
<p>SAMPLE REQUIREMENTS: If the study requires biologic samples from the CIBMTR Repository, the proposal should also include: 1) A detailed description of the proposed testing methodology and sample requirements; 2) A summary of the investigator's previous e</p>	<p>This study does not request biologic samples from the CIBMTR Repository. Focus: The project will use existing registry data (TED Forms, CRFs, PROs, and linked structural data) only. Testing methodology: No assays or biospecimen-based analyses are planned. PI experience: While Dr. Sainvil has experience with biospecimen-based projects (e.g., disparities in biorepository participation), the current proposal does not require samples, and thus, no assay expertise is needed here. No sample requests will be made, and this proposal is feasible using only existing registry and PRO data.</p>

Field	Response
<p>NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required.</p>	<p>External Data Sources: This study will link CIBMTR patient-level data with publicly available, nationally standardized geographic indices: 1. Area Deprivation Index (ADI): - Derived from U.S. Census and American Community Survey data. - Calculated at the 9-digit or 5-digit ZIP code level. - Captures socioeconomic disadvantage across multiple domains (income, education, employment, housing quality). 2. Rural Urban Commuting Area (RUCA) Codes: - Developed by the U.S. Department of Agriculture. - Classifies residential ZIP codes into metropolitan, micropolitan, small town, or rural categories. 3. Distance to Transplant Center: - Computed using the patient’s residential ZIP code (Form 2400, Q9) and the transplant center’s ZIP code (from the CIBMTR Center Database). - Reported as great-circle distance in miles, and categorized (≤ 50 miles, 51 – 100 miles, >100 miles). Rationale for Linkage: - CIBMTR collects clinical, demographic, and PRO data but does not include area-level socioeconomic measures or geographic access indicators. - ADI and RUCA linkage provide validated proxies of structural disadvantage that cannot be derived from CIBMTR data alone. - Distance to center is not directly collected but can be calculated using ZIP-level data from CIBMTR and center location files. - Linking these datasets is essential to answer the research question: whether structural disadvantage provides incremental prognostic value beyond clinical indices for predicting functional recovery after HCT. Feasibility: These linkages have been successfully performed in prior CIBMTR studies evaluating survival and health service outcomes [8 – 13], demonstrating that the linkage is feasible, validated, and compliant with data use restrictions.</p>

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Field	Response
	<p>cell transplantation in the United States. <i>Cancer</i>. 2021 Feb 15;127(4):609-618. doi:10.1002/cncr.33232. PMID: 33270323; PMCID: PMC7821122. 10. Bona K, Brazauskas R, He N, et al. Neighborhood poverty and pediatric allogeneic hematopoietic cell transplantation outcomes: a CIBMTR analysis. <i>Blood</i>. 2021 Jan 28;137(4):556-568. doi:10.1182/blood.2020006252. PMID: 33237888; PMCID: PMC7849812. 11. Wolfson JA, Bhatia S, Hageman L, et al. Neighborhood disadvantage, health status, and health care utilization after blood or marrow transplant: BMTSS report. <i>Blood Adv</i>. 2023 Feb 14;7(3):293-301. doi:10.1182/bloodadvances.2022007548. PMID: 36694626; PMCID: PMC9910330. 12. Fu S, Rybicki L, Abounader D, et al. Association of socioeconomic status with long-term outcomes in 1-year survivors of allogeneic hematopoietic cell transplantation. <i>Bone Marrow Transplant</i>. 2015 Oct;50(10):1326-1330. doi:10.1038/bmt.2015.166. PMID: 26192657. 13. Hong S, Majhail NS. Increasing access to allotransplants in the United States: the impact of race, geography, and socioeconomics. <i>Hematology Am Soc Hematol Educ Program</i>. 2021 Dec 10;2021(1):275-280. doi:10.1182/hematology.2021000259. PMID: 34889366. 14. Knight JM, Rizzo JD, Logan BR, et al. Low socioeconomic status, adverse gene expression profiles, and clinical outcomes in hematopoietic stem cell transplant recipients. <i>Clin Cancer Res</i>. 2016 Jan 1;22(1):69-78. doi:10.1158/1078-0432.CCR-15-1344. PMID: 26463708; PMCID: PMC4696604. 15. Taylor MR, Cole SW, Strom J, et al. Unfavorable transcriptome profiles and social disadvantage in hematopoietic cell transplantation: a CIBMTR analysis. <i>Blood Adv</i>. 2023 Nov 28;7(22):6830-6838. doi:10.1182/bloodadvances.2023010746. PMID: 37992686; PMCID: PMC10670894. 16. Rotz SJ, Bhatt NS, Hamilton BK, et al. International recommendations for screening and preventative practices for long-term survivors of transplantation and cellular therapy: a 2023 update. <i>Transplant Cell Ther</i>. 2024 Apr;30(4):349-385. doi:10.1016/j.jtct.2023.12.001. Epub 2023 Dec 28. PMID: 38159390; PMCID: PMC10874858.</p>
<p>CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning?</p>	<p>No, I do not have any conflicts of interest pertinent to this proposal</p>

