Not for publication or presentation

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 HST

Co-Chair:	**Hélène Schoemans, MD, PhD; University Hospitals Leuven and KU Leuven; Telephone: 321-634-6889; Email: helene.schoemans@uzleuven.be**
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Statistician:	**Andrew Peterson, MS; CIBMTR® (Center for International Blood and Marrow Transplant Research), Milwaukee, WI; Telephone: 414-805-8163; E-mail: andpeterson@mcw.edu**

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1. **Introduction**
   a. Minutes from February 2024 (Attachment 1)

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, Sorror 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, Sorror 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. **LE19-01c** Cheng G, Smith M, Phelan R, Brazauskas R, Strom J, Ahn KW, Hamilton B, Peterson A, Savani B, Schoemans H, Schoettler M, Sorror 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.***

e. **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.***

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 (P Satwani/ L 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 2410-248** Impact of Li Fraumeni syndrome upon outcomes of Hematopoietic stem cell transplant recipients of hematologic malignancies (K Singh Sandhu/ R Nakamura)(Attachment 4)
b. **PROP 2410-02** Association of fludarabine exposure on car-t outcomes (K Sweiss/ S Ahmed) (Attachment 5)
c. **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 6)

d. **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 7)
e. **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 8)
f. **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 9)
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)
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 (J Holter Chakrabarty/ P Vallabhaneni) (Attachment 11)

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 Fraint). ***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

MINUTES AND OVERVIEW PLAN
CIBMTR WORKING COMMITTEE FOR MORBIDITY, RECOVERY, AND SURVIVORSHIP
San Antonio, TX
Friday, February 23, 2024, 1:00 – 3:00 PM CT

Co-Chair:	**Betty Hamilton, MD; Cleveland Clinic Foundation, Cleveland, OH; Phone: 216-445-7580; E-mail: hamiltb2@ccf.org**
Co-Chair:	**Hélène Schoemans, MD, PhD; EBMT, University Hospitals Leuven and KU Leuven, Leuven, Belgium; Phone: 32 16 34 68 80; E-mail: helene.schoemans@uzleuven.be**
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Co-Chair:	**Mohamed Sorror, MD, MSc; Fred Hutchinson Cancer Research Center, Seattle, WA; Phone: 206-667-6298; Email: msorror@fredhutch.org**
Co-Chair:	**Sairah Ahmed, MD, PhD; M.D. Anderson Cancer Center, Houston, TX; E-mail: sahmed3@mdanderson.org**
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Statistical Director:	**Kwang Woo Ahn, PhD; CIBMTR® (Center for International Blood and Marrow Transplant Research), Medical College of Wisconsin, Milwaukee, WI; Telephone: 414-955-7387; Email: kwooahn@mcw.edu**
Statistician:	**Andy Peterson, MS; CIBMTR® (Center for International Blood and Marrow Transplant Research), Medical College of Wisconsin, Milwaukee, WI; E-mail: andpeterson@mcw.edu**

1. Introduction

a. Minutes and Overview Plan from February 2023 meeting

The CIBMTR Morbidity Recovery and Survivorship Working Committee (MRSWC) meeting was called to order at 1:00 CT on Friday, February 23, 2024 by Dr. Bipin Savani. He began by welcoming all the in-person and virtual attendees and providing the CIBMTR's Industry Funding Disclosure. Then, he introduced all the committee's leadership listed above, including Dr. Michelle Schoettler as our Working Committee Training and Leadership representative, Rebecca Higgins and Brandon Nuechterlein as our CAC representatives, and Dr. Amy Moskop (Co-Scientific Director) and Dr. Sairah Ahmed (Chair) joining us from the Cellular Immunotherapy WC. After reviewing the committee's COI disclosures, Dr. Savani explained that everyone attending this session has

been added to MRSWC membership! If you are unable to participate in a research study this year, we invite you to utilize the publicly available datasets on our website (cibmtr.org/datasets).

Dr. Hélène Schoemans then explained the scoring process for the proposals on a 1-9 (highest to lowest) scale based on scientific impact. Each presentation will be about 5 minutes with a 5-minute Q&A. We hope to select studies moving forward in one month. If your study is selected, anyone is welcome to have authorship given that they provide contributions to every stage of the study's lifecycle. Dr. Schoemans then explained our Transplant Essential Data (TED), which all patients contribute to, and our Comprehensive Report Forms, which only a subset of patients receives to contribute to more in-depth transplant research. Cellular therapy patients receive a different set of forms. CIBMTR has also begun collecting Patient-Reported Outcome (PRO) data across different physical, mental, and social health topics. For investigators that are early in your career, we invite you to participate in our WC's Training and Leadership Program, which will get you more involved in our committee's activities and statistical meetings.

2. Accrual Summary

3. Presentations, published or submitted papers

Dr. Rachel Phelan then introduced the studies in progress. Currently, we have 5 in protocol development, 5 in data file preparation, 1 in analysis, 4 in manuscript preparation, and 1 waiting to be published. She then gave a brief synopsis of each of these studies and their stage in the process.

a. **RT18-01a:** Broglie L, Friend BD, Chhabra S, Logan BR, Bupp C, Schiller G, Savani BN, Stadtmauer E, Abraham AA, Aljurf M, Badawy SM, Perez MAD, Guinan EC, Hashem H, Krem MM, Lazarus HM, Rotz SJ, Wirk B, Yared JA, Pasquini M, Thakar MS, Sorror ML. Expanded HCT-CI definitions capture comorbidity better for younger patients of allogeneic HCT for nonmalignant diseases. ***Transplantation and Cellular Therapy. 2023 Feb 1; 29(2):125.e1-125.e9. doi:10.1016/j.jtct.2022.11.020. Epub 2022 Nov 25. PMC9911359.***

b. **RT18-01b:** Friend BD, Broglie L, Logan BR, Chhabra S, Bupp C, Schiller G, Beitinjaneh A, Perez MAD, Guilcher G, Hashem H, Hildebrandt GC, Krem MM, Lazarus HM, Nishihori T, Nusrat R, Rotz SJ, Wirk B, Wieduwilt M, Pasquini M, Savani BN, Stadtmauer EA, Sorror ML, Thakar MS. Adapting the HCT-CI definitions for children, adolescents, and young adults with hematologic malignancies undergoing allogeneic hematopoietic cell transplantation. ***Transplantation and Cellular Therapy. 2023 Feb 1; 29(2):123.e1-123.e10. doi:10.1016/j.jtct.2022.11.019. Epub 2022 Nov 26. PMC9911376.***

c. **LE19-01a:** Zinter M, Brazauskas R, Strom J, Chen S, Bo-Subait S, Sharma A, Beitinjaneh A, Dimitrova D, Guilcher G, Preussler J, Myers K, Bhatt N, Ringden O, Hematti P, Hayashi R, Patel S, De Oliveira S, Rotz S, Badawy S, Nishihori T, Buchbinder D, Hamilton B, Savani B, Schoemans H, Sorror M, Winestone L, Duncan C, Phelan R, Dvorak C. Intensive care risk and long-term outcomes in pediatric allogeneic hematopoietic cell transplant recipients. ***Blood Advances. doi:10.1182/bloodadvances.2023011002. Epub 2023 Dec 21.***

d. **LE20-02:** Taylor MR, Cole SW, Strom J, Brazauskas R, Baker KS, Phelan R, Buchbinder D, Hamilton B, Schoemans H, Shaw BE, Sharma A, Bhatt NS, Badawy SM, Winestone LE, Preussler JM, Mayo S, Jamani K, Nishihori T, Lee MA, Knight JM. Unfavorable transcriptome profiles and social disadvantage in hematopoietic cell transplantation: A CIBMTR analysis. ***Blood Advances. 2023 Nov 28; 7(22):6830-6838. doi:10.1182/bloodadvances.2023010746. Epub 2023 Sep 29.***

e. **LE16-02b** Late effects after AlloHCT for pediatric patients with non-malignant diseases. (J Kahn/ P Satwani) ***Submitted.***

4. Studies in progress

a. **LE12-03a:** Outcomes for patients undergoing hematopoietic cell transplantation followed by solid organ transplants (M Gupta/ PL Abt/ M Levine) **Manuscript Preparation.**
b. **LE12-03b:** Outcomes for patients undergoing solid organ transplants followed by hematopoietic cell transplantation (M Gupta/ PL Abt/ M Levine) **Manuscript Preparation.**
c. **LE17-01a:** Late effects after hematopoietic stem cell transplantation for sickle cell disease. (E Stenger/ R Phelan/ S Shenoy/ L Krishnamurti) **Manuscript Preparation.**
d. **LE17-01b:** Comparison of survival between transplanted and non-transplanted SCD patients. (E Stenger/ R Phelan/ S Shenoy/ L Krishnamurti) **Data File Preparation.**
e. **LE18-01:** Trends in late mortality amongst two-year survivors of pediatric allogeneic hematopoietic cell transplantation for hematologic malignancies. (L Broglie/ P Satwani) **Manuscript Preparation.**
f. **LE19-01b:** POP TA-DAH! - Predictors of Pediatric Transplant Associated Diffuse Alveolar Hemorrhage (M Zinter/ C Dvorak/ C Duncan) **Data File preparation.**
g. **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. (M Veeraputhiran/ S Pingali/ A Mukherjee/ L Muffly) **Analysis.**
h. **LE20-01:** Cardiometabolic risk after total body irradiation during childhood. (D Novetsky Friedman/ E Chow) **Protocol Development.**
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) **Data File Preparation.**
k. **RT19-02:** Hemorrhagic cystitis as a complication of hematopoietic stem cell transplantation in the post-transplant cyclophosphamide graft-versus-host disease prophylaxis era compared to other allogeneic stem cell transplants (K Adekola/ N Ali/ O Frankfurt/ L Metheny/ J Moreira/ M de Lima) **Protocol Development.**
l. **RT20-01:** Toxicities of older adults receiving allogeneic hematopoietic cell transplant compared to younger patients (R Jayani/ H Murff) **Data File Preparation.**
m. **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/ C Duncan/ L Jimenez-Kurlander) **Protocol Development.**
n. **MRS22-02:** Post-transplant cyclophosphamide related cardiomyopathy; incidence, risk factors and outcome: A retrospective review from CIBMTR database (K Poonsombudlert/ C Strouse) **Protocol Development.**
o. **MRS23-01:** Updated Analysis of Long-Term Survival and Late Deaths after Allogeneic Hematopoietic Cell Transplantation for Hematologic Malignancies and Severe Aplastic Anemia (U Rao/ M Battiwalla) **Protocol Pending.**

5. Future/Proposed Studies

a. **PROP 2305-05/2310-55:** Defibrotide prophylaxis for hepatic sinusoidal obstructive syndrome in hematopoietic cellular therapy recipients: real-world outcomes and health care utilization implications (M Pamukcuoglu/ M Schoettler/ K Williams)

Dr. Betty Hamilton introduced Dr. Michelle Schoettler. This proposal is a case-control study with a pediatric and adult arm. The primary aim is to determine the difference in cumulative incidence of severe SOS in patients who received defibrotide prophylaxis for SOS vs. a matched cohort who did not receive defibrotide prophylaxis. This will be done for both the pediatric and adult arms separately. CIBMTR identified 215 adult patients with defibrotide prophylaxis and 86539 patients without that are eligible for the study in the TED retrieval (2009-2020). CIBMTR also identified 517 pediatric patients with defibrotide prophylaxis and 11788 without defibrotide prophylaxis that are eligible.

After the presentation, Dr. Phelan clarified that we hope to have more data available up until the present day as we continue to update our new database (HCT Essentials).

The first question from the audience noted that there is an increase in the utilization of defibrotide prophylaxis after 2015. This makes sense since defibrotide was approved by the FDA in March 2016. He was wondering if it would be worth amending the proposal to start at the FDA approval date instead of 2019. Dr. Schoettler said that they would use the timepoint in which they received defibrotide prophylaxis.

The second question noted that there may be a bit of bias in matching the patients across centers; they should figure out if the centers have set some scoring criteria to select defibrotide prophylaxis or classify VOD. Dr. Schoettler said that the study is limited by what is reported for SOS to the CIBMTR. In terms of severity, they can pull data from the forms and PHIS to collect data on renal failure.

The next question asked how the older patients at transplant in the pediatric group will be classified once they reach 18 years of age. They will need to look closer at the distribution of ages if the study progresses. It may be a good idea to combine the pediatric and adult cohorts together to avoid the center bias.

The fourth question asked if the PIs would compare defibrotide to those that did not receive prophylaxis or those that received a different type of prophylaxis. Dr. Schoettler said there should exist data on how other prophylaxis types perform. The intention is that the cohorts will be whether you got defibrotide, regardless of other prophylaxis.

The last question noted that there is a higher frequency of VOD on the prophylaxis arm. Since patients that got defibrotide may be a higher risk of VOD, they may need to take this into consideration as a confounder. They may do propensity score matching to address this. Also, it was asked if we have data on the dose of defibrotide or when it was stopped, which we do not.

b. **PROP 2310-28:** Toxicity profile and survival of patients with BMI >30 undergoing allogeneic stem cell transplantation (N Tijaro Ovalle/ A Jakubowski)

Dr. Hamilton introduced Dr. Natalia Tijaro Ovalle, who gave a virtual presentation. The primary aim of this proposal is to determine if increasing obesity impacts post-transplant toxicities in allogeneic transplant patients. Among the adult first allo-HCT patients for AML and MDS/MPN, CIBMTR identified 9887 eligible patients with BMI 25-29, 7174 patients with BMI 30-39, and 1226 patients with BMI 40+ from the CRF retrieval (2000-2020).

The first question noted that this study will have a lot of value in the BMI 40+ group. He asked if it would be reasonable to even further subdivide the BMI 40+ group. Dr. Tijaro Ovalle said that it would be interesting to look into these BMIs further and see if this is a possibility.

The second question asked if we have information on if the chemotherapy was adjusted and how much it was adjusted. Sometimes (especially with very high BMIS), physicians will make up a little more adjustment or not be sure what to do. She said that it will be very important for toxicity and relapse risk. Dr. Tijaro Ovalle replied that the old version of the 2000 form does ask about dose adjustments by weight. However, there are other ways to infer if there is any adjustment since we know the weight at transplant. She has reached out to Andy Peterson (Statistician for MRS) and confirmed that we can calculate adjusted weights in the SAS code.

The last question recommended looking at the cell dose because there is a discrepancy between the weight of the donor and the patient. Dr. Tijaro Ovalle said that this is something that she plans to include in the multivariate analysis.

c. **PROP 2310-35/2310-210:** Incidence, risk factors, and characteristics of subsequent neoplasms in CAR-T recipients and its impact on survival (M Shah/ V Irizarry Gatell/ R Faramand)

Dr. Hamilton introduced Dr. Vivian Irizarry Gatell. The primary aim of this proposal is to define the incidence, risk factors, and pattern of subsequent neoplasms and second hematological malignancies following CAR-T for adults with NHL or MM. Among the adult CAR-T patients that achieved remission at day 100, CIBMTR identified 3783 patients with NHL and 926 patients with MM that are eligible (This data will become available in 2 years, or with company approval, after the end of the data embargo. With this embargo applied, we currently have 3312 NHL patients and 128 MM/PCD patients eligible).

The first question asked why the PIs selected a landmark of 100 days. Dr. Irizarry Gatell said they want to make sure that they are not capturing patients who relapsed within the first 100 days. In the inclusion criteria, they select patients that achieved complete CR up until day 100. She also asked if we are confident that the cases of NHL and ALL defined as second malignancies are not relapse. Dr. Irizarry Gatell responded that since there are only a couple in which this is the case, they will go back to the path reports to confirm. Dr. Moskop said that some of these path reports have queries out, and some are still under review and actively being updated.

The second question alluded to a publication that came out a day before this meeting. This publication showed a model that is associated with myeloid neoplasms. He asked if there is an added benefit of this study compared to the publication. Dr. Irizarry Gatell added that they are not only looking at myeloid neoplasms, but also other solid tumors. We would hope to characterize T-cell lymphomas as well. He also asked about the baseline features that they want to explore. The PIs are interested in treatment related features, like whether they had a stem cell transplant and other therapies. They are also interested in the amount of inflammation that happens, so it would be good to look at the presence of CRS.

The next question was a suggestion that there may be a benefit to having a control group of patients that did not undergo CAR-T, or perhaps having a cohort of transplant patients. Dr. Irizarry Gatell acknowledged that this is a great suggestion and was initially not included in

case there were not enough patients. However, as they continue to look into the data, this may be a great option.

The last question asked why the PIs decided to exclude pediatric patients. Since they are stratifying by indication for CAR-T, they are unsure if they had enough patients. However, they are very happy to include pediatrics and ALL patients given that they have the numbers to power the analysis.

In the interest of time, we made this the last question for this proposal.

d. **PROP 2310-45:** The impact of obesity and body weight on immune mediated toxicities and outcomes of patients with relapsed/refractory large B cell lymphoma treated with CD19 CAR T cells (K Wudhikarn)

Dr. Hamilton introduced Dr. Kitsada Wudhikarn. The primary aim of this proposal is to explore if obesity affects toxicities and outcomes after CAR-T for large B-cell lymphoma patients. Amongst the adult CAR-T cell patients with large B-cell lymphoma, CIBMTR identified 1495 patients with BMI < 25, 1384 patients with BMI 25-29, and 1169 patients with BMI 30+ that are eligible for this study (This data will become available in 2 years, or with company approval, after the end of the data embargo. With this embargo applied, we currently have 1107 BMI < 25 patients, 1045 BMI 25-29 patients, and 922 BMI 30+ patients eligible).

The first question asked if we plan to stratify by disease burden for comparing outcomes. Dr. Wudhikarn said that this would be a great baseline characteristic for multivariate analysis, but the primary question will have us stratify by BMI.

The second question mentioned that it may be hard to explore interesting aspects of body habitus using CIBMTR data. She noted a paper that looks at visceral fat, which had a different impact compared to BMI. Dr. Wudhikarn notes that this may be a limitation of this study, and perhaps it would be something captured by another study in the future. She also asked why the PIs decided to stratify based on 100 kg. Dr. Wudhikarn said that for certain products, the cell dose has a cap according to the body weight, while other CAR-T products have a total cell dose captured by the form. She also asked if this question could be addressed using the publicly available datasets on the CIBMTR website. Dr. Moskop said that we have several lymphoma studies that are to be completed in the future, with some missing variables like chemo dose.

e. **PROP 2310-53/2310-232:** Impact of renal injury before CAR-T therapy (H Murthy/ M Iqbal/ A Mirza /L Gowda)

Dr. Hamilton introduced Dr. Sayeef Mirza. The primary aim of this proposal is to determine if renal insufficiency can predict an increase in toxicities and inferior survival in patients receiving CAR-T. Among the adult CAR-T patients, CIBMTR identified 296 patients with a renal injury comorbidity (sCR > 2 mg/dL) and 11724 patients without the comorbidity (This data will become available in 2 years, or with company approval, after the end of the data embargo. With this embargo applied, we currently have 8365 patients without renal injury and 146 patients with renal injury eligible).

The first question noted that they may need to tease out that renal insufficiency is part of the disease process for myeloma patients. Dr. Mirza said that it is a good point to study two different groups, lymphoma and myeloma, by nature of the disease. He also asked if it would be more informative to look at post-CAR-T renal injury instead of pre-Car-T renal injury. Dr. Mirza said that it is definitely of interest, and we would like to look at these outcomes.

The second question asked if there is more than just the level of serum creatinine captured in the forms, such as creatinine clearance and eGFR. Dr. Mirza said that this data is collected, but not all of it is reported. The best way to capture all these patients is to use the comorbidity score. They could do this with eGFR, but they would use a smaller subset of patients. Dr. Moskop noted that the eGFR question was recently added and thus has low reporting.

The last question asked why the PIs are using an eGFR cutoff of 60. For instance, fludarabine can be adjusted by over 20%. Some references use a cutoff of 30. Dr. Mirza said that they can look at different benchmarks and would be happy to incorporate suggestions. This eGFR cutoff was discussed amongst the CIBMTR team and would be subject to change as needed. She also asked about capping the serum creatine for the elderly and the type of weight that they use. They are happy to clarify the body weight standard used if the study moves forward.

f. **PROP 2310-128/2310-136/2310-212/2310-245**: Immune effector cell associated HLH-like Syndrome (IEC-HS) in patients undergoing CAR T cell therapy (T Jain/ K McNerney/ J Roman Diaz/ C Freeman/ L Gowda/ A Mirza/ S Gupta/ V Bachanova)

Dr. Hamilton introduced Dr. Tania Jain. The primary aim of this proposal is to describe the real-world incidence and clinical outcomes of IEC-HS in CAR-T patients. Among CAR-T patients, CIBMTR identified 143 patients that reported IEC-HS in follow-up and 8338 patients that did not (This data will become available in 2 years, or with company approval, after the end of the data embargo. With this embargo applied, we currently have 5931 patients without IEC-HS and 93 with IEC-HS eligible).

The first question was a comment that took note on the number of events. Although more may be added at the time of the study, the statistical power may be a concern if they are to do a predictive score and have a training and a validation set.

The second question asked what kind of statistical methods they would use to model the internal and external validation. Dr. Jain said that for the matched cohort, they will probably use propensity score matching. For the validation cohort, perhaps they can explore an external cohort like EBMT.

The last question was another comment that said there are a few working committees that are looking at this disease, such as adult lymphoma and multiple myeloma. However, these studies may not have overlapping patients because they are not all CAR-T.

g. **PROP 2310-160:** Determinants of Immune Effector Cell-Associated Hematotoxicity (ICAHT) following CAR-T therapy across Disease Entities (K Rejeski/ R Shouval)

Dr. Hamilton introduced Dr. Kai Rejeski. The primary aim of this proposal is to identify predictive markers for immune effector cell-associated hematotoxicity (ICAHT) at time of

leukapheresis and lymphodepletion in CAR-T patients. Since there is ongoing work in another committee focused on multiple myeloma, the PIs were encouraged to focus on the lymphoma population. Among the adult patients with B-cell lymphoma, CIBMTR found 8294 patients that are eligible (This data will become available in 2 years (or with company approval) after the end of the data embargo. With this embargo applied, we currently have 7098 patients eligible).

The first question asked if there is any thought in including ALL patients because prolonged cytopenias are a huge problem in this patient population as well. Dr. Rejeski said that it would be interesting to look at this in a subgroup. They were asked to focus on lymphoma due to the overlapping MM study, but it would be very interesting to validate the CAR-HEMATOTOX score and other predictive factors for ALL.

The second question asked if they would account for bridging therapies since they will look at apheresis as our timepoint. Dr. Rejeski said that they would look at both LD and validate the CAR-HEMATOTOX, which would be after bridging. Nonetheless, if they want to collect stem cells for a potential stem cell boost, they will need to do it earlier. It would be good to look at the types of bridging therapies associated with hematological toxicities. Nevertheless, if they want to develop a tool that is helpful at a very early timepoint, going to apheresis is the nature of the game. Dr. Moskop added that the data we collect is pre-LD chemo, and we do have data on bridging therapies.

The last question asked if they know how many patients have all the labs, since it appears that each patient needs all the lab values to calculate the score. Dr. Rejeski responded that they anticipate a CBC that's going to be available in more patients closer to 5000. By doing univariate modeling, they can look at the impact of specific markers. However, to have all 5 markers, the limiting factor is the inflammatory markers (CRP and ferritin). Conservatively, 1,500-1,600 patients would be used to calculate this score and being the largest validation of the score to date.

h. **PROP 2310-173:** Return to work among adolescent and young adult survivors of autologous stem cell transplantation in the US (N Khan)

Dr. Hamilton introduced Dr. Niloufer Khan. The primary aim of this proposal is to determine the incidence and associated factors of not returning to work after autologous transplant. Among autologous transplant patients in the U.S. at ages 18-39 with malignant conditions, CIBMTR found 862 patients that are eligible for this study in the CRF retrieval (2008-2020).

The first question said that he was involved in a prior project with a similar topic. However, since autologous transplants are voluntarily collected, they considered excluding autologous and using allogeneic instead. He also mentioned that there was some missingness in the employment data they used for their project. Thus, the voluntary reporting and missingness may cause a skewed perspective. Also, the employment question was revised in 2021 with more detailed information on employment. Dr. Khan said that this is helpful to know and potentially using the PRO data, specifically financial toxicity, would be a great addition. Although the numbers seem a bit small, these updated questions will contribute to more granular data in the future.

Proposed studies; not accepted for consideration at this time

a. **PROP 2305-04:** Comparing Icteric Veno-occlusive disease with Anicteric Veno-occlusive disease (VOD) according to Overall Survival (OS), VOD resolution time (RT) under the Defibrotide treatment. *Dropped due to unavailability of bilirubin data.*

b. **PROP 2309-07**: Cardiac Toxicity in Haploidentical transplant with PTCy vs Matched transplant with PTCy vs Matched Transplant with CNI. *Dropped due to overlap with MRS 22-02.*

c. **PROP 2309-10:** Use of Anakinra for the Treatment of ICANS after Anti-CD19 Autologous CART in B-cell Lymphoma. *Dropped due to lower impact.*

d. **PROP 2310-48:** Psychiatric and Cognitive Health Among Survivors of Chimeric Antigen Receptor Therapy in the United States. *Dropped due to not enough PRO data.*

e. **PROP 2310-65:** Machine Learning based Mortality Risk Assessment in Stem cell Transplant for Non-Malignant Bone Marrow Disorders. *Dropped due to low power with rare disease and low mortality.*

f. **PROP 2310-69:** Trends in Primary Graft Failure in allogeneic hematopoietic stem Cell Transplant Recipients. *Dropped due to lower impact.*

g. **PROP 2310-95:** Merging CIBMTR and SEER data to provide a resource for studying rare prior and subsequent neoplasms. *May consider as a separate effort.*

h. **PROP 2310-148:** Incidence and risk factors of engraftment syndrome in autologous hematopoietic cell transplant recipients and its impact on outcomes. *Dropped due to lower impact.*

i. **PROP 2310-159:** Early Platelet count recovery before white cell count recovery after allogeneic hematopoietic cell transplantation and effect on transplant outcomes. *Dropped due to lower impact.*

j. **PROP 2310-163:** Risk factors for long-term osteoporosis and fragility fractures after pediatric HCT. *Dropped due to not enough data for pediatric osteoporosis/fracture.*

k. **PROP 2310-189:** Updated Analysis of the Prevalence of Cellular Therapy Survivors in the United States. *May consider as a separate effort.*

l. **PROP 2310-195:** A comparison of Melphalan (Mel) dosing in the setting of post-transplant cyclophosphamide (PTCy) GVHD prophylaxis. *Dropped due to limitations on Mel dosing data.*

m. **PROP 2310-211:** Sexual Health Among Survivors of Chimeric Antigen Receptor T-cell Therapy in the United States. *Dropped due to not enough PRO data.*

n. **PROP 2310-216:** Long-term survival and late mortality among patients treated with allogeneic hematopoietic cell transplant for inborn errors of metabolism. *Dropped due to two MRSWC studies looking at late mortality.*

o. **PROP 2310-217:** Comprehensive Assessment of Health-Related Quality of Life (HRQoL), Toxicity and Clinical Outcomes Following Chimeric Antigen Receptor T-Cell Therapy for Hematological Malignancies. *Dropped due to not enough PRO data.*

p. **PROP 2310-218:** Efficacy of Three Prophylactic Measures to Mitigate the Toxicities in Chimeric Antigen Receptor (CAR) T-cell Therapy in Lymphoma. *Dropped due to low numbers of patients*

receiving prophylactic therapies.

q. **PROP 2310-250:** Incidence of hypogammaglobulinemia following CD19-directed CAR-T therapy and its impact on CAR-T persistence and outcomes. *Dropped due to not enough data on this topic.*

r. **PROP 2310-269:** Late mortality and standardized mortality ratio (SMR) in patients surviving after allogeneic hematopoietic cell transplantation (HCT). *Dropped due to overlap with MRS 23-01.*

6. Closing Remarks

Dr. Phelan provided the closing remarks, starting with additional information and website links to find out more on what we have available and ongoing studies. We will send out a quarterly newsletter after we make decisions on proposals moving forward. Next, Dr. Phelan announced that "International Recommendations for Screening and Preparative Regimens for Long-Term Survivors of Transplantation and Cellular Therapy: A 2023 Update" has been published in TCT and BMT on February 27, 2024! Also, we have put out a call for systematic review on female-specific late effects. We have over 180 responses in our call for volunteers. Chosen volunteers will be selected shortly after Tandem and thank you all for your interest!

We would like to acknowledge our 2 outgoing chairs: Dr. Betty Hamilton from Cleveland Clinic Foundation and Dr. Bipin Savani from Vanderbilt University Medical Center. Thank you so much for your contributions!

We would like to welcome our incoming chair: Dr. Seth Rotz from Cleveland Clinic Foundation. We are excited to have you on the team!

Thank you everyone, and please reach out if you would like to talk through projects!

Working Committee Overview Plan for 2024-2025		
Study Number and Title	**Current Status**	**Chairs Priority**
LE12-03a: Outcomes for patients undergoing hematopoietic cell transplantation followed by solid organ transplants	Manuscript preparation	1
LE12-03b: Outcomes for patients undergoing solid organ transplants followed by hematopoietic cell transplantation	Manuscript preparation	1
LE17-01: Late effects after hematopoietic stem cell transplantation for sickle cell disease.	Data file preparation	1
LE19-01b: POP TA-DAH! - Predictors of Pediatric Transplant Associated Diffuse Alveolar Hemorrhage	Submitted	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	Analysis	1
LE21-01: Risk of subsequent neoplasms in patients with post-transplant cyclophosphamide use for graft-versus-host disease prophylaxis	Data file preparation	3
RT19-01: Analysis of comorbidity-associated toxicity at a regimen-based level	Data file preparation	2
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	Protocol development	3
RT20-01: Toxicities of older adults receiving allogeneic hematopoietic cell transplant compared to younger patients	Data file preparation	1
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	3
MRS22-02: Post-transplant cyclophosphamide related cardiomyopathy; incidence, risk factors and outcome: A retrospective review from CIBMTR database	Protocol development	3
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 pending	3
MRS24-02: Determinants of immune effector cell-associated hematotoxicity (ICAHT) following CAR-T therapy across disease entities	Protocol pending	3

Table 1. TED vs. CRF Follow-up of adult patients (age >= 18) after allogeneic transplant reported to CIBMTR, 1990-2024

Characteristic	TED	Research
All patients	125775	63677
3-year survivors	49442	23508
5-year survivors	35287	17729
10-year survivors	14652	7526
15-year survivors	4666	2429
AML	48390	20921
3-year survivors	17927	7299
5-year survivors	12346	5516
10-year survivors	4520	2300
ALL	18543	7834
3-year survivors	6910	2565
5-year survivors	4731	1920
10-year survivors	1675	780
CML	15580	9120
3-year survivors	7372	3242
5-year survivors	5700	2584
10-year survivors	3018	1543
MDS/MPS	16588	12147
3-year survivors	6043	4885
5-year survivors	4029	3527
10-year survivors	1440	1138
MM	2288	1141
3-year survivors	856	371
5-year survivors	609	260
10-year survivors	277	99
LY	12021	5477
3-year survivors	4963	2081
5-year survivors	3871	1650
10-year survivors	1890	825

Characteristic	TED	Research
Other malignant	6082	3102
3-year survivors	2279	1135
5-year survivors	1677	843
10-year survivors	782	355
SAA	4331	2900
3-year survivors	2152	1443
5-year survivors	1687	1079
10-year survivors	833	373
Immun def disorder	279	120
3-year survivors	152	56
5-year survivors	101	40
10-year survivors	14	9
Other non-malignant	1479	914
3-year survivors	750	431
5-year survivors	509	310
10-year survivors	186	104

Table 2. Ted vs. CRF Follow-up of adult patients (age >= 18) after autologous transplant reported to CIBMTR, 1990-2024

Characteristic	TED	Research
All patients	207022	35656
3-year survivors	118363	19002
5-year survivors	83916	13418
10-year survivors	30567	4332
15-year survivors	8015	1029
AML	5832	1329
3-year survivors	2160	431
5-year survivors	1620	300
10-year survivors	919	133
ALL	940	208
3-year survivors	261	41
5-year survivors	182	26
10-year survivors	96	11
CML	453	207
3-year survivors	189	94
5-year survivors	133	54
10-year survivors	64	20
MDS/MPS	210	44
3-year survivors	93	22
5-year survivors	64	11
10-year survivors	30	2
MM	91443	14933
3-year survivors	59626	10259
5-year survivors	40981	7551
10-year survivors	11696	2170
LY	82537	11182
3-year survivors	45098	5680
5-year survivors	33349	4097
10-year survivors	13873	1596

Characteristic	TED	Research
Other malignant	24331	7614
3-year survivors	10456	2393
5-year survivors	7286	1318
10-year survivors	3766	367
SAA	11	3
3-year survivors	2	1
5-year survivors	1	1
10-year survivors	0	0
Immun def disorder	14	2
3-year survivors	10	2
5-year survivors	9	1
10-year survivors	0	0
Other non-malignant	1150	133
3-year survivors	417	78
5-year survivors	250	58
10-year survivors	95	32

Table 3. Ted vs. CRF Follow-up of pediatric (age < 18) patients after allogeneic transplant reported to CIBMTR, 1990-2024

Characteristic	TED	Research
All patients	33322	22424
3-year survivors	16232	10792
5-year survivors	12354	8499
10-year survivors	5552	4124
15-year survivors	1884	1304
AML	6413	3843
3-year survivors	2721	1524
5-year survivors	2026	1227
10-year survivors	941	640
ALL	9074	5541
3-year survivors	3960	2157
5-year survivors	3030	1726
10-year survivors	1412	896
CML	1350	854
3-year survivors	648	412
5-year survivors	502	342
10-year survivors	241	191
MDS/MPS	1789	1287
3-year survivors	858	582
5-year survivors	649	476
10-year survivors	280	297
MM	23	5
3-year survivors	12	3
5-year survivors	8	2
10-year survivors	4	0
LY	768	431
3-year survivors	311	156
5-year survivors	240	125
10-year survivors	112	53

Characteristic	TED	Research
Other malignant	687	415
3-year survivors	286	180
5-year survivors	203	147
10-year survivors	93	77
SAA	3185	2092
3-year survivors	1878	1216
5-year survivors	1481	937
10-year survivors	704	391
Immun def disorder	2874	2458
3-year survivors	1497	1464
5-year survivors	1104	1206
10-year survivors	480	588
Other non-malignant	7129	5498
3-year survivors	4050	3098
5-year survivors	3105	2311
10-year survivors	1285	991

Table 4. CRF Follow-up of pediatric (age < 18) patients after autologous transplant reported to CIBMTR, 1990-2024

Characteristic	TED	Research
All patients	13748	2756
3-year survivors	6513	1171
5-year survivors	4737	833
10-year survivors	2069	375
15-year survivors	664	103
AML	730	245
3-year survivors	343	49
5-year survivors	278	28
10-year survivors	149	14
ALL	266	122
3-year survivors	108	18
5-year survivors	80	7
10-year survivors	47	0
CML	20	3
3-year survivors	11	1
5-year survivors	7	0
10-year survivors	4	0
MDS/MPS	19	4
3-year survivors	7	0
5-year survivors	5	0
10-year survivors	3	0
MM	99	2
3-year survivors	16	1
5-year survivors	10	1
10-year survivors	3	0
LY	2515	347
3-year survivors	1221	178
5-year survivors	896	129
10-year survivors	376	41

Characteristic	TED	Research
Other malignant	9881	1967
3-year survivors	4709	882
5-year survivors	3398	633
10-year survivors	1464	314
SAA	4	2
3-year survivors	2	1
5-year survivors	2	1
10-year survivors	1	0
Immun def disorder	16	45
3-year survivors	12	32
5-year survivors	5	25
10-year survivors	0	2
Other non-malignant	171	19
3-year survivors	76	9
5-year survivors	50	9
10-year survivors	19	4

Table 5. First CAR-T infusions

Characteristic	N (%)
No. of patients	16516
No. of centers	244
Patient Characteristics	
Age, by decades - no. (%)	
Median (min-max)	63 (0-91)
0-9	562 (3)
10-19	712 (4)
20-29	670 (4)
30-39	629 (4)
40-49	1203 (7)
50-59	2992 (18)
60-69	5348 (32)
70+	4400 (27)
Recipient Sex - no. (%)	
Male	10285 (62)
Female	6228 (38)
Not reported	3 (0)
Recipient race - no. (%)	
White	12508 (76)
Black or African American	1186 (7)
Asian	777 (5)
Native Hawaiian or other Pacific Islander	41 (0)
American Indian or Alaska Native	71 (0)
Other	109 (1)
More than one race	837 (5)
Not reported	987 (6)
Ethnicity - no. (%)	
Hispanic or Latino	2139 (13)
Non-Hispanic or Latino	12555 (76)
Non-resident of the U.S.	1305 (8)
Not reported	517 (3)
Karnofsky performance score prior to CT - no. (%)	
90-100	6871 (42)
80	4859 (29)
< 80	3021 (18)
Not reported	1765 (11)

Characteristic	N (%)
HCT-CI Score - no. (%)	
0	5077 (31)
1	3261 (20)
2	2227 (13)
3	2363 (14)
4	1520 (9)
5+	1804 (11)
Not reported	264 (2)
Disease related	
Disease - no. (%)	
Acute myeloid leukemia (AML)	47 (0)
Acute lymphoblastic leukemia (ALL)	2031 (12)
Other leukemia (including CLL/PLL)	36 (0)
Chronic myeloid leukemia (CML)	4 (0)
Myelodysplastic/myeloproliferative diseases (MDS/MPN)	3 (0)
Acute leukemia of ambiguous lineage and other myeloid neoplasms	10 (0)
Non-Hodgkin lymphoma (NHL)	11006 (67)
Hodgkin lymphoma (HD)	23 (0)
Plasma cell disorder/multiple myeloma (PCD/MM)	3269 (20)
Solid tumor	24 (0)
Autoimmune diseases	1 (0)
Other indication	6 (0)
Not reported	56 (0)
Disease status prior to infusion	
Disease status prior to CT for leukemia - no. (%)	
Disease is not leukemia	14428 (87)
CR1	237 (1)
CR2	363 (2)
CR3+	235 (1)
Relapse, 1st	519 (3)
Relapse, other	473 (3)
PIF/Untreated	215 (1)
Not reported	46 (0)
Disease status prior to CT for lymphoma - no. (%)	
Disease is not lymphoma	5487 (33)
CR	767 (5)
PR	2340 (14)
Resistant	6582 (40)

Characteristic	N (%)
Untreated	669 (4)
Unknown	623 (4)
Not reported	48 (0)
Disease status prior to CT for PCD - no. (%)	
Disease is not MM/PCD	13247 (80)
Stringent complete remission (sCR)	23 (0)
Complete remission (CR)	51 (0)
Very good partial remission (VGPR)	310 (2)
Partial response (PR)/ Not Complete Remission	405 (2)
Stable disease (SD)	534 (3)
Progressive disease (PD)	1863 (11)
Relapse from CR (Rel) (untreated)	62 (0)
Not reported	21 (0)
Infusion related	
Lymphodepleting regimen - no. (%)	
Fludarabine + Cyclophosphamide	12843 (78)
Bendamustine only	1100 (7)
Others	2513 (15)
None	58 (0)
Not reported	2 (0)
Product - no. (%)	
Kymriah	2908 (18)
Yescarta	6500 (39)
Tecartus	1387 (8)
Breyanzi	1199 (7)
Abecma	1549 (9)
Carvykti	1372 (8)
Other	1601 (10)
Commercial vs. noncommercial CAR-T product - no. (%)	
Commercial	14915 (90)
Noncommercial	1601 (10)
Is the recipient participating in a cellular therapy clinical trial? - no. (%)	
No	14557 (88)
Yes	1956 (12)
Not reported	3 (0)
2-year product embargo - no. (%)	
No	13117 (79)
Yes	3399 (21)

Characteristic	**N (%)**
Year of infusion - no. (%)	
Before 2017	82 (0)
2017	122 (1)
2018	813 (5)
2019	1409 (9)
2020	1669 (10)
2021	2352 (14)
2022	3802 (23)
2023	4742 (29)
2024	1525 (9)
Follow-up of survivors, months - median (range)	14 (0-4880)

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

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Number of patients	50520	24709	13268
Source of data			
CRF	25730 (51)	9079 (37)	5980 (45)
TED	24790 (49)	15630 (63)	7288 (55)
Number of centers	265	245	396
Disease at transplant			
AML	17660 (35)	9401 (38)	4437 (33)
ALL	7264 (14)	3073 (12)	2113 (16)
Other leukemia	1493 (3)	488 (2)	335 (3)
CML	3610 (7)	1233 (5)	1063 (8)
MDS	7617 (15)	4675 (19)	1739 (13)
Other acute leukemia	565 (1)	301 (1)	151 (1)
NHL	4389 (9)	1657 (7)	983 (7)
Hodgkin Lymphoma	970 (2)	305 (1)	224 (2)
Plasma Cell Disorders, MM	952 (2)	300 (1)	211 (2)
Other malignancies	61 (<1)	15 (<1)	22 (<1)
Breast cancer	7 (<1)	3 (<1)	1 (<1)
SAA	1644 (3)	746 (3)	582 (4)
Inherited abnormalities erythrocyte diff fxn	733 (1)	256 (1)	226 (2)
Inherited bone marrow failure syndromes	63 (<1)	67 (<1)	39 (<1)
Hemoglobinopathies	40 (<1)	44 (<1)	25 (<1)
Paroxysmal nocturnal hemoglobinuria	6 (<1)	11 (<1)	5 (<1)
SCIDs	893 (2)	408 (2)	401 (3)
Inherited abnormalities of platelets	43 (<1)	18 (<1)	13 (<1)
Inherited disorders of metabolism	311 (1)	100 (<1)	163 (1)
Histiocytic disorders	408 (1)	148 (1)	140 (1)
Autoimmune disorders	32 (<1)	28 (<1)	15 (<1)
MPN	1705 (3)	1406 (6)	354 (3)
Others	54 (<1)	26 (<1)	26 (<1)
AML Disease status at transplant			
CR1	9875 (56)	6142 (65)	2275 (51)
CR2	3296 (19)	1521 (16)	868 (20)
CR3+	354 (2)	128 (1)	102 (2)
Advanced or active disease	3951 (22)	1571 (17)	1045 (24)
Missing	184 (1)	39 (<1)	147 (3)

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Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
ALL Disease status at transplant			
CR1	3664 (50)	1842 (60)	906 (43)
CR2	2067 (28)	760 (25)	616 (29)
CR3+	599 (8)	202 (7)	196 (9)
Advanced or active disease	852 (12)	244 (8)	274 (13)
Missing	82 (1)	25 (1)	121 (6)
MDS Disease status at transplant			
Early	1612 (21)	864 (18)	388 (22)
Advanced	5026 (66)	3561 (76)	1002 (58)
Missing	979 (13)	250 (5)	349 (20)
NHL Disease status at transplant			
CR1	638 (15)	349 (21)	143 (15)
CR2	826 (19)	337 (20)	160 (16)
CR3+	383 (9)	149 (9)	90 (9)
PR	446 (10)	111 (7)	99 (10)
Advanced	2003 (46)	685 (42)	457 (47)
Missing	73 (2)	18 (1)	31 (3)
Recipient age at transplant			
0-9 years	4138 (8)	1425 (6)	1714 (13)
10-17 years	3290 (7)	1118 (5)	1202 (9)
18-29 years	5989 (12)	2237 (9)	1733 (13)
30-39 years	5608 (11)	2226 (9)	1529 (12)
40-49 years	7457 (15)	3016 (12)	1884 (14)
50-59 years	10282 (20)	4730 (19)	2288 (17)
60-69 years	10984 (22)	7231 (29)	2356 (18)
70+ years	2772 (5)	2726 (11)	562 (4)
Median (Range)	49 (0-84)	56 (0-83)	43 (0-84)
Recipient race			
White	44161 (91)	21667 (91)	9821 (87)
Black or African American	2423 (5)	1007 (4)	651 (6)
Asian	1334 (3)	750 (3)	604 (5)
Native Hawaiian or other Pacific Islander	75 (<1)	36 (<1)	41 (<1)
American Indian or Alaska Native	208 (<1)	112 (<1)	64 (1)
Other	49 (<1)	27 (<1)	28 (<1)
More than one race	304 (1)	146 (1)	67 (1)
Unknown	1966 (N/A)	964 (N/A)	1992 (N/A)
Recipient ethnicity			
Hispanic or Latino	4313 (10)	1880 (8)	1238 (11)
Non Hispanic or non-Latino	38348 (88)	20014 (90)	7032 (64)
Non-resident of the U.S.	889 (2)	302 (1)	2769 (25)