Population characteristics of first HCT patients in the U.S. with 1 year PRO data, 2010-2023

Characteristic	Allogeneic	Autologous	Total
No. of patients	270	447	717
No. of centers	26	22	31
Patient-Related Characteristics			
Age, by decades, no. (%)			
Median (range)	61 (21-79)	62 (19-77)	62 (19-79)
18-19	0 (0)	1 (0)	1 (0)
20-29	14 (5)	10 (2)	24 (3)
30-39	25 (9)	13 (3)	38 (5)
40-49	36 (13)	42 (9)	78 (11)
50-59	54 (20)	124 (28)	178 (25)
60-69	100 (37)	185 (41)	285 (40)
70+	41 (15)	72 (16)	113 (16)
Sex, no. (%)			
Male	163 (60)	262 (59)	425 (59)
Female	107 (40)	185 (41)	292 (41)
Race, no. (%)			
White	218 (81)	358 (80)	576 (80)
Black or African American	4 (1)	48 (11)	52 (7)
Asian	24 (9)	13 (3)	37 (5)
Native Hawaiian or other Pacific Islander	1 (0)	1 (0)	2 (0)
American Indian or Alaska Native	0 (0)	1 (0)	1 (0)
More than one race	1 (0)	1 (0)	2 (0)
Not reported	22 (8)	25 (6)	47 (7)
Ethnicity, no. (%)			
Hispanic or Latino	26 (10)	44 (10)	70 (10)
Non-Hispanic or Latino	237 (88)	388 (87)	625 (87)
Not reported	7 (3)	15 (3)	22 (3)
Current CCN region of patient, no. (%)			
US	270 (100)	447 (100)	717 (100)
Karnofsky score prior to HCT, no. (%)			
90-100%	168 (62)	247 (55)	415 (58)
< 90%	102 (38)	199 (45)	301 (42)
Not reported	0 (0)	1 (0)	1 (0)
ECOG prior to HCT, no. (%)			
Asymptomatic	168 (62)	247 (55)	415 (58)
Symptomatic but completely ambulatory	101 (37)	192 (43)	293 (41)

Characteristic	Allogeneic	Autologous	Total
Symptomatic, < 50% in bed during the day	1 (0)	7 (2)	8 (1)
Not reported	0 (0)	1 (0)	1 (0)
HCT-CI, no. (%)			
0	65 (24)	115 (26)	180 (25)
1	43 (16)	84 (19)	127 (18)
2	46 (17)	76 (17)	122 (17)
3	39 (14)	71 (16)	110 (15)
4	39 (14)	47 (11)	86 (12)
5+	34 (13)	53 (12)	87 (12)
Not reported	4 (1)	1 (0)	5 (1)
Disease-Related Characteristics			
Primary disease, no. (%)			
AML	114 (42)	1 (0)	115 (16)
ALL	34 (13)	0 (0)	34 (5)
CLL	2 (1)	0 (0)	2 (0)
CML	8 (3)	0 (0)	8 (1)
MDS	68 (25)	0 (0)	68 (9)
Other acute leukemia	4 (1)	0 (0)	4 (1)
NHL	7 (3)	85 (19)	92 (13)
HD	4 (1)	19 (4)	23 (3)
MM	0 (0)	309 (69)	309 (43)
Other PCD	0 (0)	20 (4)	20 (3)
Solid tumor	0 (0)	5 (1)	5 (1)
Aplastic anemia	10 (4)	0 (0)	10 (1)
Paroxysmal nocturnal hemoglobinuria (PNH)	1 (0)	0 (0)	1 (0)
Autoimmune diseases	1 (0)	8 (2)	9 (1)
MPN	17 (6)	0 (0)	17 (2)
Interval from diagnosis to HCT, months, median (range)	6 (1-390)	8 (2-244)	7 (1-390)
Transplant-Related Characteristics			
Conditioning regimen intensity (F2400 pre-TED data), no. (%)			
MAC	110 (41)	0 (0)	110 (15)
RIC	108 (40)	0 (0)	108 (15)
NMA	33 (12)	0 (0)	33 (5)
N/A, not malignant disease	12 (4)	0 (0)	12 (2)
N/A, auto-HCT	0 (0)	447 (100)	447 (62)
Not reported	7 (3)	0 (0)	7 (1)
Conditioning regimen, no. (%)			
TBI/Cy	11 (4)	0 (0)	11 (2)