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Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Unknown	6970 (N/A)	2513 (N/A)	2229 (N/A)
Recipient sex			
Male	29289 (58)	14449 (58)	7866 (59)
Female	21231 (42)	10260 (42)	5402 (41)
Karnofsky score			
10-80	17764 (35)	9943 (40)	4214 (32)
90-100	30913 (61)	14082 (57)	8398 (63)
Missing	1843 (4)	684 (3)	656 (5)
HLA-A B DRB1 groups - low resolution			
<=3/6	30 (<1)	111 (<1)	12 (<1)
4/6	298 (1)	130 (1)	70 (1)
5/6	6900 (14)	2920 (13)	1821 (15)
6/6	42187 (85)	19862 (86)	10249 (84)
Unknown	1105 (N/A)	1686 (N/A)	1116 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	908 (2)	167 (1)	86 (1)
6/8	1853 (4)	237 (1)	253 (3)
7/8	9291 (19)	3166 (16)	1966 (22)
8/8	36454 (75)	16187 (82)	6834 (75)
Unknown	2014 (N/A)	4952 (N/A)	4129 (N/A)
HLA-DPB1 Match			
Double allele mismatch	12440 (28)	3578 (23)	1263 (24)
Single allele mismatch	23579 (54)	8083 (52)	2693 (52)
Full allele matched	7901 (18)	3896 (25)	1211 (23)
Unknown	6600 (N/A)	9152 (N/A)	8101 (N/A)
High resolution release score			
No	15052 (30)	24646 (>99)	12759 (96)
Yes	35468 (70)	63 (<1)	509 (4)
KIR typing available			
No	36672 (73)	24684 (>99)	13197 (99)
Yes	13848 (27)	25 (<1)	71 (1)
Graft type			
Marrow	16860 (33)	5544 (22)	5029 (38)
PBSC	33538 (66)	18919 (77)	8167 (62)
BM+PBSC	22 (<1)	29 (<1)	6 (<1)
PBSC+UCB	40 (<1)	191 (1)	11 (<1)
Others	60 (<1)	26 (<1)	55 (<1)
Conditioning regimen			
Myeloablative	30248 (60)	12189 (49)	8090 (61)
RIC/Nonmyeloablative	20037 (40)	12441 (50)	4995 (38)

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Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
TBD	235 (<1)	79 (<1)	183 (1)
Donor age at donation			
To Be Determined/NA	778 (2)	952 (4)	373 (3)
0-9 years	4 (<1)	30 (<1)	1 (<1)
10-17 years	1 (<1)	11 (<1)	1 (<1)
18-29 years	25102 (50)	13722 (56)	5750 (43)
30-39 years	14053 (28)	6255 (25)	3900 (29)
40-49 years	8127 (16)	2853 (12)	2459 (19)
50+ years	2455 (5)	886 (4)	784 (6)
Median (Range)	30 (0-69)	28 (0-89)	32 (4-77)
Donor/Recipient CMV serostatus			
+/+	12758 (25)	6857 (28)	3524 (27)
+/-	5937 (12)	3179 (13)	1622 (12)
-/+	16579 (33)	7438 (30)	4066 (31)
-/-	14540 (29)	6518 (26)	3533 (27)
CB - recipient +	36 (<1)	151 (1)	10 (<1)
CB - recipient -	4 (<1)	47 (<1)	2 (<1)
CB - recipient CMV unknown	0	1 (<1)	0
Missing	666 (1)	518 (2)	511 (4)
GvHD Prophylaxis			
No GvHD Prophylaxis	208 (<1)	162 (1)	70 (1)
Ex vivo T-cell depletion alone	127 (<1)	45 (<1)	63 (<1)
Ex vivo T-cell depletion +- other	1122 (2)	305 (1)	382 (3)
CD34 select alone	309 (1)	182 (1)	117 (1)
CD34 select +- other	537 (1)	291 (1)	147 (1)
Cyclophosphamide alone	233 (<1)	94 (<1)	58 (<1)
Cyclophosphamide +- others	5003 (10)	6053 (24)	1208 (9)
FK506 + MMF +- others	5513 (11)	2213 (9)	1006 (8)
FK506 + MTX +- others(not MMF)	21115 (42)	9671 (39)	3662 (28)
FK506 +- others(not MMF,MTX)	2501 (5)	1377 (6)	493 (4)
FK506 alone	1202 (2)	532 (2)	226 (2)
CSA + MMF +- others(not FK506)	3118 (6)	1008 (4)	1067 (8)
CSA + MTX +- others(not MMF,FK506)	7022 (14)	1956 (8)	3542 (27)
CSA +- others(not FK506,MMF,MTX)	1089 (2)	337 (1)	467 (4)
CSA alone	467 (1)	132 (1)	401 (3)
Other GVHD Prophylaxis	772 (2)	296 (1)	225 (2)
Missing	182 (<1)	55 (<1)	134 (1)
Donor/Recipient sex match			
Male-Male	20319 (40)	9586 (39)	5081 (38)
Male-Female	12469 (25)	5846 (24)	2904 (22)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Female-Male	8717 (17)	4479 (18)	2664 (20)
Female-Female	8572 (17)	4094 (17)	2399 (18)
CB - recipient M	18 (<1)	108 (<1)	3 (<1)
CB - recipient F	22 (<1)	91 (<1)	9 (<1)
Missing	403 (1)	505 (2)	208 (2)
Year of transplant			
1986-1990	347 (1)	47 (<1)	103 (1)
1991-1995	1837 (4)	439 (2)	745 (6)
1996-2000	3305 (7)	1184 (5)	1213 (9)
2001-2005	5347 (11)	1070 (4)	1880 (14)
2006-2010	9591 (19)	1921 (8)	1878 (14)
2011-2015	13348 (26)	3589 (15)	2650 (20)
2016-2020	10394 (21)	7186 (29)	2816 (21)
2021-2024	6351 (13)	9273 (38)	1983 (15)
Follow-up among survivors, Months			
N Eval	23098	14565	6370
Median (Range)	49 (0-384)	20 (0-362)	36 (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	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Number of patients	6426	1862	2353
Source of data			
CRF	4570 (71)	1180 (63)	1105 (47)
TED	1856 (29)	682 (37)	1248 (53)
Number of centers	155	146	230
Disease at transplant			
AML	2441 (38)	651 (35)	768 (33)
ALL	1319 (21)	404 (22)	520 (22)
Other leukemia	102 (2)	30 (2)	37 (2)
CML	137 (2)	37 (2)	57 (2)
MDS	579 (9)	180 (10)	188 (8)
Other acute leukemia	101 (2)	26 (1)	49 (2)
NHL	414 (6)	109 (6)	140 (6)
Hodgkin Lymphoma	103 (2)	27 (1)	35 (1)
Plasma Cell Disorders, MM	38 (1)	12 (1)	13 (1)
Other malignancies	12 (<1)	1 (<1)	3 (<1)
SAA	96 (1)	36 (2)	52 (2)
Inherited abnormalities erythrocyte diff fxn	171 (3)	51 (3)	45 (2)
Inherited bone marrow failure syndromes	8 (<1)	5 (<1)	6 (<1)
Hemoglobinopathies	3 (<1)	1 (<1)	1 (<1)
SCIDs	294 (5)	97 (5)	183 (8)
Inherited abnormalities of platelets	21 (<1)	6 (<1)	10 (<1)
Inherited disorders of metabolism	404 (6)	138 (7)	156 (7)
Histiocytic disorders	111 (2)	31 (2)	54 (2)
Autoimmune disorders	8 (<1)	0	6 (<1)
MPN	54 (1)	17 (1)	20 (1)
Others	10 (<1)	3 (<1)	10 (<1)
AML Disease status at transplant			
CR1	1292 (53)	377 (58)	393 (51)
CR2	647 (27)	159 (24)	198 (26)
CR3+	67 (3)	11 (2)	28 (4)
Advanced or active disease	427 (17)	101 (16)	143 (19)
Missing	8 (<1)	3 (<1)	6 (1)
ALL Disease status at transplant			
CR1	591 (45)	173 (43)	225 (43)

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Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
CR2	500 (38)	150 (37)	189 (36)
CR3+	151 (11)	56 (14)	64 (12)
Advanced or active disease	76 (6)	24 (6)	40 (8)
Missing	1 (<1)	1 (<1)	2 (<1)
MDS Disease status at transplant			
Early	177 (31)	43 (24)	75 (40)
Advanced	349 (60)	122 (68)	90 (48)
Missing	53 (9)	15 (8)	23 (12)
NHL Disease status at transplant			
CR1	66 (16)	12 (11)	26 (19)
CR2	77 (19)	26 (24)	35 (25)
CR3+	47 (11)	11 (10)	12 (9)
PR	68 (17)	12 (11)	16 (12)
Advanced	153 (37)	47 (43)	47 (34)
Missing	0	1 (1)	3 (2)
Recipient age at transplant			
0-9 years	1939 (30)	672 (36)	848 (36)
10-17 years	675 (11)	174 (9)	270 (11)
18-29 years	765 (12)	167 (9)	252 (11)
30-39 years	617 (10)	172 (9)	233 (10)
40-49 years	681 (11)	179 (10)	223 (9)
50-59 years	877 (14)	226 (12)	296 (13)
60-69 years	750 (12)	232 (12)	212 (9)
70+ years	122 (2)	40 (2)	19 (1)
Median (Range)	27 (0-85)	23 (0-84)	20 (0-78)
Recipient race			
White	4512 (74)	1293 (74)	1426 (72)
Black or African American	952 (16)	257 (15)	293 (15)
Asian	383 (6)	137 (8)	179 (9)
Native Hawaiian or other Pacific Islander	36 (1)	4 (<1)	21 (1)
American Indian or Alaska Native	61 (1)	18 (1)	24 (1)
Other	1 (<1)	1 (<1)	1 (<1)
More than one race	133 (2)	41 (2)	39 (2)
Unknown	348 (N/A)	111 (N/A)	370 (N/A)
Recipient ethnicity			
Hispanic or Latino	1352 (22)	349 (19)	401 (18)
Non Hispanic or non-Latino	4863 (78)	1416 (79)	1395 (61)
Non-resident of the U.S.	54 (1)	27 (2)	494 (22)
Unknown	157 (N/A)	70 (N/A)	63 (N/A)
Recipient sex			

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Male	3569 (56)	1060 (57)	1338 (57)
Female	2857 (44)	802 (43)	1015 (43)
Karnofsky score			
10-80	1714 (27)	477 (26)	584 (25)
90-100	4483 (70)	1261 (68)	1553 (66)
Missing	229 (4)	124 (7)	216 (9)
HLA-A B DRB1 groups - low resolution			
<=3/6	181 (3)	103 (6)	65 (3)
4/6	2414 (41)	642 (39)	822 (40)
5/6	2526 (43)	657 (40)	858 (42)
6/6	764 (13)	230 (14)	310 (15)
Unknown	541 (N/A)	230 (N/A)	298 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	2802 (55)	669 (54)	881 (53)
6/8	1233 (24)	299 (24)	387 (23)
7/8	734 (14)	181 (14)	246 (15)
8/8	370 (7)	101 (8)	133 (8)
Unknown	1287 (N/A)	612 (N/A)	706 (N/A)
HLA-DPB1 Match			
Double allele mismatch	896 (37)	163 (32)	225 (37)
Single allele mismatch	1289 (53)	294 (58)	320 (53)
Full allele matched	240 (10)	50 (10)	63 (10)
Unknown	4001 (N/A)	1355 (N/A)	1745 (N/A)
High resolution release score			
No	4954 (77)	1812 (97)	2320 (99)
Yes	1472 (23)	50 (3)	33 (1)
KIR typing available			
No	5153 (80)	1856 (>99)	2325 (99)
Yes	1273 (20)	6 (<1)	28 (1)
Graft type			
UCB	6025 (94)	1663 (89)	2210 (94)
BM+UCB	1 (<1)	0	0
PBSC+UCB	369 (6)	191 (10)	129 (5)
Others	31 (<1)	8 (<1)	14 (1)
Number of cord units			
1	5387 (84)	0	1968 (84)
2	1037 (16)	0	384 (16)
3	1 (<1)	0	0
Unknown	1 (N/A)	1862 (N/A)	1 (N/A)
Conditioning regimen			

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Myeloablative	4181 (65)	1192 (64)	1481 (63)
RIC/Nonmyeloablative	2229 (35)	664 (36)	850 (36)
TBD	16 (<1)	6 (<1)	22 (1)
Donor/Recipient CMV serostatus			
+/+	0	0	1 (<1)
-/-	0	0	1 (<1)
CB - recipient +	4036 (63)	1133 (61)	1432 (61)
CB - recipient -	2288 (36)	662 (36)	843 (36)
CB - recipient CMV unknown	102 (2)	67 (4)	76 (3)
GvHD Prophylaxis			
No GvHD Prophylaxis	25 (<1)	10 (1)	17 (1)
Ex vivo T-cell depletion alone	1 (<1)	0	0
Ex vivo T-cell depletion +- other	27 (<1)	9 (<1)	9 (<1)
CD34 select alone	0	2 (<1)	1 (<1)
CD34 select +- other	286 (4)	147 (8)	85 (4)
Cyclophosphamide alone	0	0	1 (<1)
Cyclophosphamide +- others	18 (<1)	11 (1)	11 (<1)
FK506 + MMF +- others	1913 (30)	595 (32)	486 (21)
FK506 + MTX +- others(not MMF)	218 (3)	57 (3)	77 (3)
FK506 +- others(not MMF,MTX)	235 (4)	69 (4)	93 (4)
FK506 alone	147 (2)	44 (2)	27 (1)
CSA + MMF +- others(not FK506)	2914 (45)	730 (39)	1132 (48)
CSA + MTX +- others(not MMF,FK506)	100 (2)	30 (2)	50 (2)
CSA +- others(not FK506,MMF,MTX)	342 (5)	116 (6)	236 (10)
CSA alone	51 (1)	18 (1)	73 (3)
Other GVHD Prophylaxis	137 (2)	21 (1)	45 (2)
Missing	12 (<1)	3 (<1)	10 (<1)
Donor/Recipient sex match			
Male-Female	0	0	1 (<1)
Female-Male	0	0	1 (<1)
CB - recipient M	3569 (56)	1060 (57)	1336 (57)
CB - recipient F	2857 (44)	802 (43)	1014 (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 (5)	34 (1)
2006-2010	1850 (29)	427 (23)	618 (26)
2011-2015	2678 (42)	513 (28)	840 (36)
2016-2020	1340 (21)	529 (28)	552 (23)
2021-2024	445 (7)	306 (16)	304 (13)

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Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Follow-up among survivors, Months			
N Eval	3180	1050	1246
Median (Range)	61 (0-196)	38 (0-213)	37 (0-240)

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

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Number of patients	12809	2225	1080
Source of data			
CRF	4126 (32)	601 (27)	337 (31)
TED	8683 (68)	1624 (73)	743 (69)
Number of centers	96	81	68
Disease at transplant			
AML	4215 (33)	718 (32)	375 (35)
ALL	2158 (17)	447 (20)	202 (19)
Other leukemia	230 (2)	43 (2)	19 (2)
CML	375 (3)	54 (2)	32 (3)
MDS	1702 (13)	272 (12)	148 (14)
Other acute leukemia	200 (2)	37 (2)	11 (1)
NHL	1041 (8)	192 (9)	91 (8)
Hodgkin Lymphoma	229 (2)	43 (2)	31 (3)
Plasma Cell Disorders, MM	265 (2)	41 (2)	22 (2)
Other malignancies	24 (<1)	1 (<1)	1 (<1)
Breast cancer	1 (<1)	0	0
SAA	621 (5)	94 (4)	40 (4)
Inherited abnormalities erythrocyte diff fxn	493 (4)	71 (3)	18 (2)
Inherited bone marrow failure syndromes	43 (<1)	3 (<1)	5 (<1)
Hemoglobinopathies	247 (2)	47 (2)	19 (2)
Paroxysmal nocturnal hemoglobinuria	3 (<1)	1 (<1)	0
SCIDs	279 (2)	46 (2)	18 (2)
Inherited abnormalities of platelets	11 (<1)	0	0
Inherited disorders of metabolism	24 (<1)	7 (<1)	2 (<1)
Histiocytic disorders	73 (1)	9 (<1)	6 (1)
Autoimmune disorders	12 (<1)	0	1 (<1)
MPN	540 (4)	97 (4)	39 (4)
Others	23 (<1)	2 (<1)	0
AML Disease status at transplant			
CR1	2813 (67)	494 (69)	242 (65)
CR2	632 (15)	94 (13)	46 (12)
CR3+	50 (1)	16 (2)	2 (1)
Advanced or active disease	713 (17)	109 (15)	85 (23)
Missing	7 (<1)	5 (1)	0

Refresh date: Dec 2024

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
ALL Disease status at transplant			
CR1	1275 (59)	268 (60)	131 (65)
CR2	649 (30)	120 (27)	50 (25)
CR3+	140 (6)	31 (7)	9 (4)
Advanced or active disease	94 (4)	28 (6)	12 (6)
MDS Disease status at transplant			
Early	300 (18)	39 (14)	25 (17)
Advanced	1349 (79)	220 (81)	116 (78)
Missing	53 (3)	13 (5)	7 (5)
NHL Disease status at transplant			
CR1	207 (20)	46 (24)	19 (21)
CR2	197 (19)	37 (19)	14 (15)
CR3+	107 (10)	24 (13)	7 (8)
PR	68 (7)	13 (7)	7 (8)
Advanced	453 (44)	71 (37)	44 (48)
Missing	5 (<1)	0	0
Recipient age at transplant			
0-9 years	1386 (11)	209 (9)	86 (8)
10-17 years	1313 (10)	179 (8)	77 (7)
18-29 years	1508 (12)	298 (13)	121 (11)
30-39 years	980 (8)	192 (9)	114 (11)
40-49 years	1503 (12)	277 (12)	122 (11)
50-59 years	2584 (20)	471 (21)	228 (21)
60-69 years	2950 (23)	498 (22)	275 (25)
70+ years	585 (5)	101 (5)	57 (5)
Median (Range)	49 (0-82)	49 (0-77)	51 (0-83)
Recipient race			
White	9481 (78)	1519 (74)	791 (79)
Black or African American	1717 (14)	311 (15)	121 (12)
Asian	616 (5)	172 (8)	65 (6)
Native Hawaiian or other Pacific Islander	48 (<1)	8 (<1)	3 (<1)
American Indian or Alaska Native	87 (1)	11 (1)	9 (1)
More than one race	162 (1)	19 (1)	13 (1)
Unknown	698 (N/A)	185 (N/A)	78 (N/A)
Recipient ethnicity			
Hispanic or Latino	2441 (19)	543 (25)	231 (22)
Non Hispanic or non-Latino	9996 (80)	1598 (74)	805 (76)
Non-resident of the U.S.	128 (1)	26 (1)	18 (2)
Unknown	244 (N/A)	58 (N/A)	26 (N/A)
Recipient sex			

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Male	7507 (59)	1306 (59)	629 (58)
Female	5302 (41)	919 (41)	451 (42)
Karnofsky score			
10-80	4626 (36)	880 (40)	471 (44)
90-100	7728 (60)	1270 (57)	552 (51)
Missing	455 (4)	75 (3)	57 (5)
HLA-A B DRB1 groups - low resolution			
<=3/6	2995 (25)	510 (25)	280 (32)
4/6	889 (7)	170 (8)	92 (11)
5/6	272 (2)	50 (2)	25 (3)
6/6	7882 (65)	1287 (64)	471 (54)
Unknown	771 (N/A)	208 (N/A)	212 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	3713 (32)	629 (33)	327 (42)
6/8	171 (1)	46 (2)	13 (2)
7/8	186 (2)	31 (2)	18 (2)
8/8	7594 (65)	1203 (63)	420 (54)
Unknown	1145 (N/A)	316 (N/A)	302 (N/A)
HLA-DPB1 Match			
Double allele mismatch	14 (<1)	0	1 (<1)
Single allele mismatch	3168 (30)	410 (32)	226 (42)
Full allele matched	7462 (70)	887 (68)	316 (58)
Unknown	2165 (N/A)	928 (N/A)	537 (N/A)
High resolution release score			
No	6504 (51)	2196 (99)	1069 (99)
Yes	6305 (49)	29 (1)	11 (1)
Graft type			
Marrow	3705 (29)	490 (22)	282 (26)
PBSC	8988 (70)	1694 (76)	789 (73)
UCB	2 (<1)	14 (1)	0
BM+PBSC	19 (<1)	6 (<1)	1 (<1)
BM+UCB	46 (<1)	13 (1)	2 (<1)
PBSC+UCB	1 (<1)	2 (<1)	5 (<1)
Others	48 (<1)	6 (<1)	1 (<1)
Conditioning regimen			
Myeloablative	7117 (56)	1224 (55)	553 (51)
RIC/Nonmyeloablative	5628 (44)	984 (44)	510 (47)
TBD	64 (<1)	17 (1)	17 (2)
Donor age at donation			
To Be Determined/NA	17 (<1)	7 (<1)	2 (<1)

Refresh date: Dec 2024

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
0-9 years	897 (7)	132 (6)	39 (4)
10-17 years	1030 (8)	171 (8)	62 (6)
18-29 years	2369 (18)	408 (18)	233 (22)
30-39 years	2002 (16)	389 (17)	208 (19)
40-49 years	2042 (16)	360 (16)	168 (16)
50+ years	4452 (35)	758 (34)	368 (34)
Median (Range)	40 (0-82)	40 (0-79)	40 (0-80)
Donor/Recipient CMV serostatus			
+/+	5191 (41)	995 (45)	442 (41)
+/-	1374 (11)	190 (9)	108 (10)
-/+	3232 (25)	540 (24)	284 (26)
-/-	2788 (22)	439 (20)	214 (20)
CB - recipient +	31 (<1)	17 (1)	6 (1)
CB - recipient -	18 (<1)	12 (1)	1 (<1)
Missing	175 (1)	32 (1)	25 (2)
GvHD Prophylaxis			
No GvHD Prophylaxis	191 (1)	26 (1)	17 (2)
Ex vivo T-cell depletion alone	122 (1)	37 (2)	12 (1)
Ex vivo T-cell depletion +- other	119 (1)	30 (1)	12 (1)
CD34 select alone	83 (1)	26 (1)	11 (1)
CD34 select +- other	96 (1)	28 (1)	9 (1)
Cyclophosphamide alone	80 (1)	12 (1)	10 (1)
Cyclophosphamide +- others	4566 (36)	754 (34)	452 (42)
FK506 + MMF +- others	851 (7)	105 (5)	35 (3)
FK506 + MTX +- others(not MMF)	4357 (34)	659 (30)	359 (33)
FK506 +- others(not MMF,MTX)	867 (7)	339 (15)	72 (7)
FK506 alone	118 (1)	19 (1)	5 (<1)
CSA + MMF +- others(not FK506)	246 (2)	41 (2)	18 (2)
CSA + MTX +- others(not MMF,FK506)	756 (6)	96 (4)	44 (4)
CSA +- others(not FK506,MMF,MTX)	81 (1)	10 (<1)	3 (<1)
CSA alone	83 (1)	12 (1)	4 (<1)
Other GVHD Prophylaxis	181 (1)	23 (1)	17 (2)
Missing	12 (<1)	8 (<1)	0
Donor/Recipient sex match			
Male-Male	4269 (33)	790 (36)	365 (34)
Male-Female	2718 (21)	451 (20)	234 (22)
Female-Male	3203 (25)	496 (22)	261 (24)
Female-Female	2566 (20)	457 (21)	213 (20)
CB - recipient M	31 (<1)	18 (1)	3 (<1)
CB - recipient F	18 (<1)	11 (<1)	4 (<1)

Refresh date: Dec 2024

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Missing	4 (<1)	2 (<1)	0
Year of transplant			
2006-2010	604 (5)	71 (3)	58 (5)
2011-2015	3685 (29)	504 (23)	215 (20)
2016-2020	5016 (39)	902 (41)	407 (38)
2021-2024	3504 (27)	748 (34)	400 (37)
Follow-up among survivors, Months			
N Eval	8318	1467	694
Median (Range)	25 (0-150)	24 (0-147)	24 (0-148)

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A RESEARCH COLLABORATION BETWEEN THE MEDICAL COLLEGE OF WISCONSIN AND NMDP

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: 2024-2025 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 2025.