Characteristic	Allogeneic	Autologous	Total
TBI/Cy/Flu	52 (19)	0 (0)	52 (7)
TBI/Cy/Flu/TT	1 (0)	0 (0)	1 (0)
TBI/Mel	16 (6)	0 (0)	16 (2)
TBI/Flu	22 (8)	0 (0)	22 (3)
TBI/other(s)	5 (2)	0 (0)	5 (1)
Bu/Cy	26 (10)	10 (2)	36 (5)
Flu/Bu/TT	12 (4)	0 (0)	12 (2)
Flu/Bu	59 (22)	0 (0)	59 (8)
Flu/Mel	56 (21)	0 (0)	56 (8)
Cy/Flu	4 (1)	0 (0)	4 (1)
Cy alone	1 (0)	0 (0)	1 (0)
CBV	0 (0)	16 (4)	16 (2)
BEAM	0 (0)	68 (15)	68 (9)
BEAM like	0 (0)	2 (0)	2 (0)
Mel alone	2 (1)	326 (73)	328 (46)
Carb/Etop	0 (0)	5 (1)	5 (1)
TLI	1 (0)	0 (0)	1 (0)
Other(s)	2 (1)	17 (4)	19 (3)
Missing	0 (0)	3 (1)	3 (0)
Donor type, no. (%)			
Autologous HCT	0 (0)	447 (100)	447 (62)
HLA identical sibling	50 (19)	0 (0)	50 (7)
Twin	1 (0)	0 (0)	1 (0)
Haploidentical donor	39 (14)	0 (0)	39 (5)
Other related	5 (2)	0 (0)	5 (1)
Well-matched unrelated (8/8)	130 (48)	0 (0)	130 (18)
Partially-matched unrelated (7/8)	24 (9)	0 (0)	24 (3)
Multi-donor	1 (0)	0 (0)	1 (0)
Unrelated (matching cannot be determined)	15 (6)	0 (0)	15 (2)
Cord blood	5 (2)	0 (0)	5 (1)
Donor/recipient sex match, no. (%)			
M-M	104 (39)	0 (0)	104 (15)
M-F	56 (21)	0 (0)	56 (8)
F-M	48 (18)	0 (0)	48 (7)
F-F	44 (16)	0 (0)	44 (6)
CB - recipient M	5 (2)	0 (0)	5 (1)
Autologous HCT	0 (0)	447 (100)	447 (62)
Not reported	13 (5)	0 (0)	13 (2)

Characteristic	Allogeneic	Autologous	Total
GVHD prophylaxis, no. (%)			
CD34 selection	11 (4)	0 (0)	11 (2)
PtCy + other(s)	133 (49)	0 (0)	133 (19)
TAC + MMF +/- other(s) (except PtCy)	23 (9)	0 (0)	23 (3)
TAC + MTX +/- other(s) (except MMF, PtCy)	80 (30)	0 (0)	80 (11)
TAC + other(s) (except MMF, MTX, PtCy)	5 (2)	0 (0)	5 (1)
TAC alone	13 (5)	0 (0)	13 (2)
CSA + MMF +/- other(s) (except PtCy,TAC)	1 (0)	0 (0)	1 (0)
CSA + MTX +/- other(s) (except PtCy,TAC,MMF)	1 (0)	0 (0)	1 (0)
Other(s)	1 (0)	0 (0)	1 (0)
Autologous HCT	0 (0)	447 (100)	447 (62)
Missing	2 (1)	0 (0)	2 (0)
Donor age, by decades, no. (%)			
Median (range)	32 (0-71)	N/A	32 (0-71)
0-9	1 (0)	0 (0)	1 (0)
10-19	9 (3)	0 (0)	9 (1)
20-29	97 (36)	0 (0)	97 (14)
30-39	76 (28)	0 (0)	76 (11)
40-49	29 (11)	0 (0)	29 (4)
50-59	26 (10)	0 (0)	26 (4)
60-69	14 (5)	0 (0)	14 (2)
70+	1 (0)	0 (0)	1 (0)
Not reported	17 (6)	447 (100)	464 (65)
Year of current transplant, no. (%)			
2020	3 (1)	7 (2)	10 (1)
2021	54 (20)	111 (25)	165 (23)
2022	132 (49)	242 (54)	374 (52)
2023	81 (30)	87 (19)	168 (23)
PRO data availability			
PRO data availability, no. (%)			
Baseline + 1-year + 1 other timepoint	62 (23)	64 (14)	126 (18)
Baseline + 1-year	0 (0)	1 (0)	1 (0)
1-year + 1 other post-HCT timepoint	203 (75)	375 (84)	578 (81)
Only 1-year	5 (2)	7 (2)	12 (2)
Follow-up of survivors, median (range), months	24 (6-51)	25 (1-52)	25 (1-52)