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 analysis due to inclusion of a more modern cohort. The goal of this study is to be in manuscript prep by June 2025.

Status: **Analysis**

LE18-01 Trends in late mortality amongst two-year survivors of pediatric allogeneic hematopoietic cell transplantation for hematologic malignancies (P Satwani/ L Broglie). The goal of this study is to evaluate trends in late mortality rates in children and young adults with hematologic malignancies and whether this has changed over time. It also aims to determine whether the incidence of certain late effects can be associated with potential mortality and its change over time. This study is currently in manuscript preparation. The goal of this study is to submit by June 2025.

Status: **Manuscript preparation**

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 2025.

Status: **Manuscript Preparation**

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). This study will evaluate the incidence of late effects within the elderly population and evaluate the association between age and cGVHD with the development of late effects. This study is in analysis. The goal of this study is to be in manuscript prep June 2025.

Status: **Analysis**

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 2025.

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 2025.

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 manuscript preparation by June 2025.

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. The goal of this study is to be in manuscript prep by June 2025.

Status: **Data File Preparation**

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 is currently in analysis. The goal of this study is to be in manuscript prep by June 2025. This study is accepted for a poster presentation this year at Tandem.

Status: **Analysis**

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. The goal of this study is to be in data file preparation by June 2025.

Status: **Protocol Development**

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 data file preparation. The goal of this study is to be in manuscript prep by June 2025.

Status: **Data File Preparation**

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. The goal of this study is to be in data file preparation by June 2025.

Status: **Protocol Development**

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 protocol development. The goal of this study is to be in data file preparation by June 2025.

Status: **Protocol Received**

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 2025.

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 2025.

Status: **Protocol Received**

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). The primary goal of this study is to compare PFS and other outcomes for Flu/Cy vs. Bendamustine in NHL patients receiving CAR-T. This study is currently in manuscript preparation. The goal of this study is to be submitted by June 2025.

Status: **Manuscript Preparation**

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 2025.

Status: **Protocol Pending**

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 2025.

Status: **Protocol Received**

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 protocol development. The goal of this study is to be in protocol development by June 2025.

Status: **Protocol Development**

Field	Response
Proposal Number	2410-248-SANDHU
Proposal Title	Impact of Li Fraumeni syndrome upon outcomes of Hematopoietic stem cell transplant recipients of hematologic malignancies
Key Words	Li Fraumeni, Hematopoietic stem cell transplant, hematologic malignancies
Principal Investigator #1: - First and last name, degree(s)	Karamjeet Singh Sandhu, MD
Principal Investigator #1: - Email address	ksandhu@coh.org
Principal Investigator #1: - Institution name	City of Hope National Cancer Center
Principal Investigator #1: - Academic rank	Assistant Professor
Junior investigator status (defined as ≤5 years from fellowship)	No
Do you identify as an underrepresented/minority?	No
Principal Investigator #2 (If applicable): - First and last name, degree(s):	Ryotaro Nakamura, MD
Principal Investigator #2 (If applicable): - Email address:)	rnakamura@coh.org
Principal Investigator #2 (If applicable): - Institution name:	City of Hope National 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:	Karamjeet Singh Sandhu
If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:	-
Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.	Prediction of Graft-Versus-Host Disease in Recipients of Hematopoietic Cell Transplant from a Single Mismatched Unrelated Donor Using a Highly Multiplexed Proteomics Assay: MHC-PepSeq
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

Field	Response
If you have already spoken with a scientific director or working committee chair regarding this study, then please specify who:	-
RESEARCH QUESTION:	Analyze Impact of Li Fraumeni syndrome upon outcomes of Hematopoietic stem cell transplant recipients of hematologic malignancies
RESEARCH HYPOTHESIS:	We hypothesize that hematopoietic stem cell transplant is curative for hematologic malignancies even among individual risk of Li Fraumeni syndrome with acceptable risk of secondary malignancies.
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	Primary: 1. Non relapse mortality: Incidence and impact of conditioning regimen on non-relapse mortality in first year post Hematopoietic Stem Cell Transplant among patients with Li Fraumeni syndrome Secondary: 1. Acute GVHD: Cumulative incidence of acute graft versus host disease by 100 post Hematopoietic Stem Cell Transplant 2. Chronic GVHD: Cumulative incidence of chronic graft versus host disease by 2 years post Hematopoietic Stem Cell Transplant 3. Relapse: Cumulative incidence and time to recurrence of disease 4. Overall survival: Time to death from any cause 5. Secondary malignancies: Incidence of second malignancies among recipients of Hematopoietic Stem Cell Transplant and impact of conditioning regimen and GVHD prophylaxis regimen on incidence of secondary malignancy
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 Cell Transplant is curative treatment for several hematological malignancies which could be seen in about 4% of patients with Li Fraumeni syndrome. Impact of Hematopoietic Stem Cell Transplant on outcomes among recipients with LFS will allow better optimize therapeutic regimen with increase recognition of LFS with expanding application of next generation sequencing for genetic characterization of hematological malignancies.

Field	Response
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.	Li Fraumeni syndrome (LFS) is an autosomal dominant disorder characterized by germline Tp53 mutation. It was described in 1969 by Li and Fraumeni. It predisposes to several solid tumors and hematological malignancies which could be denovo or therapy related are reported in about 4% of patients with LFS.1,2,3 However in current era of multi gene sequencing will identify many more patients which otherwise would have missed using traditional phenotype-based testing approach7. Characterization of hematological malignancies among LFS and its impact on choice of treatments especially impact of HCT treatment modalities on outcomes has been sporadically reported in small case series which limits its implication in otherwise curative approach by optimizing ideal conditioning and graft versus host preventive strategies.4,5 Notably use of radiation in comparison to chemotherapy radiation has been associated with increased risk of secondary malignancies thus it becomes even more important to analyze outcomes of Hematopoietic Stem Cell Transplant among patients with LFS as its use has been reported successfully in pediatric patients.4,6

Field	Response
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	Patient-related variables: • Age at transplant: in years • Patient sex: male vs. female • Karnofsky performance status at transplant: ≥ 90 vs. < 90 vs. missing • HCT comorbidity index at transplant: 0 vs. 1-2 vs. ≥ 3 vs. missing • Previous malignancies • Chemotherapy for previous and current malignancy • Radiation for previous and current malignancy • Post transplant second malignancy Disease-related variables: • Disease: AML vs. ALL vs. MDS vs MPN • Cytogenetics • Type of Tp53 pathogenic variant • Disease status at transplant Transplant-related variables: • Graft source: peripheral blood vs. bone marrow • Donor type: Matches Sibling donor vs 8/8 matched unrelated donor vs. 7/8 mismatched unrelated donor vs Haploidentical donor vs Umbilical cord graft source. • Donor-recipient gender match: male-male vs. male-female vs. female-male vs. female-female vs. missing • GVHD prophylaxis: Descriptive all regimens • Time from diagnosis to transplant: continuous • Donor-recipient CMV status: -/+ vs. others vs. missing • Year of transplant: continuous • Conditioning intensity: Myeloablative (MAC) vs. reduced intensity conditioning (RIC)
Does this study include pediatric patients?	Yes
If this study does not include pediatric patients, please provide justification:	-

Field	Response
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.	Patient-related variables: • Age at transplant: in years • Patient sex: male vs. female • Karnofsky performance status at transplant: ≥ 90 vs. < 90 vs. missing • HCT comorbidity index at transplant: 0 vs. 1-2 vs. ≥ 3 vs. missing • Previous malignancies • Chemotherapy for previous and current malignancy • Radiation for previous and current malignancy • Post transplant second malignancy Disease-related variables: • Disease: AML vs. ALL vs. MDS vs MPN • Cytogenetics • Type of Tp53 pathogenic variant • Disease status at transplant Transplant-related variables: • Graft source: peripheral blood vs. bone marrow • Donor type: Matches Sibling donor vs 8/8 matched unrelated donor vs. 7/8 mismatched unrelated donor vs Haploidentical donor vs Umbilical cord graft source. • Donor-recipient gender match: male-male vs. male-female vs. female-male vs. female-female vs. missing • GVHD prophylaxis: Descriptive all regimens • Time from diagnosis to transplant: continuous • Donor-recipient CMV status: -/+ vs. others vs. missing • Year of transplant: continuous • Conditioning intensity: Myeloablative (MAC) vs. reduced intensity conditioning (RIC) • Radiation in conditioning: dose of radiation • ATG use in conditioning: no vs. yes vs. missing.
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	NA
MACHINE LEARNING: Please indicate if the study requires methodology related to machine-learning and clinical predictions.	NA
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	NA

Field	Response
NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required.	I have communicated with Dr Fabio Ciceri at EBMT who has expressed willingness to survey centers to supplement our initiative. I have previously communicated in 2023 and such population meeting criteria for Li Fraumeni receiving hematopoietic stem cell transplant
REFERENCES:	1. Roloff GW, Drazer MW, Godley LA. Inherited Susceptibility to Hematopoietic Malignancies in the Era of Precision Oncology. JCO Precis Oncol. 2021; 5:107-122. doi:10.1200/PO.20.00387 2. Bougeard G, Renaux-Petel M, Flaman JM, et al. Revisiting Li-Fraumeni Syndrome From TP53 Mutation Carriers. J Clin Oncol. 2015;33(21):2345-2352. doi:10.1200/JCO.2014.59.5728 3. Kleihues P, Schäuble B, zur Hausen A, Estève J, Ohgaki H. Tumors associated with p53 germline mutations: a synopsis of 91 families. Am J Pathol. 1997;150(1):1-13. 4. Winter G, Kirschner-Schwabe R, Groeneveld-Krentz S, et al. Clinical and genetic characteristics of children with acute lymphoblastic leukemia and Li-Fraumeni syndrome. Leukemia. 2021;35(5):1475-1479. doi:10.1038/s41375-021-01163-y 5. Swaminathan M, Bannon SA, Routbort M, et al. Hematologic malignancies and Li-Fraumeni syndrome. Cold Spring Harb Mol Case Stud. 2019;5(1):a003210. Published 2019 Feb 1. doi:10.1101/mcs.a003210 6. Thariat J, Chevalier F, Orbach D, et al. Avoidance or adaptation of radiotherapy in patients with cancer with Li-Fraumeni and heritable TP53-related cancer syndromes. Lancet Oncol. 2021;22(12):e562-e574. doi:10.1016/S1470-2045(21)00425-3 7. Foulkes WD, Polak P. Li-Fraumeni Syndrome in the Cancer Genomics Era. J Natl Cancer Inst. 2021 Nov 29;113(12):1615-1617. doi: 10.1093/jnci/djab118. PMID: 34240211; PMCID: PMC8634324.
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
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.	-

Patient characteristics of patients with Li Fraumeni syndrome, 2008-present

Characteristic	N (%)
No. of patients	42
No. of centers	36
Patient-Related Characteristics	
TED or RES (RF) track determined for this event - no. (%)	
TED	29 (69)
CRF (RES)	13 (31)
Age, by decades - no. (%)	
Median (min-max)	24 (5-69)
0-9	5 (12)
10-19	12 (29)
20-29	9 (21)
30-39	6 (14)
40-49	2 (5)
50-59	4 (10)
60-69	4 (10)
Sex - no. (%)	
Male	22 (52)
Female	20 (48)
Race - no. (%)	
White	32 (76)
Asian	3 (7)
More than one race	3 (7)
Not reported	4 (10)
Ethnicity - no. (%)	
Hispanic or Latino	7 (17)
Non-Hispanic or Latino	27 (64)
Non-resident of the U.S.	8 (19)
Current CCN region of patient - no. (%)	
US	32 (76)
Canada	4 (10)
Australia/New Zealand	4 (10)
Central/South America	2 (5)
Karnofsky score prior to HCT - no. (%)	
90-100%	24 (57)
< 90%	17 (40)
Not reported	1 (2)

Characteristic	N (%)
HCT-CI - no. (%)	
0	5 (12)
1	2 (5)
2	4 (10)
3	16 (38)
4	5 (12)
5+	9 (21)
Not reported	1 (2)
Disease-Related Characteristics	
Primary disease - no. (%)	
AML	12 (29)
ALL	12 (29)
MDS	18 (43)
Interval from diagnosis to HCT, months - median (min-max)	5 (1-36)
Disease Status	
AML pre-HCT disease stage - no. (%)	
Disease is not AML	30 (71)
CR1	6 (14)
Advanced or active disease	6 (14)
ALL pre-HCT disease stage - no. (%)	
Disease is not ALL	30 (71)
CR1	8 (19)
CR2	3 (7)
CR3+	1 (2)
MDS pre-HCT disease stage - no. (%)	
Disease is not MDS/MPN	24 (57)
Early	3 (7)
Advanced	15 (36)
Transplant-Related Characteristics	
transplant type - Auto/Allo - no. (%)	
Allogeneic	42 (100)
Conditioning intensity reported by center - no. (%)	
MAC	30 (71)
NMA	1 (2)
RIC	11 (26)
Conditioning regimen - no. (%)	
TBI/Cy	1 (2)
TBI/Cy/Flu	3 (7)

Characteristic	N (%)
TBI/Cy/TT	2 (5)
TBI/VP	1 (2)
TBI/Mel	1 (2)
TBI/Flu	1 (2)
Bu/Cy/Mel	2 (5)
Bu/Cy	2 (5)
Bu/Mel	1 (2)
Flu/Bu/TT	3 (7)
Flu/Bu	15 (36)
Flu/Mel	6 (14)
Treosulfan	2 (5)
Other(s)	2 (5)
TBI usage - no. (%)	
TBI (single dose > 500 cGy or fractionated > 800 cGy)	5 (12)
TBI (single dose > 200 and <= 500 cGy, or fractionated > 200 and <= 800 cGy)	2 (5)
TBI = 200 cGy	2 (5)
Non-TBI regimen	28 (67)
Not reported	5 (12)
Donor type - no. (%)	
HLA identical sibling	6 (14)
Haploidentical donor	11 (26)
Other related	1 (2)
Well-matched unrelated (8/8)	15 (36)
Partially-matched unrelated (7/8)	4 (10)
Multi-donor	1 (2)
Unrelated (matching cannot be determined)	2 (5)
Cord blood	2 (5)
Donor/recipient sex match - no. (%)	
M-M	12 (29)
M-F	8 (19)
F-M	10 (24)
F-F	10 (24)
CB - recipient F	2 (5)
GVHD prophylaxis - no. (%)	
None	1 (2)
Ex-vivo T-cell depletion	2 (5)
CD34 selection	2 (5)
PtCy + other(s)	9 (21)

Characteristic	**N (%)**
PtCy alone	1 (2)
TAC + MMF +- other(s) (except PtCy)	4 (10)
TAC + MTX +- other(s) (except MMF, PtCy)	14 (33)
TAC + other(s) (except MMF, MTX, PtCy)	1 (2)
TAC alone	1 (2)
CSA + MMF +- other(s) (except PtCy,TAC)	2 (5)
CSA + MTX +- other(s) (except PtCy,TAC,MMF)	3 (7)
CSA alone	1 (2)
Other(s)	1 (2)
Product type - no. (%)	
BM	11 (26)
PBSC	29 (69)
UCB	2 (5)
Year of HCT - no. (%)	
2012-2015	3 (7)
2016-2019	14 (33)
2020-2023	23 (55)
2024	2 (5)
Follow-up of survivors - median (range)	27.8 (5.9-74.8)

Field	Response
Proposal Number	2410-02-SWEISS
Proposal Title	ASSOCIATION OF FLUDARABINE EXPOSURE ON CAR-T OUTCOMES
Key Words	fludarabine, lymphodepletion, pharmacokinetics, CAR-T, CRS/ICANS
Principal Investigator #1: - First and last name, degree(s)	Karen Sweiss, PharmD
Principal Investigator #1: - Email address	ksweis2@uic.edu
Principal Investigator #1: - Institution name	University of Illinois at Chicago
Principal Investigator #1: - Academic rank	Assistant Professor
Junior investigator status (defined as ≤5 years from fellowship)	No
Do you identify as an underrepresented/minority?	No
Principal Investigator #2 (If applicable): - First and last name, degree(s):	Sairah Ahmed
Principal Investigator #2 (If applicable): - Email address:)	Sahmed3@mdanderson.org
Principal Investigator #2 (If applicable): - Institution name:	MD Anderson Cancer Center
Principal Investigator #2 (If applicable): - Academic rank:	-
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:	-
If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:	-
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.	Yes
If you have already spoken with a scientific director or working committee chair regarding this study, then please specify who:	Sairah Ahmed

Field	Response
RESEARCH QUESTION:	Is there an association between population-predicted fludarabine lymphodepletion exposure (AUC) and clinical outcomes after CAR-T therapy in lymphoma and multiple myeloma?
RESEARCH HYPOTHESIS:	We hypothesize that fludarabine exposure, determined by using a previously published population PK model is associated with CAR-T efficacy and toxicity A therapeutic window that will balance these two outcomes needs to be identified and used to prospectively dose patients in a personalized fashion.
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	• To determine the effect of predicted Flu exposure on clinical outcomes, including disease response, duration of response, PFS, OS, grade 3/4 CRS, ICANS, and cytopenias in relapsed/refractory B cell lymphoma patients undergoing anti-CD19 CAR-T • To determine the effect of predicted Flu exposure on clinical outcomes, including disease response, duration of response, PFS, OS, grade 3/4 CRS, ICANS, and cytopenias in relapsed/refractory multiple myeloma patients undergoing anti-BCMA CAR-T
SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.	We will gain insight on how fludarabine exposure impacts outcomes after CAR-T in R/R lymphoma and myeloma, when compensating for known prognostic markers. We will identify the predicted fludarabine exposure window that results in maximal efficacy and minimal toxicity. This will lay the groundwork for future prospective evaluation of personalized dosing of fludarabine in CAR-T to optimize outcomes.

Field	Response
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.	Chimeric antigen receptor-engineered (CAR) T-cell therapy has transformed the treatment landscape for relapsed or refractory B-cell malignancies and myeloma, but remains limited by non-durable responses and severe toxicities, such as cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS). Optimizing the in-vivo expansion and persistence of CD19 CAR T cells is a promising approach to maximize anti-tumor effects while minimizing toxicities. With first generation CAR-T cells, the only modifiable factor to improve CAR-T expansion and persistence is lymphodepleting chemotherapy. Lymphodepletion (LD) mediates elimination of sinks for homeostatic cytokines and eradication of immunosuppressive regulatory T cells and myeloid-derived suppressor cells. Unfortunately, LD is entirely empiric, with little scientific rationale governing the preferred agents or dosing schedules. The foundational drugs, fludarabine (Flu) and cyclophosphamide (Cy) exhibit extreme PK variability (up to 10-fold) thus leading to unpredictable dose-exposure (AUC) profiles. It has been suggested that the predicted fludarabine (Flu) exposure could be associated with improved outcomes in children with B-cell acute lymphoblastic leukemia (B-ALL) undergoing CD19 CAR T-cell therapy (Fabrizio et al., 2022). Our group has started a line of inquiry in this area, with investigation in both lymphoma and myeloma. Using CARTITUDE-1 patients, we predicted fludarabine exposure and observed a significant association with response (this data will be presented at the ASH conference in New Orleans in December 2022). Since smaller datasets have provided signals towards the importance of fludarabine AUC, a larger dataset like CIBMTR will allow for validation of these findings, both in lymphoma and myeloma.
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	• Adult patients ? 18 years of age • Relapsed/refractory large B cell lymphoma or multiple myeloma receiving anti-CD19 or anti-BCMA CAR-T therapy
Does this study include pediatric patients?	No
If this study does not include pediatric patients, please provide justification:	We are specifically asking this question for adults with lymphoma and myeloma

Field	Response
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.	• Fludarabine covariates include total body weight (on first day of fludarabine), estimated GFR (on first day of fludarabine dose), fludarabine doses received • Fludarabine PK parameters, including clearance and area under the curve, will be estimated using a population approach that is based on non-linear mixed-effects modeling, using the software package NONMEM version 7.5. R version 4.1.2 will be used for data handling and visualization. • Clinical outcomes of interest include: PFS, OS, disease response, duration of response, and toxicities (i.e., grade 3/4 CRS, ICANS/neurotoxicity). • Variables to be included in multivariate analysis for lymphoma (i.e., bulky disease, stage, LDH, etc) and myeloma (R-ISS, karyotype, prior lines of therapy, etc)
Types of cellular therapy data this proposal includes:	Chimeric Antigen Receptor (CAR) T-Cell Therapy (CAR-T)
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	-
MACHINE LEARNING: Please indicate if the study requires methodology related to machine-learning and clinical predictions.	-
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	-
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.	-