Field	Response
Proposal Number	2509-222-EPSTEIN
Proposal Title	Incidence and risk factors of head and neck cancers in HCT recipients
Key Words	head and neck cancers, squamous cell carcinoma, HPV
Principal Investigator #1: - First and last name, degree(s)	Joel Epstein, DMD
Principal Investigator #1: - Email address	jepstein@coh.org
Principal Investigator #1: - Institution name	City of Hope
Principal Investigator #1: - Academic rank	Professor
Junior investigator status (defined as 助、5 years from fellowship)	No
Do you identify as an underrepresented/minority?	No
We encourage a maximum of two Principal Investigators per study. If more than one author is listed, please indicate who will be identified as the corresponding PI below:	Dr. Joel Epstein
Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.	none
Do any of the PI(s) within this proposal have a CIBMTR WC study in manuscript preparation >6 months?	No
PROPOSED WORKING COMMITTEE:	Morbidity, Recovery and Survivorship
Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.	No
RESEARCH QUESTION:	What is the incidence and risk factors for head and neck cancers in patients who underwent allogeneic HCT?
RESEARCH HYPOTHESIS:	We hypothesize that 1) head and neck cancers are rare, but 2) have poor prognosis if developed, and 3) its occurrence is associated with a few key clinical factors such as chronic GVHD, intensive immunosuppression, use of FTBI, and h/o smoking.
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	Primary: to define the incidence of head and neck cancers in allogeneic HCT recipients Secondary: 1) to describe clinical characteristics and prognosis of head and neck cancers in HCT recipients 2) to identify risk factors associated with development of head and neck cancers

Field	Response
SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.	It is known that the incidence of head and neck cancers is increased in HCT survivors. Understanding of the incidence and risk factors of head and neck cancers will inform the risk-stratified approaches for screening and prevention, possibly early treatment for leukoplakia as preemption. The outcome data will also help identify the gap in care and understanding of the specific biology (i.e. immunosuppression, involvement of HPV, etc.), which may lead to unique treatment approaches including the use of checkpoint inhibitors.

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

Hematopoietic cell transplantations (HCT) has increased over the last decades and with increased survival (1) (2), resulting in increased need for management of survivors in clinical practice. Following HCT secondary cancers have been identified at increased risk independent of the prior cancer leading to HCT, of these oral squamous cell carcinoma (OSCC) and oropharyngeal squamous cell carcinoma (OPC), as well as other secondary cancers including lymphoma and salivary gland cancer are reported (4) (5). It has also been suggested that OSCC/OPC occurring in this setting may be multifocal and may have a more aggressive course (6). Increased risk of secondary oral cancers are reported in allogeneic HCT survivors, estimated to be 7-16 times the risk in the general population (4) (5) (7) (8). In addition, patients are also at risk of secondary oral dysplasia. The risk may be higher in patients with chronic Graft versus Host Disease (cGVHD) and specifically in those with oral involvement (9). Chronic mucosal inflammation, immunosuppression may increase risk for dysplastic change and progression (10) (11). Additional risk has been suggested with azathioprine, disease type and pre-SCT treatment, conditioning regimen, stem cell source, young as well as advanced age at HCT, male gender, and genetic predisposition (4) (12) (10) (13) (14). The risk for oral cancer risk following autologous and reduced intensity conditioning regimen may also occur (15), (16). Some studies report an association between HPV and oral cancer post HCT (17) (18).

The previous registration study (19) evaluated all solid cancers including head and neck cancer and demonstrated a significantly increased risk of these cancers in HCT survivors. However, the report included mostly younger patients (over 90% were age <50) using myeloablative conditioning. Since age is a major risk factor for head and neck cancers, more contemporary data are needed. Moreover, since then there have been significant advances in both HCT and treatment of head and neck cancers such as checkpoint inhibitors. Therefore, there is clear needs in understanding the incidence, risk factors, and outcomes of head and neck cancers occurring in HCT recipients in more contemporary era. Clinical relevance and practical considerations - Increased risk for oral second malignancies in allogeneic HCT survivors - Oral cancer surveillance, with additional care in patients with cGVHD - Patients should be educated about the risk of secondary cancers and should reduce all risk factors: (smoking, alcohol abuse,

Field	Response
	<p>sun exposure of the lips) - Effective management of oral cGVHD with thorough, regular clinical follow up, may be more challenging due to presence of oral GVHD and assessment to determine need for tissue evaluation - Evaluation of potential prevention (eg: comparing those on metformin and those not); continuing immunosuppression, HPV infection etc</p> <ul style="list-style-type: none"> Outcomes of cancer therapy in HCT patents treated for oral cancer, including local and systemic toxicity of therapy and cancer outcomes Evaluation of potential risk factors for oral leukoplakia, dysplastic lesions and SCC Patients with Fanconi Anemia (FA) and dyskeratosis congenita (DKC) have increased risk for oral cancer which may be impacted by HCT.
<p>PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.</p>	<p>- any patients who underwent allogeneic HCT (up to 2023) - no age restrictions - all genders - any donor types - any conditioning regimens - any indications for HCTs - both malignant and non-malignant diseases</p>
<p>Does this study include pediatric patients?</p>	<p>Yes</p>
<p>DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Outline any supplementary data required.</p>	<p>Patient characteristics: Age (years), gender Primary cancer, leading to SCT: date of DX, date of transplant, prior tx Primary disease status: remission, active Donor type graft source Conditioning - MAC vs. RIC, TBI usage/dose GVHD prophylaxis Mucositis during SCT if available; candidiasis, opioid use (y/n) Dental pain/infection; dental cavities/abscess, gum disease GVHD prophylaxis aGVHD: sites, grade; management cGVHD: sites, grade, management cGVHD: oral involvement (y/n) Mucosal lesions: leukoplakia, ulceration HNC: Time from HCT Site, stage at Dx Oral/dental care: plaque/gingivitis/xerostomia Tobacco Hx/current Alcohol Hx/current Tumor DX Date (month/year) (repeat if multiple): histologic finding/diagnosis Pathology: HPV? Candida (repeat if multiple)? Complications of HNC TX if available</p> <ul style="list-style-type: none"> . Mucositis Candidiasis Pain trismus dysphagia esthetics Outcome: time post HNC TX of last followup: NED, AWD, progression Additional HNC (if yes repeat above)
<p>Types of cellular therapy data this proposal includes:</p>	<p>Hematopoietic Cell Transplantation (HCT)</p>

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Field	Response
	<p>2016;45(7):469-74. 12. Bhatia S, Louie AD, Bhatia R, O'Donnell MR, Fung H, Kashyap A, et al. Solid cancers after bone marrow transplantation. J Clin Oncol. 2001;19(2):464-71. 13. Demarosi F, Lodi G, Carrassi A, Soligo D, Sardella A. Oral malignancies following HSCT: graft versus host disease and other risk factors. Oral Oncol. 2005;41(9):865-77. 14. Morton LM, Saber W, Baker KS, Barrett AJ, Bhatia S, Engels EA, et al. National Institutes of Health Hematopoietic Cell Transplantation Late Effects Initiative: The Subsequent Neoplasms Working Group Report. Biol Blood Marrow Transplant. 2017;23(3):367-78. 15. Ringden O, Brazauskas R, Wang Z, Ahmed I, Atsuta Y, Buchbinder D, et al. Second solid cancers after allogeneic hematopoietic cell transplantation using reduced-intensity conditioning. Biol Blood Marrow Transplant. 2014;20(11):1777-84. 16. Bilton IA, Ashton LJ, Le Marsney RE, Dodds AJ, O'Brien TA, Wilcox L, et al. Second cancer risk in adults receiving autologous haematopoietic SCT for cancer: a population-based cohort study. Bone Marrow Transplant. 2014;49(5):691-8. 17. Zhang L, Epstein JB, Poh CF, Berean K, Lam WL, Zhang X, et al. Comparison of HPV infection, p53 mutation and allelic losses in post-transplant and non-posttransplant oral squamous cell carcinomas. J Oral Pathol Med. 2002;31(3):134-41. 18. Zhao H, Duan Z, Li M, Chiao E, Ahmed S, Shih YT, et al. Increased Incidence of Human Papillomavirus-Related Precancer or Second Malignancy Among Allogeneic Stem Cell Transplantation Patients: A SEER-Medicare Population Study. Transplant Cell Ther. 2021;27(12):1016 e1-e9. 19. Rizzo JD, Curtis RE, Soci G, Sobocinski KA, Gilbert E, Landgren O, et al. Solid cancers after allogeneic hematopoietic cell transplantation. Blood. 2009;113:1175-83.</p>
<p>CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning?</p>	<p>Yes, I have conflicts of interest pertinent to this proposal</p>