Field	Response
REFERENCES:	1. Hirayama AV, et al. The response to lymphodepletion impacts PFS in patients with aggressive non-Hodgkin lymphoma treated with CD19 CAR T cells. Blood. 2019 Apr 25;133(17):1876-1887. 2. Fabrizio VA, et al. Optimal fludarabine lymphodepletion is associated with improved outcomes following CAR T-cell therapy. Blood Adv. 2021 Nov 17:bloodadvances.2021006418. doi: 10.1182/bloodadvances.2021006418. Online ahead of print. 3. Langenhorst JB, Dorlo TPC, van Maarseveen EM, Nierkens S, Kuball J, Boelens JJ, van Kesteren C, Huitema ADR. Population Pharmacokinetics of Fludarabine in Children and Adults during Conditioning Prior to Allogeneic Hematopoietic Cell Transplantation. Clin Pharmacokinet. 2019 May;58(5):627-637. 4. Langenhorst JB, Dorlo TPC, van Kesteren C, van Maarseveen EM, Nierkens S, de Witte MA, Boelens JJ, Huitema ADR. Clinical Trial Simulation To Optimize Trial Design for Fludarabine Dosing Strategies in Allogeneic Hematopoietic Cell Transplantation. CPT Pharmacometrics Syst Pharmacol. 2020 May;9(5):272-281.
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
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.	-

Patient characteristics of adult CAR-T patients with LBCL/MM hat received fludarabine in their lymphodepleting regimen

Characteristic	NHL	MM	Total
No. of patients	6829	2558	9387
No. of centers	167	93	170
Patient Characteristics			
Age, by decades - no. (%)			
Median (min-max)	65 (18-91)	65 (29-89)	65 (18-91)
10-19	13 (0)	0 (0)	13 (0)
20-29	173 (3)	2 (0)	175 (2)
30-39	323 (5)	27 (1)	350 (4)
40-49	563 (8)	160 (6)	723 (8)
50-59	1326 (19)	570 (22)	1896 (20)
60-69	2294 (34)	1062 (42)	3356 (36)
70+	2137 (31)	737 (29)	2874 (31)
Recipient Sex - no. (%)			
Male	4274 (63)	1461 (57)	5735 (61)
Female	2555 (37)	1095 (43)	3650 (39)
Not reported	0 (0)	2 (0)	2 (0)
Recipient race - no. (%)			
White	5231 (77)	1976 (77)	7207 (77)
Black or African American	337 (5)	394 (15)	731 (8)
Asian	419 (6)	65 (3)	484 (5)
Native Hawaiian or other Pacific Islander	13 (0)	5 (0)	18 (0)
American Indian or Alaska Native	24 (0)	7 (0)	31 (0)
Other	31 (0)	10 (0)	41 (0)
More than one race	315 (5)	56 (2)	371 (4)
Missing	459 (7)	45 (2)	504 (5)
Ethnicity - no. (%)			
Hispanic or Latino	665 (10)	188 (7)	853 (9)
Non-Hispanic or Latino	5295 (78)	2284 (89)	7579 (81)
Non-resident of the U.S.	662 (10)	23 (1)	685 (7)
Not reported	207 (3)	63 (2)	270 (3)
Current CCN region of patient - no. (%)			
US	6164 (90)	2528 (99)	8692 (93)
Canada	344 (5)	12 (0)	356 (4)
Europe	57 (1)	13 (1)	70 (1)

Characteristic	NHL	MM	Total
Asia	87 (1)	0 (0)	87 (1)
Australia/New Zealand	59 (1)	4 (0)	63 (1)
Mideast/Africa	107 (2)	0 (0)	107 (1)
Central/South America	11 (0)	0 (0)	11 (0)
Not reported	0 (0)	1 (0)	1 (0)
Karnofsky performance score prior to CT - no. (%)			
90-100	2718 (40)	1000 (39)	3718 (40)
80	2066 (30)	892 (35)	2958 (32)
< 80	1360 (20)	429 (17)	1789 (19)
Not reported	685 (10)	237 (9)	922 (10)
HCT-CI Score - no. (%)			
0	2101 (31)	728 (28)	2829 (30)
1	1321 (19)	467 (18)	1788 (19)
2	921 (13)	364 (14)	1285 (14)
3	978 (14)	404 (16)	1382 (15)
4	647 (9)	249 (10)	896 (10)
5+	782 (11)	323 (13)	1105 (12)
Not reported	79 (1)	23 (1)	102 (1)
EGFR - no. (%)			
Median (min-max)	86 (0-191)	78 (3-147)	83 (0-191)
Unknown	4775 (70)	918 (36)	5693 (61)
Known	2054 (30)	1640 (64)	3694 (39)
Disease related			
Interval from diagnosis to HCT, months - median (min-max)	14 (0-447)	71 (0-424)	20 (0-447)
Disease status prior to infusion			
Disease status prior to CT for lymphoma - no. (%)			
Disease is not lymphoma	0 (0)	2558 (100)	2558 (27)
CR	428 (6)	0 (0)	428 (5)
PR	1446 (21)	0 (0)	1446 (15)
Resistant	4182 (61)	0 (0)	4182 (45)
Untreated	398 (6)	0 (0)	398 (4)
Unknown	372 (5)	0 (0)	372 (4)
Not reported	3 (0)	0 (0)	3 (0)
Disease status prior to CT for PCD - no. (%)			
Disease is not MM/PCD	6829 (100)	0 (0)	6829 (73)
Stringent complete remission (sCR)	0 (0)	17 (1)	17 (0)

Characteristic	NHL	MM	Total
Complete remission (CR)	0 (0)	44 (2)	44 (0)
Very good partial remission (VGPR)	0 (0)	251 (10)	251 (3)
Partial response (PR)/ Not Complete Remission	0 (0)	317 (12)	317 (3)
Stable disease (SD)	0 (0)	409 (16)	409 (4)
Progressive disease (PD)	0 (0)	1465 (57)	1465 (16)
Relapse from CR (Rel) (untreated)	0 (0)	39 (2)	39 (0)
Not reported	0 (0)	16 (1)	16 (0)
Infusion related			
Prior HCT - no. (%)			
No	5325 (78)	406 (16)	5731 (61)
Yes	1483 (22)	2150 (84)	3633 (39)
Not reported	21 (0)	2 (0)	23 (0)
Bridging therapy - no. (%)			
No	2734 (40)	739 (29)	3473 (37)
Yes	3422 (50)	1370 (54)	4792 (51)
Systemic therapy given as bridging therapy	2871 (42)	1323 (52)	4194 (45)
Intrathecal therapy given as bridging therapy	227 (3)	0 (0)	227 (2)
Intraocular therapy given as bridging therapy	5 (0)	0 (0)	5 (0)
Radiation therapy given as bridging therapy	927 (14)	166 (6)	1093 (12)
Surgery given as bridging therapy	21 (0)	0 (0)	21 (0)
Not reported	673 (10)	449 (18)	1122 (12)
Lymphodepleting regimen - no. (%)			
Fludarabine + Cyclophosphamide	6769 (99)	2541 (99)	9310 (99)
Others	60 (1)	17 (1)	77 (1)
Fludarabine dose - no. (%)			
Unknown	2477 (36)	201 (8)	2678 (29)
Known	4352 (64)	2357 (92)	6709 (71)
Commercial vs. noncommercial CAR-T product - no. (%)			
Commercial	6353 (93)	2223 (87)	8576 (91)
Noncommercial	476 (7)	335 (13)	811 (9)
Product - no. (%)			
Kymriah	1258 (18)	0 (0)	1258 (13)
Yescarta	4106 (60)	0 (0)	4106 (44)
Tecartus	4 (0)	0 (0)	4 (0)
Breyanzi	985 (14)	0 (0)	985 (10)
Abecma	0 (0)	1088 (43)	1088 (12)
Carvykti	0 (0)	1135 (44)	1135 (12)
Other	476 (7)	335 (13)	811 (9)

Characteristic	NHL	MM	Total
Is the recipient participating in a cellular therapy clinical trial? - no. (%)			
No	6272 (92)	2041 (80)	8313 (89)
Yes	556 (8)	517 (20)	1073 (11)
Not reported	1 (0)	0 (0)	1 (0)
2-year product embargo - no. (%)			
No	5797 (85)	1311 (51)	7108 (76)
Yes	1032 (15)	1247 (49)	2279 (24)
Year of infusion - no. (%)			
Before 2017	9 (0)	3 (0)	12 (0)
2017	21 (0)	5 (0)	26 (0)
2018	516 (8)	49 (2)	565 (6)
2019	963 (14)	70 (3)	1033 (11)
2020	1129 (17)	84 (3)	1213 (13)
2021	1220 (18)	332 (13)	1552 (17)
2022	1556 (23)	686 (27)	2242 (24)
2023	1203 (18)	1031 (40)	2234 (24)
2024	212 (3)	298 (12)	510 (5)
Follow-up of survivors, months - median (range)	25 (0-86)	13 (1-86)	23 (0-86)

CIBMTR Study Proposal

Study Title
Comparing the Toxicity Profile of AYA Patients vs Older Patients following anti-CD19 CAR T-cell Therapy for B-cell malignancies

Key words
LBCL, ALL, AYA, CAR T cell, CRS, ICANS, infection, neurotoxicity

PI #1
Irtiza Sheikh, DO
PI #2
Sairah Ahmed, MD
PI#3
Partow Kebriaei, MD

Current Ongoing work with CIBMTR
Sairah: PBL LY23-01 – pending stats

Do any of the PIs within this proposal have a CIBMTR WC study in manuscript prep for >6 months:
no

Research Question

What is the impact of the toxicity profile in AYA (age 15-39 years old) patients who receive CD 19 directed CAR T cell therapy for B-cell malignancies including large B-cell lymphoma (LBCL) and acute lymphoblastic leukemia (ALL) compared to older adults?

Research Hypothesis

Adolescents and young adults (AYA) receiving CAR T cell therapy for relapsed/refractory (r/r) CD-19 positive leukemia and lymphoma may have a distinct toxicity profile, including severity of CRS/ICANS, than what is described in the current literature. The impact of toxicities attributed to CAR T cells has not been well studied in the AYA population specifically, indicating a need for targeted studies in this population.

Specific Objectives to be investigated

- Primary Objective
    - To compare CRS/ICANS in AYA patients (age 15-39 years old) to older patients following anti-CD19 CAR T cell therapy for r/r LBCL and ALL, including rates, grades, frequency, and severity.

- Secondary Objectives
    - To determine outcomes including overall response rate, complete response rate, relapse rate, non-relapse mortality in AYA patients versus older adults with r/r LBCL or ALL treated with anti-CD19 CAR T-cell therapy.
    - To compare cytopenias in AYA patients to older patients who receive CAR T cell therapy for r/r LBCL or ALL.
    - To compare the rate and severity of infections in AYA patients to older patients

- To compare the toxicities, including CRS/ICANS, infection, cytopenias and outcomes (ORR, CRR, RR, NRM) between AYA patients that receive Kymriah versus Tecartus for r/r ALL

Scientific Impact (Briefly state how the completion of the aims will impact participant care / outcomes and how it will advance science or clinical care.

While the impact of CART cell therapy has been described in the literature, there is a gap in knowledge specific to the AYA population in terms of the toxicity profile of CAR T cell therapy. Studies in patients with acute leukemia show that AYA patients differ from older and younger patients in terms of physiology, age related changes, and response to various chemotherapy protocols. AYA patients with lymphoma or leukemia may share similar characteristics, however, this has not been specifically investigated. Moreover, depending on the age of patients with ALL, AYA patients can be treated with different CAR T cell products in Kymriah (≤ 25 years old) or Tecartus (> 25). There is a need in the literature to describe the difference in toxicities and outcomes between the two products in the AYA population, along with comparing these factors to older adults. The importance in understanding the difference between the two CAR T cell products in the AYA population is underscored by the fact that a third CAR T cell product, obecabtagene autolecuel, has been recently approved in patients ≥18 years old for the treatment of relapsed ALL. The data obtained from this project will be used to determine if there is a correlation of toxicities to factors such as outcomes including overall survival (OS), event free survival/progression free survival (EFS/PFS), and non-relapsed mortality (NRM), infection rates, re-hospitalization rates, and length of B-cell aplasia.

Scientific Justification:

CAR T cell therapy has led to significant progress in the treatment of patients with relapsed/refractory (R/R) high-grade B cell malignancies and numerous publications have demonstrated differing toxicity profiles based on tumor burden, organ dysfunction, CAR product etc., and subgroups of patients have been identified to be at higher risk for CAR specific toxicity (i.e. older patients with higher rates of CRS/ICANS)[1]. The AYA population has not been specifically studied in current real world or registry analyses. Logue et al (2021) published their experience describing infections in the first 30 days after axicabtagene ciloleucel (axi-cel) infusion for LBCL[2]. Strati et al (2023) reported that prolonged cytopenias (PCs) following CAR T cell therapy for LBCL were associated with inferior outcomes including higher CRS frequency of any grade, higher rates of ICANS, including grade 3-4, and had shorter overall survival compared to those without PCs[3]. Following CAR T cell therapy for ALL, Jain et al (2020) and Juluri et al (2022) demonstrate that prolonged cytopenias increase rates of bacterial and viral infections and higher-grade CRS is associated with similar prolonged cytopenias in all cell lines that increase NRM and worsen quality of life, respectively[4, 5]. While these studies are vital to understanding the toxicities associated with CAR T cell therapy, and subsequent burden of care, the median age of patients in these studies was over 50 years old. It is difficult to ascertain if AYAs suffer from these toxicities at a higher or lower rate, requiring differing management due to their physiological differences from older patients. While current studies establish a correlation between toxicities such as infection, neurotoxicity, and prolonged cytopenias with outcomes like overall survival, this analysis has not been performed specifically in the AYA population. Our study will help in bridging the gap in understanding the downstream impact of CAR T cell toxicity in AYA patients with B-cell malignancies and is uniquely suited to a large registry based study.

Inclusion criteria
Patients ≥15 years old with LBCL or ALL treated with CD19 directed CAR T cells

Variables

Patient Characteristics

- Age
- Sex
- Race
- ECOG score
- Karnofsky scale
- HCTCI Score
- Time since diagnosis
- Prior malignancy: LBCL or CD-19 positive lymphoblastic leukemia
- Prior cellular therapies, DATE
- Prior HCT, days prior to cell infusion
- History of prior stem cell transplant
    - Type of SCT: Allo vs. auto

Malignancy Related Variables

- Lymphoma histology
- Number and agents utilized for prior lines of therapy
- CNS involvement at diagnosis and relapse (yes vs no)
- Bone marrow involvement at diagnosis and relapse (yes vs. no)
- Extranodal involvement at diagnosis and relapse (yes vs. no)
- Number of prior therapies (<2 vs. ≥2)
- Disease status at the time of HCT: CR vs PR vs SD/PD
- Extramedullary involvement (yes vs. no)
    - Site: Skin, soft tissue, testes/ovaries, etc.
- Blasts in blood prior to cell infusion
- Blasts in marrow prior to cell infusion
- Received CNS prophylaxis (yes vs. no)
    - Type of prophylaxis
- Radiation therapy given prior to lymphodepletion (yes vs. no)
    - Site of radiation

CAR-T Related Variables and Salvage Therapy

- Name of cellular therapy product
- Most recent CBC, including WBC, Neutrophil, lymphocytes, and platelets prior to infusion, at Day 30 following infusion, Day 100 following infusion, and day 180 following infusion
    - Presence of cytopenia following cell infusion
- Bridging therapy
- Drugs used in lymphodepleting therapy prior to cellular therapy

  - Total prescribed dose
- Use of toxicity prophylaxis
  - Therapy given for prevention of CRS
  - Therapy given for prevention of neurotoxicity
- Best response to cellular therapy
- Day 30, Day 100, and day 180 Response to CAR T cell therapy
- CRS, Grades
  - Did the patient experience CRS (yes/no)
  - Duration of CRS
  - Day of fever onset, day of hypotension onset
  - Therapy given for CRS
  - Symptoms of CRS
  - Did CRS resolve (yes/no)
  - Date CRS resolved
- Receipt of tocilizumab, dose
- Receipt of corticosteroids, duration
- Other specific therapies given for CRS
- Need for pressors
- Need for positive pressure ventilation (yes/no/unknown)
- ICANS, Grades, duration
- Specific therapy given for neurotoxicity
  - Resolution (yes/no)
- Length of Admission
- ICU admissions – duration of ICU admission
- Presence of primary HLH/ Immune effector cell associated HLH/HLH-like toxicities (yes/no/unknown)
    - Resolution (yes/no)
    - Days following infusion of onset and resolution
- Specific therapy given for primary HLH/ Immune effector cell associated HLH /HLH-like toxicities
- Confirmation of hemophagocytosis confirmed by bone marrow biopsy or aspirate
- Peripheral blood count recovery
  - Evidence of initial recovery (yes/no/not applicable)
  - Days post infusion when first ANC >/ 500/mm^3
  - Platelet count recovery >20 x 10^9/L (yes/no/NA)
    - Days post infusion
- Disease or progression
- Evidence of B cell recovery
  - Were B-cell counts monitored after infusion? (yes/no/unknown)
  - Days post infusion of initial B cell recovery
  - B cell presence at Day 30, Day 100, and Day 180
- Receipt of immunoglobulin replacement therapy (yes/no)
  - Is patient still requiring replacement therapy (yes/no)

        - Reason for immunoglobulin therapy (symptomatic or prophylactic)
    - IgG level prior to IVIG
    - IgG levels at 30, 100, and 180 days following infusion
    - Has the recipient's immunoglobulin level recovered (yes/no/NA)
    - Recovery of immunoglobulin level, days following infusion of recovery
- Grade 3 or grade 4 toxicity (yes/no/unknown)
    - Day following infusion of onset
    - Organs involved
    - Type of toxicity
    - Resolution of toxicity
- Development of infection
    - Type of infection, organism
    - Site of infection
    - Days following cell infusion
- Admission to hospital post-infusion (yes/no)
    - Days following cell infusion, duration of admission

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

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

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Patient characteristics of ALL CAR-T patients at least 15 years old, stratified by age

Characteristic	< 40	40+	Total
No. of patients	874	301	1175
No. of centers	152	93	173
Patient Characteristics			
Age, by decades - no. (%)			
Median (min-max)	22 (15-40)	57 (40-84)	24 (15-84)
10-19	346 (40)	0 (0)	346 (29)
20-29	398 (46)	0 (0)	398 (34)
30-39	130 (15)	0 (0)	130 (11)
40-49	0 (0)	89 (30)	89 (8)
50-59	0 (0)	99 (33)	99 (8)
60-69	0 (0)	82 (27)	82 (7)
70+	0 (0)	31 (10)	31 (3)
Recipient Sex - no. (%)			
Male	565 (65)	155 (51)	720 (61)
Female	309 (35)	146 (49)	455 (39)
Recipient race - no. (%)			
White	581 (66)	221 (73)	802 (68)
Black or African American	50 (6)	25 (8)	75 (6)
Asian	34 (4)	14 (5)	48 (4)
Native Hawaiian or other Pacific Islander	2 (0)	1 (0)	3 (0)
American Indian or Alaska Native	10 (1)	2 (1)	12 (1)
Other	10 (1)	2 (1)	12 (1)
More than one race	108 (12)	25 (8)	133 (11)
Missing	79 (9)	11 (4)	90 (8)
Ethnicity - no. (%)			
Hispanic or Latino	396 (45)	77 (26)	473 (40)
Non-Hispanic or Latino	378 (43)	210 (70)	588 (50)
Non-resident of the U.S.	73 (8)	10 (3)	83 (7)
Not reported	27 (3)	4 (1)	31 (3)
Current CCN region of patient - no. (%)			
US	805 (92)	292 (97)	1097 (93)
Canada	44 (5)	4 (1)	48 (4)
Europe	4 (0)	0 (0)	4 (0)
Asia	4 (0)	0 (0)	4 (0)
Australia/New Zealand	10 (1)	1 (0)	11 (1)
Mideast/Africa	4 (0)	4 (1)	8 (1)

Characteristic	< 40	40+	Total
Central/South America	3 (0)	0 (0)	3 (0)
Karnofsky performance score prior to CT - no. (%)			
90-100	483 (55)	90 (30)	573 (49)
80	186 (21)	106 (35)	292 (25)
< 80	137 (16)	70 (23)	207 (18)
Not reported	68 (8)	35 (12)	103 (9)
HCT-CI Score - no. (%)			
0	260 (30)	64 (21)	324 (28)
1	191 (22)	62 (21)	253 (22)
2	123 (14)	46 (15)	169 (14)
3	128 (15)	48 (16)	176 (15)
4	74 (8)	38 (13)	112 (10)
5+	67 (8)	37 (12)	104 (9)
Not reported	31 (4)	6 (2)	37 (3)
Disease related			
Interval from diagnosis to HCT, months - median (min-max)	26 (1-318)	19 (0-315)	23 (0-318)
Disease status prior to infusion			
Disease status prior to CT for leukemia - no. (%)			
CR1	105 (12)	31 (10)	136 (12)
CR2	142 (16)	50 (17)	192 (16)
CR3+	93 (11)	29 (10)	122 (10)
Relapse, 1st	202 (23)	87 (29)	289 (25)
Relapse, other	227 (26)	69 (23)	296 (25)
PIF/Untreated	87 (10)	31 (10)	118 (10)
Not reported	18 (2)	4 (1)	22 (2)
Infusion related			
Prior HCT - no. (%)			
No	617 (71)	168 (56)	785 (67)
Yes	244 (28)	133 (44)	377 (32)
Not reported	13 (1)	0 (0)	13 (1)
Bridging therapy - no. (%)			
No	213 (24)	96 (32)	309 (26)
Yes	447 (51)	152 (50)	599 (51)
Systemic therapy given as bridging therapy	432 (49)	147 (49)	579 (49)
Radiation therapy given as bridging therapy	46 (5)	14 (5)	60 (5)
Not reported	214 (24)	53 (18)	267 (23)
CRS (during follow-up for this CT) - no. (%)			
No	276 (32)	57 (19)	333 (28)

Characteristic	< 40	40+	Total
Yes	597 (68)	244 (81)	841 (72)
Not reported	1 (0)	0 (0)	1 (0)
Lymphodepleting regimen - no. (%)			
Fludarabine + Cyclophosphamide	811 (93)	273 (91)	1084 (92)
Bendamustine only	1 (0)	9 (3)	10 (1)
Others	53 (6)	19 (6)	72 (6)
None	9 (1)	0 (0)	9 (1)
Commercial vs. noncommercial CAR-T product - no. (%)			
Commercial	719 (82)	262 (87)	981 (83)
Noncommercial	155 (18)	39 (13)	194 (17)
Product - no. (%)			
Kymriah	519 (59)	0 (0)	519 (44)
Tecartus	200 (23)	262 (87)	462 (39)
Other	155 (18)	39 (13)	194 (17)
Is the recipient participating in a cellular therapy clinical trial? - no. (%)			
No	713 (82)	257 (85)	970 (83)
Yes	161 (18)	44 (15)	205 (17)
2-year product embargo - no. (%)			
No	689 (79)	104 (35)	793 (67)
Yes	185 (21)	197 (65)	382 (33)
Year of infusion - no. (%)			
Before 2017	20 (2)	3 (1)	23 (2)
2017	29 (3)	5 (2)	34 (3)
2018	66 (8)	6 (2)	72 (6)
2019	111 (13)	12 (4)	123 (10)
2020	113 (13)	2 (1)	115 (10)
2021	104 (12)	10 (3)	114 (10)
2022	178 (20)	96 (32)	274 (23)
2023	175 (20)	118 (39)	293 (25)
2024	78 (9)	49 (16)	127 (11)
Follow-up of survivors, months - median (range)	25 (1-108)	13 (1-74)	20 (1-108)

Patient characteristics of LBCL CAR-T patients at least 15 years old, stratified by age

Characteristic	< 40	40+	Total
No. of patients	658	8283	8941
No. of centers	129	174	188
Patient Characteristics			
Age, by decades - no. (%)			
Median (min-max)	32 (15-40)	66 (40-91)	65 (15-91)
10-19	22 (3)	0 (0)	22 (0)
20-29	231 (35)	0 (0)	231 (3)
30-39	405 (62)	0 (0)	405 (5)
40-49	0 (0)	751 (9)	751 (8)
50-59	0 (0)	1735 (21)	1735 (19)
60-69	0 (0)	3056 (37)	3056 (34)
70+	0 (0)	2741 (33)	2741 (31)
Recipient Sex - no. (%)			
Male	400 (61)	5200 (63)	5600 (63)
Female	258 (39)	3082 (37)	3340 (37)
Not reported	0 (0)	1 (0)	1 (0)
Recipient race - no. (%)			
White	396 (60)	6377 (77)	6773 (76)
Black or African American	83 (13)	360 (4)	443 (5)
Asian	49 (7)	469 (6)	518 (6)
Native Hawaiian or other Pacific Islander	5 (1)	16 (0)	21 (0)
American Indian or Alaska Native	5 (1)	33 (0)	38 (0)
Other	12 (2)	34 (0)	46 (1)
More than one race	52 (8)	384 (5)	436 (5)
Missing	56 (9)	610 (7)	666 (7)
Ethnicity - no. (%)			
Hispanic or Latino	116 (18)	800 (10)	916 (10)
Non-Hispanic or Latino	445 (68)	6319 (76)	6764 (76)
Non-resident of the U.S.	85 (13)	880 (11)	965 (11)
Not reported	12 (2)	284 (3)	296 (3)
Current CCN region of patient - no. (%)			
US	570 (87)	7390 (89)	7960 (89)
Canada	44 (7)	484 (6)	528 (6)
Europe	11 (2)	73 (1)	84 (1)
Asia	9 (1)	78 (1)	87 (1)
Australia/New Zealand	9 (1)	84 (1)	93 (1)

Characteristic	< 40	40+	Total
Mideast/Africa	9 (1)	140 (2)	149 (2)
Central/South America	6 (1)	34 (0)	40 (0)
Karnofsky performance score prior to CT - no. (%)			
90-100	306 (47)	3178 (38)	3484 (39)
80	178 (27)	2465 (30)	2643 (30)
< 80	99 (15)	1707 (21)	1806 (20)
Not reported	75 (11)	933 (11)	1008 (11)
HCT-CI Score - no. (%)			
0	265 (40)	2470 (30)	2735 (31)
1	139 (21)	1620 (20)	1759 (20)
2	94 (14)	1122 (14)	1216 (14)
3	83 (13)	1195 (14)	1278 (14)
4	47 (7)	790 (10)	837 (9)
5+	25 (4)	992 (12)	1017 (11)
Not reported	5 (1)	94 (1)	99 (1)
Disease related			
Interval from diagnosis to HCT, months - median (min-max)	11 (2-166)	14 (0-447)	13 (0-447)
Disease status prior to infusion			
Disease status prior to CT for lymphoma - no. (%)			
CR	27 (4)	615 (7)	642 (7)
PR	155 (24)	1796 (22)	1951 (22)
Resistant	418 (64)	4917 (59)	5335 (60)
Untreated	27 (4)	487 (6)	514 (6)
Unknown	29 (4)	461 (6)	490 (5)
Not reported	2 (0)	7 (0)	9 (0)
Infusion related			
Prior HCT - no. (%)			
No	554 (84)	6587 (80)	7141 (80)
Yes	98 (15)	1676 (20)	1774 (20)
Not reported	6 (1)	20 (0)	26 (0)
Bridging therapy - no. (%)			
No	178 (27)	2840 (34)	3018 (34)
Yes	315 (48)	3511 (42)	3826 (43)
Systemic therapy given as bridging therapy	265 (40)	2947 (36)	3212 (36)
Intrathecal therapy given as bridging therapy	23 (3)	227 (3)	250 (3)
Intraocular therapy given as bridging therapy	0 (0)	6 (0)	6 (0)
Radiation therapy given as bridging therapy	95 (14)	937 (11)	1032 (12)
Surgery given as bridging therapy	4 (1)	20 (0)	24 (0)

Characteristic	< 40	40+	Total
Not reported	165 (25)	1932 (23)	2097 (23)
CRS (during follow-up for this CT) - no. (%)			
No	147 (22)	2121 (26)	2268 (25)
Yes	510 (78)	6161 (74)	6671 (75)
Not reported	1 (0)	1 (0)	2 (0)
Lymphodepleting regimen - no. (%)			
Fludarabine + Cyclophosphamide	504 (77)	6269 (76)	6773 (76)
Bendamustine only	35 (5)	623 (8)	658 (7)
Others	119 (18)	1372 (17)	1491 (17)
None	0 (0)	18 (0)	18 (0)
Not reported	0 (0)	1 (0)	1 (0)
Commercial vs. noncommercial CAR-T product - no. (%)			
Commercial	615 (93)	7785 (94)	8400 (94)
Noncommercial	43 (7)	498 (6)	541 (6)
Product - no. (%)			
Kymriah	83 (13)	1454 (18)	1537 (17)
Yescarta	498 (76)	5219 (63)	5717 (64)
Tecartus	1 (0)	3 (0)	4 (0)
Breyanzi	33 (5)	1109 (13)	1142 (13)
Other	43 (7)	498 (6)	541 (6)
Is the recipient participating in a cellular therapy clinical trial? - no. (%)			
No	606 (92)	7657 (92)	8263 (92)
Yes	52 (8)	624 (8)	676 (8)
Not reported	0 (0)	2 (0)	2 (0)
2-year product embargo - no. (%)			
No	611 (93)	7100 (86)	7711 (86)
Yes	47 (7)	1183 (14)	1230 (14)
Year of infusion - no. (%)			
Before 2017	2 (0)	13 (0)	15 (0)
2017	1 (0)	22 (0)	23 (0)
2018	46 (7)	486 (6)	532 (6)
2019	84 (13)	934 (11)	1018 (11)
2020	105 (16)	1098 (13)	1203 (13)
2021	93 (14)	1193 (14)	1286 (14)
2022	144 (22)	1800 (22)	1944 (22)
2023	140 (21)	2089 (25)	2229 (25)
2024	43 (7)	648 (8)	691 (8)
Follow-up of survivors, months - median (range)	21 (1-81)	22 (0-86)	22 (0-86)

CIBMTR Study Proposal

Study Title: 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

Principal Investigators (Alphabetical order): Gurbakhash Kaur, Hira Javed

Co-investigators (Alphabetical order):

Caroline Schinke , Doris Hansen, Hamza Hashmi Meera Mohan, Murali Janakiram, Saad Usmani, Surbhi Sidana,

Research Hypothesis:

BCMA targeting chimeric antigen receptor T (CAR T) cell therapies idecabtagene vicleucel (ide-cel)[1,2] and ciltacabtagene autoleucel (cilta-cel) [3] have improved outcomes for patients with relapsed/refractory multiple myeloma (MM). These therapies are linked to significant including cytokine release syndrome (CRS), immune effector cell-associated neurotoxicity syndrome (ICANS), non-ICANS neurotoxicity, secondary malignancies, and the risk of infections, all contributing to non-relapse mortality (NRM). In the pivotal clinical trials of T-cell immunotherapies, there is significant variability in the attribution of treatment related adverse effects and mortality to therapy. In the absence of any clearly defined comorbidity index that predicts NRM from CAR T-cell therapy, there is an unmet clinical need to evaluate the impact of comorbidities on NRM and OS in patients undergoing CAR T-cell therapy. As such, the hematopoietic cell transplant comorbidity index (HCT-CI) is a validated scoring system designed to predict non-relapse mortality (NRM) risk following allogeneic transplants in patients with hematological malignancies, including multiple myeloma (MM). The application of HCT-CI in CAR T therapy may provide insights into a patient's overall health status and potential treatment complications. HCT CI may predict risk of short term complication such as CRS, ICANS, infections and NRM in addition to disease specific response such as PFS and - overall survival (OS) in recipients of CAR T there by offering a practical framework for assessing risk and guiding clinical decision-making.

Specific Aims:

Primary aim:

1. To assess the patient and disease characteristics that predict non-relapse mortality (NRM) at 3, 6 and 12-months post-treatment in patients undergoing BCMA targeted CAR-T therapy in RRMM

Secondary aims:

1. To evaluate the role of the Hematopoietic Cell Transplantation-Comorbidity Index (HCT-CI) in predicting non-relapse mortality at 3,6 and 12 months in patients undergoing BCMA targeted CAR-T therapy in RRMM.
2. To develop a new prognostic model (CAR-T-CI) that integrates myeloma specific disease factors (e.g., tumor burden, cardiac dysfunction, renal dysfunction) to predict non-relapse mortality at 3, 6 and 12 months. [keeping in mind that we do not know the n to develop and validate a new prognostic model if the NRM or events is low]

Scientific Impact: Identifying patients, disease and treatment specific risk factors upfront using a CAR-T CI could help provide insights into therapeutic decision making especially with the recent approval of these therapies in the earlier lines.

Scientific Justification:

CAR T-cell therapy has revolutionized the treatment of relapsed/refractory multiple myeloma (RRMM). FDA-approved therapies, such as idecabtagene vicleucel (ide-cel) and ciltacabtagene autoleucel (cilta-cel), have shown impressive response rates ranging from 80% to 98%. However, organ dysfunctions and comorbidities are known to impact treatment outcomes, especially in cancer. The **Hematopoietic Cell Transplant Comorbidity Index (HCT-CI)**, a comorbidity index consisting of a of 15 weighted pre-transplant comorbidities (scores ranging from a minimum of 0 to a maximum of 26), [8] has been useful in assessing organ dysfunction in allogeneic stem cell transplant recipients and has provided valuable prognostic information. Currently, no similar tool exists for patients undergoing CAR-T therapy.

In a recent meta-analysis of CAR-T therapy for various hematological conditions, ide-cel and cilta-cel were associated with **non-relapse mortality (NRM)** rates of up to 6.5% and 15%, respectively. [5] Additionally pivotal clinical trials for CAR-T in RRMM have shown a **treatment-related mortality (TRM)** rate of about 5-10%. However, clinical trials typically involve carefully selected patients with adequate organ function and good performance status. This selection bias limits their ability to fully reflect the true risk of NRM and other CAR-T-specific side effects.

While the risks of CAR-T therapy may be acceptable for heavily pre-treated patients, the risk-benefit ratio becomes more concerning for those in earlier lines of therapy or those considering CAR-T as a non-curative treatment in upfront settings.

We propose validating the use of the **HCT-CI** for predicting prognostic outcomes and evaluating NRM in CAR-T patients. Additionally, we aim to develop a comorbidity scoring system tailored for CAR-T therapy that can predict both **non-relapse mortality (NRM)** and **overall survival (OS)** taking into account myeloma specific disease burden, comorbidities (renal failure, history of neuropathy etc). This tool will assist in decision-making and enable more accurate patient selection for CAR-T therapy in patients with RRMM.

Patient eligibility population:

Inclusion criteria:

- Any Patient who has received BCMA CAR T cell therapy (ide-cel and cilta-cel) for relapsed refractory MM

VARIABLES TO BE DESCRIBED AND/OR ANALYZED:

Form 2100R9- Post HSCT Data

- last follow up
- survival status at last follow up
- subsequent infusions
- subsequent HCT
- received cellular therapy?
- hematopoietic recovery

Form 2400R10- Pre Transplant Essential Data

- Recipient age, sex, ethnicity, race, country and state of residence
- Prior cellular therapy and HCT history
- Recipient functional status and comorbidities
- reason for current HCT
- donor type (auto or syngeneic only)
- serum ferritin

Form 2450-R8

- date of last contact
- survival status at last contact

- subsequent infusions?
- time to hematopoietic recovery
- complications post transplant
- new malignancies post transplant.
- best response
- date of best response
- relapse/progression date
- subsequent therapy at relapse/persistent/progressive disease status- date(s), regimen, response.

Form 2900R5

- date of death
- cause

Form 4000R10 – Pre-Cellular Therapy Essential Data

- Recipient age, sex, ethnicity, race, country and state of residence
- Prior cellular therapy and HCT history
- Cellular therapy product, clinical trial versus standard of care
- LDH-
-

  Recipient functional status and comorbidities

  - Question 77, 78, and 80 re ECOG and Karnofsky
  - Question 91 RE; prior viral exposure
  - Question 92, 93 (Co-morbidity Index)
  - Co-existing Disease or Organ impairment (as outlined in question 93)
  - Question 94: prior hx of dialysis to CAR-T
  - Question 95- specific prior malignancy

Form 4001R1- Baseline data

- HCT type – autologous or allogeneic
- -lymphodepleting chemotherapy details

- Therapy given to prevent CRS and neurotoxicity

Form 4003R5

- -cellular therapy product
- -date of cell collection
- -method of product collection
- -therapy target
-

Form 2016R5 – Plasma Cell Disorders Pre-Infusion

- Disease status
- R-ISS, ISS stage at diagnosis
- High risk cytogenetics by FISH: t(4;14), t(14;16), deletion 17p, t(14;20), amp 1q
- other cytogenetics: del 1p, monosomy 13, t(11;14), t(8;14), hyperdiploidy.
- Presence of extramedullary disease
- o Marrow plasma cell percentage (>50% plasma cells in marrow will be considered high tumor burden)
- Lines of therapy (drugs given, start and stop date, and response for each line)
- Prior Akylator (Yes/No, type)
    - ♣ Carmustine
    - ♣ Bendamustine
    - ♣ Melphalan
    - ♣ Cyclophosphamide
- Prior stem cell transplant
- Prior bispecific T-cell engager (BiTE) therapy
    - ♣ Talquetamab (Yes/No)
    - ♣ Teclistamab (Yes/No)
- Prior CAR T-cell therapy
- Prior antibody-drug conjugate (ADC) therapy
    - ♣ Belantamab (Yes/No)
- Will assess for refractoriness to bortezomib, carfilzomib, lenalidomide, pomalidomide, and daratumumab

-

Form 4006R6 – Cellular Therapy Infusion

- CAR T-cell dose infused

Form 4100R0 – Cellular Therapy Essential Data Follow-Up (100 days, 6 months, 1 year, 2 years, >2 years)

- -name of cellular therapy product
- -date of infusion.
- Response and survival: best response to cellular therapy, date of death (if deceased), date of disease relapse or progression, date of last follow-up
- Subsequent cellular infusions (CD34+ stem cell boost)
- Peripheral blood count recovery– includes dates of ANC and platelet recovery
- Current hematologic findings) – includes transfusion details, growth factor use
- o Calculate time to transfusion independence
- Incidence of secondary malignancy
- B-cell recovery (yes/no, date)
- •oxicities and their management (questions 89-203) – includes CRS, MAS/HLH, neurotoxicity (ICANS), hypogammaglobulinemia, TLS, organ toxicity
    - Yes/No
- Maximum grade
    - Use of tocilizumab, siltuximab, steroids, anakinra and IVIG
- Yes/No
    - Number of doses
- Infection data – includes type, site and date

Form 4101R1

Form 2116R5 – Plasma Cell Disorders Post-Infusion (100 days, 6 months, 1 year, 2 years, >2 years)

- MM type (light chain only, nonsecretory, heavy chain type, light chain type)
- line of therapy
- date of best response
- best Response: CCR, sCR, CR, VGPR, PR, NR/SD, PD, MRD, PET/CT

- date of progression
- maintenance therapy?
- post infusion systemic therapy – regimen, date started, date stopped, reason for stopping, response.
- post infusion radiation therapy – dates, dose.
- post infusion cellular therapy – date of infusion, response
- Subsequent lines of therapy
- date of last follow up
- response status at last follow up
- survival status at last follow up.

OUTCOMES:

Primary:

- Cumulative incidence of 3 , 6 -NRM and 12-month OS in patients stratifies by pre-CAR T HCT-CI score.

Secondary:

- Multivariable models of patient, disease and therapy characteristics associated with 3, 6, and 12-month OS.
- Evaluate the cumulative incidence of CRS, and CRS, ICANS, toxicity based on HCT-CI.
- PFS
- OS at 3, 6, 12 months

7. STUDY DESIGN:

A retrospective multicenter study will be performed using the CIBMTR dataset.

Data Requirements: NA

If supplemental data is required, please review data collection forms at:

http://www.cibmtr.org/DataManagement/DataCollectionForms/Pages/index.aspx

Sample Requirements: NA

Study Design: NA

Non-CIBMTR Data Source:

If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required, i.e., neither database contains all the data required to answer the study question; 3) A list of the data elements available in both data sources that will be used to link the CIBMTR record with the external record; 4) The methodology used to link the datasets.

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8. Saad A, Mahindra A, Zhang MJ, et al. Hematopoietic cell transplant comorbidity index is predictive of survival after autologous hematopoietic cell transplantation in multiple myeloma. *Biol Blood Marrow Transplant*. 2014;20(3):402-408.e401.

Conflicts of Interest:

Do you have any conflicts of interest pertinent to this proposal concerning:

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

□ Yes

x No

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.

Insert your text here.

Patient characteristics of MM CAR-T patients

Characteristic	N (%)
No. of patients	3269
No. of centers	106
Patient Characteristics	
Age, by decades - no. (%)	
Median (min-max)	66 (29-90)
20-29	2 (0)
30-39	32 (1)
40-49	199 (6)
50-59	707 (22)
60-69	1329 (41)
70+	1000 (31)
Recipient Sex - no. (%)	
Male	1881 (58)
Female	1386 (42)
Not reported	2 (0)
Recipient race - no. (%)	
White	2510 (77)
Black or African American	508 (16)
Asian	85 (3)
Native Hawaiian or other Pacific Islander	6 (0)
American Indian or Alaska Native	9 (0)
Other	10 (0)
More than one race	82 (3)
Missing	59 (2)
Ethnicity - no. (%)	
Hispanic or Latino	244 (7)
Non-Hispanic or Latino	2912 (89)
Non-resident of the U.S.	29 (1)
Not reported	84 (3)
Current CCN region of patient - no. (%)	
US	3235 (99)
Canada	15 (0)
Europe	13 (0)
Australia/New Zealand	5 (0)
Not reported	1 (0)

Characteristic	N (%)
Karnofsky performance score prior to CT - no. (%)	
90-100	1231 (38)
80	1133 (35)
< 80	568 (17)
Not reported	337 (10)
HCT-CI Score - no. (%)	
0	898 (27)
1	590 (18)
2	475 (15)
3	520 (16)
4	332 (10)
5+	428 (13)
Not reported	26 (1)
Were there clinically significant co-existing diseases or organ impairment prior to prep. regimen? - no. (%)	
No	847 (26)
Yes	2402 (73)
Arrhythmia	369 (11)
Inflammatory bowel disease	20 (1)
Cardiac	448 (14)
Cerebrovascular disease	146 (4)
Diabetes	482 (15)
Pulmonary, severe	385 (12)
Pulmonary, moderate	528 (16)
Infection	122 (4)
Prior malignancy	578 (18)
Hepatic, mild	214 (7)
Hepatic, moderate / severe	28 (1)
Heart valve disease	88 (3)
Obesity	397 (12)
Renal, moderate / severe	164 (5)
Psychiatric disturbance	617 (19)
Peptic ulcer	33 (1)
Rheumatologic	45 (1)
Not reported	20 (1)
Disease related	
Interval from diagnosis to HCT, months - median (min-max)	71 (0-424)

Characteristic	N (%)
Disease status prior to infusion	
Disease status prior to CT for PCD - no. (%)	
Stringent complete remission (sCR)	23 (1)
Complete remission (CR)	51 (2)
Very good partial remission (VGPR)	310 (9)
Partial response (PR)/ Not Complete Remission	405 (12)
Stable disease (SD)	534 (16)
Progressive disease (PD)	1863 (57)
Relapse from CR (Rel) (untreated)	62 (2)
Not reported	21 (1)
Infusion related	
Prior HCT - no. (%)	
No	551 (17)
Yes	2714 (83)
Not reported	4 (0)
Lymphodepleting regimen - no. (%)	
Fludarabine + Cyclophosphamide	2541 (78)
Bendamustine only	253 (8)
Others	469 (14)
None	6 (0)
Bridging therapy - no. (%)	
No	832 (25)
Yes	1549 (47)
Systemic therapy given as bridging therapy	1494 (46)
Radiation therapy given as bridging therapy	190 (6)
Not reported	888 (27)
Commercial vs. noncommercial CAR-T product - no. (%)	
Commercial	2905 (89)
Noncommercial	364 (11)
Product - no. (%)	
Abecma	1543 (47)
Carvykti	1362 (42)
Other	364 (11)
Is the recipient participating in a cellular therapy clinical trial? - no. (%)	
No	2704 (83)
Yes	565 (17)
2-year product embargo - no. (%)	
No	1822 (56)

Characteristic	**N (%)**
Yes	1447 (44)
Year of infusion - no. (%)	
Before 2017	5 (0)
2017	5 (0)
2018	51 (2)
2019	70 (2)
2020	86 (3)
2021	340 (10)
2022	865 (26)
2023	1418 (43)
2024	429 (13)
Follow-up of survivors, months - median (range)	12 (1-86)

I. Study Title

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

II. Key Words

a. conditioning regimen intensity, myeloablative, reduced intensity, non-myeloablative, toxicity, non- relapse mortality

III. Principle Investigator Information

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III. Research Question

a. Can the transplant conditioning intensity (TCI) score developed by the ALWP of EBMT be externally validated through the CIBMTR database as a more predictive measurement of transplant conditioning intensity, and is this predictive value maintained when applied to patients with AML and MDS who receive an allogeneic stem cell transplantation using post-transplant Cyclophosphamide (PTCy) GVHD prophylaxis?