Population characteristics of first alloHCT patients before 2023, stratified by oropharyngeal cancer

Characteristic	No	Yes	Total
No. of patients	150968	203	151171
No. of centers	420	90	420
Patient-Related Characteristics			
Age, by decades, no. (%)			
Median (range)	49 (<1-88)	54 (2-78)	49 (<1-88)
0-9	17475 (12)	5 (2)	17480 (12)
10-19	14004 (9)	15 (7)	14019 (9)
20-29	14032 (9)	12 (6)	14044 (9)
30-39	13967 (9)	21 (10)	13988 (9)
40-49	19052 (13)	30 (15)	19082 (13)
50-59	30588 (20)	60 (30)	30648 (20)
60-69	33811 (22)	49 (24)	33860 (22)
70+	8039 (5)	11 (5)	8050 (5)
Sex, no. (%)			
Male	88287 (58)	129 (64)	88416 (58)
Female	62681 (42)	74 (36)	62755 (42)
Race, no. (%)			
White	105428 (70)	170 (84)	105598 (70)
Black or African American	10316 (7)	13 (6)	10329 (7)
Asian	10827 (7)	5 (2)	10832 (7)
Native Hawaiian or other Pacific Islander	614 (0)	1 (0)	615 (0)
American Indian or Alaska Native	653 (0)	0 (0)	653 (0)
More than one race	1733 (1)	2 (1)	1735 (1)
Not reported	21397 (14)	12 (6)	21409 (14)
Ethnicity, no. (%)			
Hispanic or Latino	15963 (11)	12 (6)	15975 (11)
Non-Hispanic or Latino	100563 (67)	171 (84)	100734 (67)
Non-resident of the U.S.	32145 (21)	18 (9)	32163 (21)
Not reported	2297 (2)	2 (1)	2299 (2)
CCN region at transplant, no. (%)			
U.S	107701 (71)	164 (81)	107865 (71)
Non U.S	43267 (29)	39 (19)	43306 (29)
Karnofsky score prior to HCT, no. (%)			
90-100%	96554 (64)	134 (66)	96688 (64)
< 90%	50343 (33)	64 (32)	50407 (33)
Not reported	4071 (3)	5 (2)	4076 (3)

Characteristic	No	Yes	Total
ECOG prior to HCT, no. (%)			
Asymptomatic	96554 (64)	134 (66)	96688 (64)
Symptomatic but completely ambulatory	47492 (31)	58 (29)	47550 (31)
Symptomatic, < 50% in bed during the day	2540 (2)	5 (2)	2545 (2)
Symptomatic, > 50% in bed, but not bedbound	214 (0)	1 (0)	215 (0)
Bedbound	97 (0)	0 (0)	97 (0)
Not reported	4071 (3)	5 (2)	4076 (3)
HCT-CI, no. (%)			
0	55299 (37)	77 (38)	55376 (37)
1	21731 (14)	19 (9)	21750 (14)
2	18501 (12)	24 (12)	18525 (12)
3	21224 (14)	30 (15)	21254 (14)
4	13120 (9)	21 (10)	13141 (9)
5+	16228 (11)	22 (11)	16250 (11)
Not reported	4865 (3)	10 (5)	4875 (3)
Disease-Related Characteristics			
Primary disease, no. (%)			
AML	52945 (35)	65 (32)	53010 (35)
ALL	22676 (15)	19 (9)	22695 (15)
Other leukemia	820 (1)	0 (0)	820 (1)
CLL	2542 (2)	6 (3)	2548 (2)
CML	4528 (3)	7 (3)	4535 (3)
MDS	20934 (14)	29 (14)	20963 (14)
Other acute leukemia	1981 (1)	2 (1)	1983 (1)
NHL	11871 (8)	32 (16)	11903 (8)
HD	2790 (2)	11 (5)	2801 (2)
MM	2428 (2)	2 (1)	2430 (2)
Other PCD	295 (0)	1 (0)	296 (0)
Solid tumor	162 (0)	0 (0)	162 (0)
Aplastic anemia	6770 (4)	6 (3)	6776 (4)
Inherited abnormal of erythrocyte differ.	2 (0)	0 (0)	2 (0)
Inherited bone marrow failure syndromes	1902 (1)	9 (4)	1911 (1)
Hemoglobinopathies	5301 (4)	1 (0)	5302 (4)
Paroxysmal nocturnal hemoglobinuria (PNH)	306 (0)	0 (0)	306 (0)
Disorders of the immune system	3995 (3)	1 (0)	3996 (3)
Inherited abnormalities of platelets	157 (0)	0 (0)	157 (0)
Inherited disorders of metabolism	1316 (1)	0 (0)	1316 (1)
Histiocytic disorders	1234 (1)	2 (1)	1236 (1)

Characteristic	No	Yes	Total
Autoimmune diseases	143 (0)	0 (0)	143 (0)
Other disease	148 (0)	0 (0)	148 (0)
Tolerance induction associated with solid organ transplant	21 (0)	0 (0)	21 (0)
Recessive dystrophic epidermolysis bullosa	1 (0)	0 (0)	1 (0)
MPN	5700 (4)	10 (5)	5710 (4)
Interval from diagnosis to HCT, months, median (range)	8 (0-1208)	12 (0-351)	8 (0-1208)
Transplant-Related Characteristics			
Conditioning regimen intensity (F2400 pre-TED data), no. (%)			
MAC	67569 (45)	80 (39)	67649 (45)
RIC	41692 (28)	69 (34)	41761 (28)
NMA	14512 (10)	22 (11)	14534 (10)
N/A, not malignant disease	21126 (14)	19 (9)	21145 (14)
Not reported	6069 (4)	13 (6)	6082 (4)
Conditioning regimen, no. (%)			
TBI/Cy	13998 (9)	15 (7)	14013 (9)
TBI/Cy/Flu	15723 (10)	16 (8)	15739 (10)
TBI/Cy/Flu/TT	1014 (1)	1 (0)	1015 (1)
TBI/Cy/TT	1287 (1)	2 (1)	1289 (1)
TBI/Cy/VP	959 (1)	0 (0)	959 (1)
TBI/VP	2599 (2)	2 (1)	2601 (2)
TBI/Mel	3736 (2)	3 (1)	3739 (2)
TBI/Flu	12751 (8)	15 (7)	12766 (8)
TBI/other(s)	1783 (1)	4 (2)	1787 (1)
Bu/Cy/Mel	537 (0)	0 (0)	537 (0)
Bu/Cy	19747 (13)	19 (9)	19766 (13)
Bu/Mel	986 (1)	0 (0)	986 (1)
Flu/Bu/TT	2932 (2)	1 (0)	2933 (2)
Flu/Bu	35300 (23)	56 (28)	35356 (23)
Flu/Mel/TT	1972 (1)	2 (1)	1974 (1)
Flu/Mel	21032 (14)	36 (18)	21068 (14)
FCR	565 (0)	3 (1)	568 (0)
Cy/Flu	4098 (3)	8 (4)	4106 (3)
Cy alone	1680 (1)	2 (1)	1682 (1)
CBV	89 (0)	1 (0)	90 (0)
BEAM	550 (0)	2 (1)	552 (0)
BEAM like	30 (0)	0 (0)	30 (0)
Mel alone	244 (0)	0 (0)	244 (0)
Mel/other(s)	356 (0)	1 (0)	357 (0)