IV. Research Hypothesis

We hypothesize that the TCI classification scoring system as a novel measurement of regimen conditioning intensity will be externally validated by the CIBMTR database as a more predictive measurement of conditioning intensity based on the primary outcome of

non-relapse mortality at day +100 and day +180 compared to the traditional RIC/MAC classification system, and that the predictive value will be maintained when applied to patients receiving PTCy GVHD prophylaxis

V. Specific Objectives/Outcomes to be investigated
   a. Primary outcomes
      i. Non-relapse mortality (NRM) at Day +100 and Day +180
   b. Secondary outcomes
      i. Relapse incidence
      ii. Leukemia-free survival
      iii. Overall survival
      iv. Incidence of acute and chronic GVHD
      v. GVHD-Relapse-free survival (GRFS)

VI. Scientific Impact

The intensity of pre-transplant conditioning regimens for allogeneic stem cell transplant have historically been defined by the degree of expected myeloablation and the necessity for stem cell rescue. The "Champlin criteria" developed at the First International Workshop of Nonmyeloablative Stem Cell Transplantation proposed that a reduced intensity regimen does not require stem cell support for hematopoietic recovery, results in low non-hematologic toxicity, and results in mixed donor-recipient chimerism in a substantial proportion of patients in the early post-transplantation period[1]. During an EBMT workshop convened in 2001, conditioning regimens were distinguished as reduced intensity based on inclusion of specific agents – total body irradiation 200 cGy, busulfan 8 mg/kg, thiotepa 10mg/kg, and melphalan 140 mg/m2[2]. Similar NMDP operational criteria for reduced intensity conditioning were accepted by an expert panel convened by NMDP and CIBMTR and generally include alkylating agents with or without TBI that is dose-reduced by ≥30% compared with MAC counterparts[3, 4]. Finally, consensus definitions indicated that myeloablative regimens cause irreversible cytopenia and stem cell support is mandatory, however this definition has been empirically determined and not defined according to transplant outcomes.

The advancement of reduced-intensity conditioning regimens have been allowed the minimization of early regimen toxicity for patients otherwise unfit to receive myeloablative conditioning, and they can achieve similar survival outcomes to those patients receiving MAC regimens[5], albeit with an increased for relapsed disease is higher[6]. As such the RIC/MAC classification system has served as an important tool for safely administering conditioning regimens, however, there remains significant variation of intensity within the broad categories of RIC/MAC. The Transplant Conditioning Intensity (TCI) score was developed as a refinement of the classical RIC/MAC classification to improve our understanding of the treatment-related toxicities of conditioning regimens on patient outcomes after allogeneic stem cell transplant and is more predictive of NRM [7].

Transplant practices have evolved over the last 2 decades as reflected by the expansion of novel reduced-toxicity regimens and improving survival outcomes. The proportion of bone marrow transplant recipients of advanced age, particularly ≥65 years, has also gradually increased since 2012[8]. To date, the RIC/MAC system to assess conditioning intensity has not been updated to

better define and standardize conditioning regimen intensities since its inception. As increasingly older patients with more complex medical comorbidities become eligible for allogeneic stem cell transplantation, it is critical to further refine the treatment-related mortality and relapse risk when making decisions regarding conditioning regimens. To broaden the knowledge and acceptance of this novel, clinically meaningful approach to transplant conditioning classification, a validation study using CIMBT data is warranted.

VII. Scientific Justification

The TCI score was developed by the Acute Leukemia Working Party (AWLP) of the European Bone Marrow Transplant (EBMT) as a tool to more effectively standardize the intensity of conditioning regimens used in allogeneic stem cell transplant compared with the traditional RIC/MAC classification system [7]. Intensity weights are assigned to the treatments frequently used in transplant conditioning regimens and the sum of these weights was used to define TCI scores for individual conditioning regimens. The TCI scoring system was retrospectively evaluated in a cohort of 8255 adult patients (ages 45-65) with acute myeloid leukemia (AML) undergoing allogeneic transplant in first remission and by concordance index was more predictive for non-relapse mortality (NRM) at days +100 and +180 versus RIC/MAC classification. In this population, the TCI scoring system was able to re-classify several commonly used conditioning regimens into “low”, “intermediate”, and “high” intensity categories for NRM. The generation of an “intermediate intensity” TCI grouping compiled primarily of borderline low-MAC and high-RIC regimens demonstrating statistically similar outcomes for NRM, relapse, and survival is an important improvement on to the RIC/MAC schema.

This innovative scoring system has been validated in diverse cohorts, including a large EBMT group of older AML patients (N=4312, aged 55-75 years) and another substantial cohort (N=1747) of AML patients in CR1, reported to the Japanese Society for Transplantation and Cellular Therapy. In both cases, the TCI score improved predictions for relapse and NRM[9]. Both cohorts comprised patients who received a variety of GVHD prophylaxis strategies, and in some cases, there were limited numbers or missing information regarding the use of PTCy (now considered standard in RIC and NMA HCT). The analysis was further confined to patients with matched, cord (JSTCT), or single-antigen mismatched donors, as well as being exclusively based on patients reported to the EBMT and JSTCT.

Our primary objective is to validate the TCI scoring system using a cohort of patients from the CIBMTR database which is similar to that cohort which was evaluated by the EBMT. However, since the development of the TCI scoring system, PTCy-based GVHD prophylaxis has emerged as a major GVHD prophylaxis strategy in the United States, particularly among mismatched HCT and RIC transplantation as supported by recent phase 2 and phase 3 data[10, 11]. The potential impact of PTCy on NRM should not be overlooked, and thus this proposal also aims to explore the application of TCI scoring in a cohort of patients who receive PTCy GVHD as it more closely aligns with current transplant practices in the United States.

VIII. Participant Selection Criteria

a. Inclusion

i. Ages ≥ 18 years
ii. Transplant received between years 2010-2022
iii. First Complete Remission (CR1) at time of HCT
iv. Transplant indication for Acute Myeloid Leukemia or Myelodysplastic syndrome
v. Allogeneic transplant recipient with matched-related donor, haploidentical, 8/8 MUD, or 7/8 MMUD
1. Conditioning regimen agents and doses available

b. Exclusion

i. Second transplant or later
ii. Syngeneic transplant
iii. Cord transplant

IX. Data Requirements

I. Demographics
- Age at HCT
- Sex/gender
- Race/ethnicity
- Karnofsky performance score
- HCT-CI score
- Follow-up post HCT (months)
- CMV status

II. Disease characteristics
- Diagnosis: AML, MDS
  - Secondary vs de Novo
  - Extramedullary
  - ELN risk (if available)
  - IPSS-R (if available)
  - MRD prior to transplant (if available)
- Remission status prior to transplant
  - CR, Cri, MRD status

III. Transplant characteristics
- Year of transplant
- Time from diagnosis to HCT
- Conditioning regimen
  - Agents used and dosing
- GVHD prophylaxis
  - PTCy vs Non-PTcy
    - Agents used and dosing
- Donor source
  - Bone marrow, Peripheral blood

        - Match Grade (8/8 MUD, 7/8 MMUD, MSD, Haploidentical)
    - Donor
        - Sex
        - age
        - CMV status

IV. Follow-up
    - Engraftment/Failure
    - aGVHD information outcomes
        - yes/no
        - max stage/grade if applicable
    - cGVHD information outcomes
        - yes/no
        - max severity if applicable
    - Survival data
        - Relapse- yes/no
            - Date of relapse if applicable
        - Survival at Day +100, day +180, and 1 year
        - Death
            - Yes/no
            - Cause

A TCI score will be computed using established criteria, utilizing data on conditioning regimen chemotherapy agents and radiation dosing as recorded in Pre-Transplant Essential Data (Pre-TED) form 2400. Patients will be categorized into three groups based on the calculated TCI scores, as outlined previously: low (≤2), intermediate (2.5-3.5), and high (≥4). First, the TCI score will be computed and validated in the cohort of patients receiving non-PTCY based GVHD prophylaxis. Sensitivity, or subgroup analyses will be performed on certain populations of interest (eg age group, MDS vs AML). Next, the TCI score will be computed and validated in the cohort of patients receiving PTCY based GVHD prophylaxis. These two groups will be evaluated separately given the clinical impression that conditioning regimens and toxicities differ between non-PTCY and PTCY based GVHD prophylaxis.

Component	Dose level			Added points for each dose level
	Low	Intermediate	High	
TBI fractionated (Gray)	≤5	6–8	≥9	1
Busulphan (mg/kg)	≤6.4 iv & ≤8 po	9.6 iv & 12 po	12.8 iv & 16 po	1
Treosulfan (g/m2)	30	36	42	1
Melphalan (mg/m2)	<140	≥140	≥200	1
Thiotepa (mg/kg)	<10	≥10	≥20	0.5
Fludarabine (mg/m2)	≤160	>160		0.5
Clofarabine (mg/m2)	≤150	>150		0.5
Cyclophosphamide (mg/kg)	<90	≥90		0.5
Carmustine (mg/m2)	≤250	280–310	≥350	0.5
Cytarabine (g/m2)	<6	≥6		0.5
Etoposide (mg/kg)	<50	≥50		0.5

X. Patient-Reported (PRO) Requirements- N/A
XI. Machine learning- N/A
XII. Sample Requirements- N/A
XIII. Non-CIBMTR Data source- N/A
XIV. References

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Population characteristics of adult patients receiving an alloHCT for AML/MDS, 2010-2022

Characteristic	AML	MDS	Total
No. of patients	35156	14343	49499
No. of centers	354	306	363
Patient-Related Characteristics			
TED or RES (RF) track determined for this event - no. (%)			
TED	28441 (81)	9151 (64)	37592 (76)
CRF (RES)	6715 (19)	5192 (36)	11907 (24)
Age, by decades - no. (%)			
Median (min-max)	56 (18-88)	62 (18-83)	58 (18-88)
18-19	511 (1)	102 (1)	613 (1)
20-29	2861 (8)	442 (3)	3303 (7)
30-39	3698 (11)	608 (4)	4306 (9)
40-49	5349 (15)	1281 (9)	6630 (13)
50-59	8972 (26)	3450 (24)	12422 (25)
60-69	10911 (31)	6432 (45)	17343 (35)
70+	2854 (8)	2028 (14)	4882 (10)
Sex - no. (%)			
Male	18924 (54)	8972 (63)	27896 (56)
Female	16232 (46)	5371 (37)	21603 (44)
Race - no. (%)			
White	26384 (75)	11511 (80)	37895 (77)
Black or African American	1793 (5)	554 (4)	2347 (5)
Asian	2103 (6)	695 (5)	2798 (6)
Native Hawaiian or other Pacific Islander	129 (0)	34 (0)	163 (0)
American Indian or Alaska Native	97 (0)	31 (0)	128 (0)
More than one race	186 (1)	62 (0)	248 (1)
Not reported	4464 (13)	1456 (10)	5920 (12)
Ethnicity - no. (%)			
Hispanic or Latino	2677 (8)	826 (6)	3503 (7)
Non-Hispanic or Latino	25602 (73)	11059 (77)	36661 (74)
Non-resident of the U.S.	6294 (18)	2228 (16)	8522 (17)
Not reported	583 (2)	230 (2)	813 (2)
Current CCN region of patient - no. (%)			
US	27209 (77)	11521 (80)	38730 (78)
Canada	1815 (5)	632 (4)	2447 (5)
Europe	1701 (5)	736 (5)	2437 (5)
Asia	1069 (3)	391 (3)	1460 (3)

Characteristic	AML	MDS	Total
Australia/New Zealand	1505 (4)	547 (4)	2052 (4)
Mideast/Africa	578 (2)	90 (1)	668 (1)
Central/South America	1279 (4)	426 (3)	1705 (3)
Karnofsky score prior to HCT - no. (%)			
90-100%	20564 (58)	7896 (55)	28460 (57)
< 90%	13972 (40)	6205 (43)	20177 (41)
Not reported	620 (2)	242 (2)	862 (2)
HCT-CI - no. (%)			
0	9060 (26)	3293 (23)	12353 (25)
1	5353 (15)	2015 (14)	7368 (15)
2	5184 (15)	1883 (13)	7067 (14)
3	5862 (17)	2469 (17)	8331 (17)
4	3979 (11)	1650 (12)	5629 (11)
5+	5006 (14)	2638 (18)	7644 (15)
Not reported	712 (2)	395 (3)	1107 (2)
Disease-Related Characteristics			
Interval from diagnosis to HCT, months - median (min-max)	5 (0-1208)	8 (0-799)	6 (0-1208)
Disease Status			
AML pre-HCT disease stage - no. (%)			
Disease is not AML	0 (0)	14343 (100)	14343 (29)
CR1	23841 (68)	0 (0)	23841 (48)
CR2	5254 (15)	0 (0)	5254 (11)
CR3+	297 (1)	0 (0)	297 (1)
Advanced or active disease	5592 (16)	0 (0)	5592 (11)
Not reported	172 (0)	0 (0)	172 (0)
MDS pre-HCT disease stage - no. (%)			
Disease is not MDS/MPN	35156 (100)	0 (0)	35156 (71)
Early	0 (0)	2582 (18)	2582 (5)
Advanced	0 (0)	11351 (79)	11351 (23)
Not reported	0 (0)	410 (3)	410 (1)
Transplant-Related Characteristics			
Conditioning intensity reported by center - no. (%)			
MAC	19292 (55)	5564 (39)	24856 (50)
NMA	3737 (11)	1988 (14)	5725 (12)
RIC	9078 (26)	5438 (38)	14516 (29)
Not MAC, either RIC or NMA	2865 (8)	1289 (9)	4154 (8)
Not reported	184 (1)	64 (0)	248 (1)
Conditioning regimen - no. (%)			

Characteristic	AML	MDS	Total
TBI/Cy	1894 (5)	240 (2)	2134 (4)
TBI/Cy/Flu	2818 (8)	1321 (9)	4139 (8)
TBI/Cy/Flu/TT	49 (0)	9 (0)	58 (0)
TBI/Cy/TT	10 (0)	2 (0)	12 (0)
TBI/Cy/VP	131 (0)	1 (0)	132 (0)
TBI/VP	185 (1)	1 (0)	186 (0)
TBI/Mel	959 (3)	400 (3)	1359 (3)
TBI/Flu	3133 (9)	1239 (9)	4372 (9)
TBI/other(s)	255 (1)	57 (0)	312 (1)
Bu/Cy/Mel	5 (0)	0 (0)	5 (0)
Bu/Cy	5766 (16)	1565 (11)	7331 (15)
Bu/Mel	182 (1)	31 (0)	213 (0)
Flu/Bu/TT	506 (1)	231 (2)	737 (1)
Flu/Bu	12415 (35)	5368 (37)	17783 (36)
Flu/Mel/TT	259 (1)	101 (1)	360 (1)
Flu/Mel	5081 (14)	2975 (21)	8056 (16)
Cy/Flu	237 (1)	142 (1)	379 (1)
Cy alone	6 (0)	6 (0)	12 (0)
BEAM	0 (0)	1 (0)	1 (0)
Mel alone	39 (0)	18 (0)	57 (0)
Mel/other(s)	84 (0)	39 (0)	123 (0)
Treosulfan	256 (1)	252 (2)	508 (1)
Carb/other(s)	1 (0)	2 (0)	3 (0)
TLI	165 (0)	84 (1)	249 (1)
Other(s)	587 (2)	144 (1)	731 (1)
None	6 (0)	9 (0)	15 (0)
Missing	127 (0)	105 (1)	232 (0)
TBI usage - no. (%)			
TBI (single dose > 500 cGy or fractionated > 800 cGy)	2904 (8)	366 (3)	3270 (7)
TBI (single dose <= 500 cGy or fractionated <= 800 cGy), other agents delivered at MA doses	183 (1)	75 (1)	258 (1)
TBI (single dose > 200 and <= 500 cGy, or fractionated > 200 and <= 800 cGy)	1960 (6)	995 (7)	2955 (6)
TBI = 200 cGy	4108 (12)	1846 (13)	5954 (12)
TBI, dose unknown	365 (1)	52 (0)	417 (1)
Non-TBI regimen	21518 (61)	9095 (63)	30613 (62)
Not reported	4118 (12)	1914 (13)	6032 (12)
Donor type - no. (%)			

Characteristic	AML	MDS	Total
HLA identical sibling	11482 (33)	4026 (28)	15508 (31)
Haploidentical donor	5205 (15)	1901 (13)	7106 (14)
Other related	816 (2)	268 (2)	1084 (2)
Well-matched unrelated (8/8)	15099 (43)	7118 (50)	22217 (45)
Partially-matched unrelated (7/8)	2411 (7)	998 (7)	3409 (7)
Mismatched unrelated (<= 6/8)	143 (0)	32 (0)	175 (0)
Donor/recipient sex match - no. (%)			
M-M	12275 (35)	5995 (42)	18270 (37)
M-F	9322 (27)	3098 (22)	12420 (25)
F-M	6567 (19)	2955 (21)	9522 (19)
F-F	6841 (19)	2264 (16)	9105 (18)
CB - recipient M	75 (0)	21 (0)	96 (0)
CB - recipient F	66 (0)	9 (0)	75 (0)
Not reported	10 (0)	1 (0)	11 (0)
GVHD prophylaxis - no. (%)			
None	200 (1)	80 (1)	280 (1)
Ex-vivo T-cell depletion	187 (1)	34 (0)	221 (0)
CD34 selection	337 (1)	105 (1)	442 (1)
PtCy + other(s)	7978 (23)	3366 (23)	11344 (23)
PtCy alone	247 (1)	56 (0)	303 (1)
TAC + MMF +- other(s) (except PtCy)	2966 (8)	1544 (11)	4510 (9)
TAC + MTX +- other(s) (except MMF, PtCy)	13163 (37)	5523 (39)	18686 (38)
TAC + other(s) (except MMF, MTX, PtCy)	1832 (5)	781 (5)	2613 (5)
TAC alone	818 (2)	271 (2)	1089 (2)
CSA + MMF +- other(s) (except PtCy,TAC)	1821 (5)	844 (6)	2665 (5)
CSA + MTX +- other(s) (except PtCy,TAC,MMF)	4641 (13)	1394 (10)	6035 (12)
CSA + other(s) (except PtCy,TAC,MMF,MTX)	26 (0)	13 (0)	39 (0)
CSA alone	554 (2)	189 (1)	743 (2)
Other(s)	350 (1)	139 (1)	489 (1)
Missing	36 (0)	4 (0)	40 (0)
Product type - no. (%)			
BM	4354 (12)	1529 (11)	5883 (12)
PBSC	30660 (87)	12784 (89)	43444 (88)
UCB	141 (0)	30 (0)	171 (0)
Not reported	1 (0)	0 (0)	1 (0)
Year of HCT - no. (%)			
2008-2011	4047 (12)	1195 (8)	5242 (11)
2012-2015	9605 (27)	3568 (25)	13173 (27)

Characteristic	AML	MDS	Total
2016-2019	12028 (34)	5199 (36)	17227 (35)
2020-2023	9476 (27)	4381 (31)	13857 (28)
Follow-up of survivors - median (range)	58.0 (0.0-172.7)	58.7 (0.0-169.7)	58.2 (0.0-172.7)

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*Revised joint proposal from a 2024 CIBMTR proposal

TITLE:

Real World Experience of Immune Effector Cell-Associated Hemophagocytic Lymphohistiocytosis-like Syndrome (IEC-HS) in CAR T-cell Recipients

KEY WORDS:

CAR T-cell therapy, Immunotherapy, Toxicity, Hemophagocytic Lymphohistiocytosis, Cytopenias

RESEARCH QUESTION:

Hemophagocytic lymphohistiocytosis (HLH)-like toxicities have been reported, usually with poor outcomes, following chimeric antigen receptor T-cell therapy (CAR T). Our consortium efforts have previously defined this phenomenon and termed it immune effector cell-associated HLH-like syndrome (IEC-HS).[1] This proposal aims to: 1) describe the incidence, clinical outcomes, associated adverse events, and management of IEC-HS in CAR T recipients and to 2) evaluate clinical factors predictive of IEC-HS and the feasibility of applying the recently developed IEC-HS criteria[1]. Upon successful completion, this work will describe this rare yet consequential complication of CAR T-cell therapy in the largest cohort to date.

Given the overall rarity of this entity, it is critical to use a larger data repository, such as the CIBMTR, to collect a sufficient sample size for meaningful analysis.

RESEARCH HYPOTHESIS:

The incidence of IEC-HS varies by underlying disease and CAR T product and contributes to prolonged morbidity and inferior outcomes following CAR T-cell therapy.

SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED

I. Part 1: Descriptive Analyses of IEC-HS

A. Primary objective: To evaluate the overall incidence of IEC-HS and outcomes in patients who develop IEC-HS. Outcomes of interest include overall survival (OS), event-free survival (EFS), complete response rate for primary malignancy, and non-relapse mortality

B. Secondary objectives:

(1) To describe management options used for IEC-HS and responses to management
(2) To describe hematopoietic recovery in patients with IEC-HS
(3) To characterize infectious complications in patients with IEC-HS
(4) To evaluate the outcomes of patients with IEC-HS, stratified by underlying disease and by CAR T construct

II. Part 2: Multivariate analysis to identify factors associated with IEC-HS and develop a risk score for IEC-HS.

A. Primary Objective:

(1) To identify risk factors predictive of the development of IEC-HS

B. Secondary Objectives:

(1) To develop a predictive risk model for IEC-HS
(2) To evaluate the feasibility of applying the recently published IEC-HS criteria[1]
(3) To determine predictors of long-term survival following development of IEC-HS.

SCIENTIFIC IMPACT:

With the increasing use of CAR T, addressing the safety and management of IEC-HS is a critical need. This study will describe the incidence, clinical outcomes, and management of IEC-HS across different disease types and CAR T constructs in part 1 and evaluate predictors of IEC-HS and the feasibility of applying consensus IEC-HS criteria[1] in part 2.

IEC-HS has been associated with severe and life-threatening complications following CAR T[2-6]. However, existing reports of IEC-HS have included limited numbers of patients (range 6-26 patients)[3,4,7-9] and have mostly focused on a single underlying malignancy and CAR T construct **(Table 1)**. Through this CIBMTR proposal, we will evaluate IEC-HS in a larger cohort of patients (n=143 as of February 2024) across CAR T constructs and underlying diseases. Evaluating IEC-HS in a larger cohort of patients will serve to validate findings from smaller reports and allow for identification of risk factors for IEC-HS. Defining risk factors associated with IEC-HS will inform patient selection for prospective clinical trials of pre-emptive anti-inflammatory therapies.