Characteristic	No	Yes	Total
Treosulfan	2732 (2)	3 (1)	2735 (2)
Carb/Etop	3 (0)	0 (0)	3 (0)
Carb/other(s)	8 (0)	0 (0)	8 (0)
TLI	838 (1)	1 (0)	839 (1)
Other(s)	2379 (2)	7 (3)	2386 (2)
None	152 (0)	0 (0)	152 (0)
Missing	888 (1)	3 (1)	891 (1)
Donor type, no. (%)			
HLA identical sibling	45849 (30)	71 (35)	45920 (30)
Twin	497 (0)	0 (0)	497 (0)
Haploidentical donor	20143 (13)	12 (6)	20155 (13)
Other related	3759 (2)	3 (1)	3762 (2)
Well-matched unrelated (8/8)	50275 (33)	84 (41)	50359 (33)
Partially-matched unrelated (7/8)	9601 (6)	7 (3)	9608 (6)
Mismatched unrelated (<= 6/8)	587 (0)	1 (0)	588 (0)
Multi-donor	929 (1)	2 (1)	931 (1)
Unrelated (matching cannot be determined)	9640 (6)	14 (7)	9654 (6)
Cord blood	9688 (6)	9 (4)	9697 (6)
Donor/recipient sex match, no. (%)			
M-M	52818 (35)	75 (37)	52893 (35)
M-F	33063 (22)	43 (21)	33106 (22)
F-M	29583 (20)	48 (24)	29631 (20)
F-F	25079 (17)	28 (14)	25107 (17)
CB - recipient M	5654 (4)	6 (3)	5660 (4)
CB - recipient F	4372 (3)	3 (1)	4375 (3)
Not reported	399 (0)	0 (0)	399 (0)
GVHD prophylaxis, no. (%)			
Ex-vivo T-cell depletion	1879 (1)	1 (0)	1880 (1)
CD34 selection	2280 (2)	7 (3)	2287 (2)
PtCy + other(s)	29877 (20)	15 (7)	29892 (20)
PtCy alone	778 (1)	0 (0)	778 (1)
TAC + MMF +/- other(s) (except PtCy)	14689 (10)	21 (10)	14710 (10)
TAC + MTX +/- other(s) (except MMF, PtCy)	44521 (29)	75 (37)	44596 (30)
TAC + other(s) (except MMF, MTX, PtCy)	6289 (4)	18 (9)	6307 (4)
TAC alone	2909 (2)	3 (1)	2912 (2)
CSA + MMF +/- other(s) (except PtCy,TAC)	13169 (9)	16 (8)	13185 (9)
CSA + MTX +/- other(s) (except PtCy,TAC,MMF)	24725 (16)	36 (18)	24761 (16)
CSA + other(s) (except PtCy,TAC,MMF,MTX)	1474 (1)	3 (1)	1477 (1)

Characteristic	No	Yes	Total
CSA alone	3687 (2)	1 (0)	3688 (2)
Other(s)	2554 (2)	4 (2)	2558 (2)
Missing	2137 (1)	3 (1)	2140 (1)
Donor age, by decades, no. (%)			
Median (range)	31 (0-152)	32 (4-69)	31 (0-152)
0-9	6864 (5)	4 (2)	6868 (5)
10-19	8984 (6)	5 (2)	8989 (6)
20-29	44943 (30)	68 (33)	45011 (30)
30-39	27128 (18)	25 (12)	27153 (18)
40-49	17320 (11)	28 (14)	17348 (11)
50-59	12880 (9)	17 (8)	12897 (9)
60-69	6625 (4)	14 (7)	6639 (4)
70+	765 (1)	0 (0)	765 (1)
Not reported	25459 (17)	42 (21)	25501 (17)
Year of current transplant, no. (%)			
2008	6634 (4)	19 (9)	6653 (4)
2009	7484 (5)	14 (7)	7498 (5)
2010	8134 (5)	21 (10)	8155 (5)
2011	8734 (6)	21 (10)	8755 (6)
2012	9111 (6)	25 (12)	9136 (6)
2013	9002 (6)	21 (10)	9023 (6)
2014	9064 (6)	14 (7)	9078 (6)
2015	9044 (6)	17 (8)	9061 (6)
2016	9396 (6)	16 (8)	9412 (6)
2017	9763 (6)	9 (4)	9772 (6)
2018	10236 (7)	5 (2)	10241 (7)
2019	10857 (7)	7 (3)	10864 (7)
2020	9791 (6)	3 (1)	9794 (6)
2021	10384 (7)	5 (2)	10389 (7)
2022	11026 (7)	4 (2)	11030 (7)
2023	12308 (8)	2 (1)	12310 (8)
Follow-up of survivors, median (range), months	61 (0-208)	144 (12-194)	61 (0-208)