Furthermore, given that patients are defined as having HLH-like criteria in the CIBMTR database using institutional definitions, which are expected to vary by site. There is a critical need to refine the ability to diagnose patients who experience IEC-HS. We will therefore explore the performance of the recently ASTCT Consensus IEC-HS criteria in identifying IEC-HS cases (**Figure 1**).[1] **Altogether, this effort will provide needed information and guidance for the recognition, management, and further study of IEC-HS.**

SCIENTIFIC JUSTIFICATION:

IEC-HS refers to HLH-like toxicities following CAR T infusion which can result in life-threatening organ dysfunction. With the increased use of CAR T-cell therapy in recent years, IEC-HS has been described anecdotally with the use of commercially approved and investigational products, but findings have been limited by use of varying definitions/criteria and/or focus on a single disease or CAR T-cell product **(Table 1)**.[3,4,7-9] Therefore, to address the unmet need for a uniform definition of HLH-like toxicities following CAR T-cell therapy, a panel of experts in diverse fields including adult and pediatric oncology, infectious disease, critical care, and rheumatology proposed a consensus definition and diagnostic criteria (**Figure 1**), and established this as an entity distinct from cytokine release syndrome **(Figure 2**).[1] These criteria have helped identify patients in practice. **As much of the existing literature on IEC-HS has been limited to single CAR T-cell constructs or single institution studies, this proposal aims to characterize IEC-HS across CAR T constructs and underlying diseases.**

IEC-HS has been associated with higher rates of infection, non-relapse mortality, progressive disease, and relapse, although these observations have varied by disease and CAR construct[2,3,5-

[7]. A larger study through the CIBMTR is crucial to validate these findings and can provide deeper insights into the mechanisms of inferior outcomes in these patients. Further, given the poor outcomes described for patients with IEC-HS, we aim to identify key factors associated with IEC-HS. Identifying key drivers of IEC-HS can inform patient selection for prospective studies that will aim at curtailing inflammation in high-risk populations through prophylactic and/or pre-emptive anti-inflammatory treatment approaches, as has been described for prevention of severe CRS or ICANS[10-12].

Cytopenias are a primary feature of IEC-HS, in addition to rapidly rising ferritin, coagulopathy, and often severe organ dysfunction. While hematopoietic recovery in the context of CAR T-cell therapy has been well-defined[13-15], recovery and clinical implications of cytopenias in the context of IEC-HS are not well-understood. Given the association between severe inflammatory toxicities and prolonged cytopenias, we hypothesize that cytopenias developed in the context of IEC-HS will be more prolonged and associated with clinical consequences of infection or bleeding. **An improved understanding of cytopenias and risk of infections will guide clinical practice of infection prophylaxis and management in patients who develop IEC-HS.** Finally, therapies used for IEC-HS in clinical practice have been poorly defined to date. Use of anakinra, steroids, ruxolitinib, emapalumab, and etoposide have been proposed using a stepwise approach[1], but additional data on real-world clinical management of IEC-HS is needed.

CIBMTR registry data involves data from all cellular therapy centers and likely houses data from the greatest number of patients who have received CAR T-cell therapy. A version of this proposal has been submitted for review at the ASTCT/CIBMTR Tandem Meetings in 2023 and in 2024 as a joint proposal. At the time of review in 2024, there were 8481 CAR T recipients in the CIBMTR registry, 143 of which had reported IEC-HS by institutional definitions, representing the largest number of described patients in a single database to date. **Given that IEC-HS is expected to be a relatively rare entity, CIBMTR registry data is best suited to describe the incidence and clinical outcomes of IEC-HS**, as well as to identify factors associated with the development IEC-HS. Hence, we hereby propose to use the CIBMTR registry data to identify patients who developed IEC-HS following CAR T-cell therapy, irrespective of the product or the disease diagnosis. This is a revised joint proposal from a submission of the same title to the ASTCT/CIBMTR Tandem meetings in 2024.

Table 1: Publications describing the incidence and outcomes of IEC-HS

Author	Population	IEC-HS Cases	Disease	CAR T	HLH-like Toxicity (IEC-HS) Criteria Used	Outcomes of group with HLH-like toxicities
Lichtenstein et al.[4]	Pediatric N=59	21	R/R B-ALL	CD22.41BB +/-TCS *NCT02315612*	Shah[4]	
Lichtenstein et al.[4]	Pediatric N=78	11	R/R B-ALL	CD19.41BB *NCT02028455*	Neelapu or clinical judgement	
Lichtenstein et al.[4]	Pediatric N=50	0	R/R B-ALL	CD19.28z *NCT01593696*	Neelapu	
Hines et al.[3]	Pediatric N=27	4	B-ALL	Tisa-cel (n=12), SJCAR (n=15)	Shah[4]	No leukemic response: 75% Median OS: 44.5 days
Ahmed et al.[2]	Adult N=105	6	R/R NHL	Axi-cel	Neelapu	PFS: 1 month Median OS: 2 months

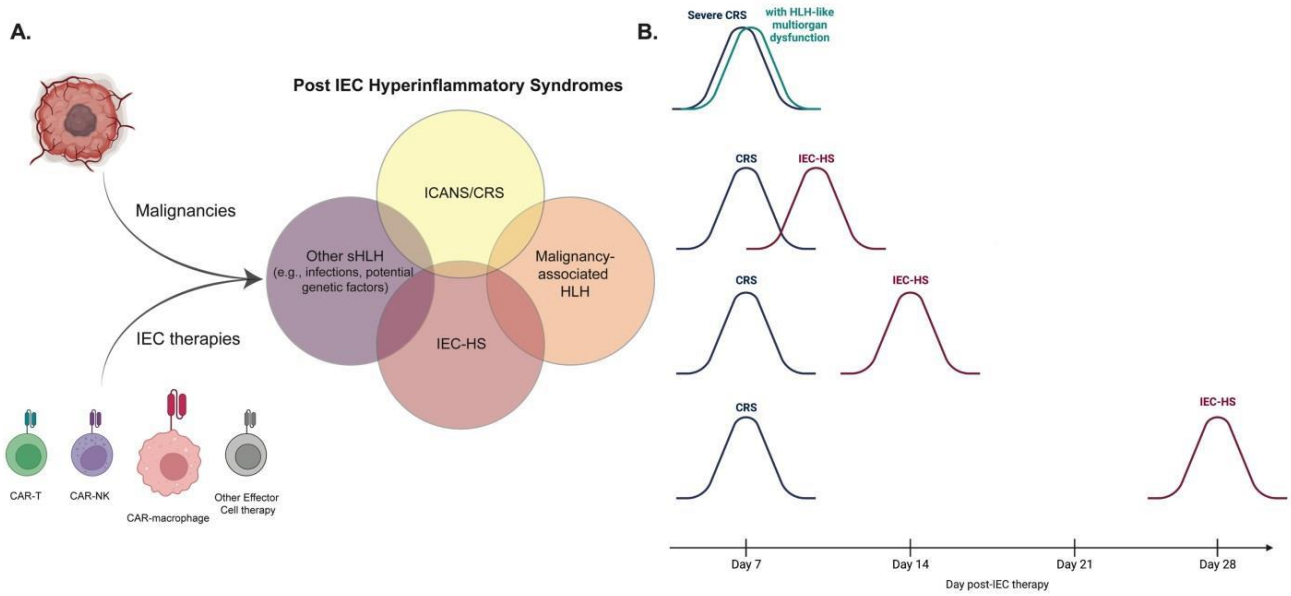
Kennedy et al.[7]	Adult N=55	12	R/R MM	BCMA CAR T	MAS-L[7]	ORR: 100% 1-year OS: 65.2% 1-year RFS: 35.2%
Priyadarshini et al.[6]	Adult and Pediatric, N=6034	121	RR B-ALL, NHL, MM	Axi-cel, Brexu-cel, Liso-cel, Tisa-cel, Ide-cel, Cita-cel	Clinical judgement	Death in 66.9%
McNerney et al.[8]	Pediatrics N=185	26	R/R B-ALL	Tisa-cel	Neelapu + coagulopathy	Median OS: 128 days Median RFS: 60 days

Abbreviations: Axi-cel, Axicabtagene ciloleucel; Brexu-cel, Brexucabtagene autoleucel; Cilta-cel, Ciltacabtagene autoleucel; Ide-cel, Idecabtagene vicleucel; MAS-L, macrophage activation syndrome-like; NHL, non-Hodgkin Lymphoma; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; RFS, relapse-free survival; R/R B-ALL, relapsed/refractory B-acute lymphoblastic leukemia; Tisa-cel, Tisagenlecleucel.

Figure 1. ASTCT Consensus IEC-HS definition[1]

Definition of IEC-HS	The development of a pathological and biochemical hyperinflammatory syndrome independent from CRS and ICANS that (1) manifests with features of macrophage activation/HLH, (2) is attributable to IEC therapy, and (3) is associated with progression or new onset of cytopenias, hyperferritinemia, coagulopathy with hypofibrinogenemia, and/or transaminitis
Criteria for Identifying IEC-HS*	**Clinical/Laboratory Manifestations**
Most common manifestations†	Required: elevated ferritin (>2 × ULN or baseline (at time of infusion)) and/or rapidly rising (per clinical assessment)
	Onset with resolving/resolved CRS or worsening inflammatory response after initial improvement with CRS-directed therapy‡
	Hepatic transaminase elevation§ (>5 × ULN (if baseline was normal) or >5 × baseline if baseline was abnormal)
	Hypofibrinogenemia (<150 mg/dL or <LLN)‖
	Hemophagocytosis in bone marrow or other tissue‖
	Cytopenias (new onset, worsening, or refractory¶)
Other manifestations that may be present	Lactate dehydrogenase elevations (>ULN)
	Other coagulation abnormalities (eg, elevated PT/PTT)
	Direct hyperbilirubinemia
	New-onset splenomegaly
	Fever (new# or persistent)‖
	Neurotoxicity
	Pulmonary manifestations (eg, hypoxia, pulmonary infiltrates, pulmonary edema)
	Renal insufficiency (new onset)
	Hypertriglyceridemia (fasting level, >265 mg/dL‖)

Figure 2. Biology and correlation of timing of IEC-HS and CRS



PATIENT ELIGIBILITY POPULATION:

For the primary analysis, we will include all adult and pediatric patients who received CAR T-cell therapy for any hematological malignancy using a commercially available or an investigational product (within the limits of protocol allowance) and reported as having developed IEC-HS (or CAR-HLH or MAS).

DATA REQUIREMENTS:

If supplemental data is required, please review data collection forms at:
http://www.cibmtr.org/DataManagement/DataCollectionForms/Pages/index.aspx

Patient and disease details:

-age/sex
-race/ethnicity
-diagnosis (BCL, multiple myeloma, ALL)
-subtype (transformed FL, double-hit BCL, triple-hit BCL, MCL, Ph Positive B-ALL, Ph negative B-ALL, MM)
-number of prior lines of therapy
-prior CNS disease involvement
-current active CNS involvement
-prior autologous stem cell transplantation (yes/no)
-days from prior autologous transplant
-prior allogeneic stem cell transplantation (yes/no)
-days from prior allogeneic transplant
-comorbidities pre-infusion
-baseline organ dysfunction (yes/no)
-if yes, which organ dysfunction
-cellular therapy comorbidity index (CT-CI) if available

-baseline (pre-lymphodepletion chemotherapy) counts (ANC, WBC, ALC, HGB, PLT)
-baseline marrow blast percentage (for B-ALL)
-Myeloma characteristics (myeloma subtype, extramedullary disease, CNS involvement, dialysis, renal insufficiency, co-existing amyloid, response to latest therapy).
-Baseline inflammatory markers and markers of cellular turnover (CRP, Ferritin, LDH)
- Disease burden prior to CAR T-cell (progressive /relapsed disease, CR, responding to bridging)

CAR T details:

-product name
-was the product a clinical trial product (4000 R10 #8)
-Was the entire product infused (4006 R6, #7)
-Did the recipient receive a subsequent infusion (4101-R1 #4)
-Any prior engineered T-cell therapy
-lymphodepletion chemotherapy
-time from diagnosis
-cell dose, viability, percent of genetically modified cells, and was target percent of genetically modified cells achieved (if available)
-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:

-peak ferritin
-days from CAR T to peak ferritin
-peak C-reactive protein
-days from CAR T to peak C-reactive protein
-peak IL-6 (if available)
-onset, duration, and severity of CRS
-treatment used for CRS
-onset, duration, and severity of ICANS
-treatment used for ICANS
-duration of hospitalization
-ICU transfer (yes/no)
-duration of ICU stay
-was IEC-HS (or HLH/MAS) diagnosed? (form 4101-R1 #68)
-features related to HLH/MAS (Form 4100 R8.0#110-120)
-Specific therapy given for MAS/HLH-like toxicity (form 4100 R9 #70)
-Soluble IL2Ralpha level
-organ involvement (hepatic, pulmonary, renal, coagulopathy)
-fibrinogen levels
-triglyceride levels if available
-was IEC-HS or HLH/MAS treated? (yes/no)
-treatment used for IEC-HS or HLH/MAS

-overall response of IEC-HS or HLH/MAS
-days to ANC recovery from CAR T (4101-R1 #16, 29)
-days to platelet recovery from CAR T (4101-R1 #20, 23)
-blood counts available post-CAR T (WBC, ANC, ALC, HGB, PLT)
-transfusions of PRBCs
-transfusion of platelets
-use of growth factors
-use of TPO-RA/stem cell boost/other treatments for cytopenias
-infections complications post CAR T
-type of infection(s)
-bleeding complications
-severity of bleeding complication
-nadir fibrinogen levels
-use of cryoprecipitate/FFP
-peak liver enzymes
-peak creatinine
-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 (will evaluate if IEC-HS related or not)
-Duration of hospitalization requirement (Form 4100 R8.0 #204-205)
-Persistence of CAR T-cells, if available (Form 4100 R8.0 #44-68)

SAMPLE REQUIREMENTS:

Not applicable

STUDY DESIGN:

In part 1, we will use a retrospective cohort study design to evaluate patients who did and did not develop IEC-HS. We will evaluate the reported incidence of IEC-HS in the overall cohort treated with CAR T. We will describe the patient characteristics and outcomes of patients who develop IEC-HS including complete response rate, OS and EFS at 1-month, 100-days, 6-months, and 1-year, median OS and EFS, cumulative incidence of non-relapse mortality at 1-month, 100-days, 6-months, and 1-year. Kaplan-Meier curves and log rank testing will be used to depict and compare survival outcomes among populations with and without IEC-HS. We will describe the incidence of infections, prolonged cytopenias and severe cytopenias in groups with and without IEC-HS. We will describe the management options used for patients with IEC-HS and the overall response of IEC-HS to treatment.

In part 2, we will use multivariable analysis of patient and treatment characteristics to identify predictors of IEC-HS. We will then 1) develop a risk score for IEC-HS using identified predictors and 2) evaluate the performance of the consensus IEC-HS criteria compared with IEC-HS cases identified by individual institutions, and 3) identify IEC-HS-related factors that are associated with poor outcomes with IEC-HS. To evaluate the performance of consensus IEC-HS criteria, we will use a peak ferritin of ≥3000 ng/mL as screening and then evaluate patients who meet ≥ 2 additional IEC-HS criteria[1] (**Table 2**) for evaluation of IEC-HS patients. Using this “post-hoc”

diagnosed IEC-HS cohort, we will compare the incidence of IEC-HS using institutional and consensus-defined criteria and evaluate clinical outcomes in this post-hoc cohort.

Table 2: Case Definition of IEC-HS:

Patients must experience a ferritin of ≥3000 ng/ml and least **2** of the following supportive criteria:	Form 4100 R9.0 #176 and 177 (maximum ferritin and date of maximum ferritin)
Onset of symptoms with resolving/resolved CRS or worsening inflammatory response after initial improvement with CRS-directed therapies	**Form 4100 R9.0 Question #67-68**
Hepatic transaminase (AST/ALT) elevation ≥ Grade 3	**Form 4100 R8.0 #182 or 189**
Hypofibrinogenemia (<150 mg/dL)	**Form 4100 R8.0 # 115**
Cytopenias (new onset, worsening, or refractory)	**Form 4100 R8.0 #16-24**
Hemophagocytosis in bone marrow or other tissue	**Form 4100 R8.0 # 113**
Elevated bilirubin levels	**Form 4100 R9.0 #156**
Splenomegaly	**Form 4100 R9.0 #72**
Neurotoxicity	**Form 4100 R8.0 #121**
Pulmonary Manifestations (hypoxia, pulmonary infiltrates, pulmonary edema)	**Form 4100 R9.0 #156 or #163 (Grade 3 or 4 pulmonary edema or respiratory failure)**
Renal insufficiency	**Form 4100 R9.0 #156 or #163 (Grade 3 or 4 acute kidney injury)**
Hypertriglyceridemia	**Form 4100 R9.0 #77 and 78**

NON-CIBMTR DATA SOURCE: Not applicable

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Patient characteristics of ALL/NHL/MM CAR-T patients, stratified by IEC-HS post-CT

Characteristic	No	Yes	Total
No. of patients	13950	313	14263
No. of centers	238	102	240
Patient Characteristics			
Age, by decades - no. (%)			
Median (min-max)	64 (0-91)	61 (4-89)	64 (0-91)
0-9	364 (3)	11 (4)	375 (3)
10-19	442 (3)	19 (6)	461 (3)
20-29	477 (3)	15 (5)	492 (3)
30-39	511 (4)	18 (6)	529 (4)
40-49	1003 (7)	30 (10)	1033 (7)
50-59	2575 (18)	60 (19)	2635 (18)
60-69	4657 (33)	80 (26)	4737 (33)
70+	3921 (28)	80 (26)	4001 (28)
Recipient Sex - no. (%)			
Male	8651 (62)	204 (65)	8855 (62)
Female	5297 (38)	109 (35)	5406 (38)
Not reported	2 (0)	0 (0)	2 (0)
Recipient race - no. (%)			
White	10560 (76)	210 (67)	10770 (76)
Black or African American	1031 (7)	24 (8)	1055 (7)
Asian	658 (5)	16 (5)	674 (5)
Native Hawaiian or other Pacific Islander	35 (0)	1 (0)	36 (0)
American Indian or Alaska Native	62 (0)	2 (1)	64 (0)
Other	81 (1)	6 (2)	87 (1)
More than one race	681 (5)	22 (7)	703 (5)
Missing	842 (6)	32 (10)	874 (6)
Ethnicity - no. (%)			
Hispanic or Latino	1709 (12)	46 (15)	1755 (12)
Non-Hispanic or Latino	10665 (76)	216 (69)	10881 (76)
Non-resident of the U.S.	1146 (8)	45 (14)	1191 (8)
Not reported	430 (3)	6 (2)	436 (3)
Current CCN region of patient - no. (%)			
US	12781 (92)	271 (87)	13052 (92)
Canada	667 (5)	11 (4)	678 (5)
Europe	97 (1)	4 (1)	101 (1)
Asia	103 (1)	0 (0)	103 (1)

Characteristic	No	Yes	Total
Australia/New Zealand	128 (1)	4 (1)	132 (1)
Mideast/Africa	123 (1)	18 (6)	141 (1)
Central/South America	50 (0)	5 (2)	55 (0)
Not reported	1 (0)	0 (0)	1 (0)
Karnofsky performance score prior to CT - no. (%)			
90-100	5794 (42)	91 (29)	5885 (41)
80	4185 (30)	89 (28)	4274 (30)
< 80	2502 (18)	96 (31)	2598 (18)
Not reported	1469 (11)	37 (12)	1506 (11)
HCT-CI Score - no. (%)			
0	4222 (30)	93 (30)	4315 (30)
1	2785 (20)	70 (22)	2855 (20)
2	1955 (14)	31 (10)	1986 (14)
3	2040 (15)	36 (12)	2076 (15)
4	1297 (9)	34 (11)	1331 (9)
5+	1533 (11)	47 (15)	1580 (11)
Not reported	118 (1)	2 (1)	120 (1)
Disease related			
Disease - no. (%)			
Acute lymphoblastic leukemia (ALL)	1436 (10)	63 (20)	1499 (11)
Non-Hodgkin lymphoma (NHL)	9429 (68)	178 (57)	9607 (67)
Plasma cell disorder/multiple myeloma (PCD/MM)	3085 (22)	72 (23)	3157 (22)
Interval from diagnosis to HCT, months - median (min-max)	24 (0-472)	19 (1-298)	24 (0-472)
Disease status prior to infusion			
Disease status prior to CT for leukemia - no. (%)			
Disease is not leukemia	12514 (90)	250 (80)	12764 (89)
CR1	194 (1)	2 (1)	196 (1)
CR2	301 (2)	4 (1)	305 (2)
CR3+	176 (1)	2 (1)	178 (1)
Relapse, 1st	331 (2)	27 (9)	358 (3)
Relapse, other	291 (2)	22 (7)	313 (2)
PIF/Untreated	137 (1)	6 (2)	143 (1)
Not reported	6 (0)	0 (0)	6 (0)
Disease status prior to CT for lymphoma - no. (%)			
Disease is not lymphoma	4521 (32)	135 (43)	4656 (33)
CR	721 (5)	13 (4)	734 (5)
PR	2064 (15)	28 (9)	2092 (15)
Resistant	5472 (39)	124 (40)	5596 (39)

Characteristic	No	Yes	Total
Untreated	598 (4)	5 (2)	603 (4)
Unknown	558 (4)	8 (3)	566 (4)
Not reported	16 (0)	0 (0)	16 (0)
Disease status prior to CT for PCD - no. (%)			
Disease is not MM/PCD	10865 (78)	241 (77)	11106 (78)
Stringent complete remission (sCR)	23 (0)	0 (0)	23 (0)
Complete remission (CR)	49 (0)	0 (0)	49 (0)
Very good partial remission (VGPR)	305 (2)	2 (1)	307 (2)
Partial response (PR)/ Not Complete Remission	396 (3)	2 (1)	398 (3)
Stable disease (SD)	510 (4)	11 (4)	521 (4)
Progressive disease (PD)	1731 (12)	57 (18)	1788 (13)
Relapse from CR (Rel) (untreated)	60 (0)	0 (0)	60 (0)
Not reported	11 (0)	0 (0)	11 (0)
Infusion related			
Prior HCT - no. (%)			
No	9075 (65)	195 (62)	9270 (65)
Yes	4837 (35)	116 (37)	4953 (35)
Not reported	38 (0)	2 (1)	40 (0)
Bridging therapy - no. (%)			
No	4346 (31)	55 (18)	4401 (31)
Yes	6039 (43)	178 (57)	6217 (44)
Systemic therapy given as bridging therapy	5356 (38)	160 (51)	5516 (39)
Intrathecal therapy given as bridging therapy	253 (2)	14 (4)	267 (2)
Intraocular therapy given as bridging therapy	7 (0)	0 (0)	7 (0)
Radiation therapy given as bridging therapy	1258 (9)	36 (12)	1294 (9)
Surgery given as bridging therapy	23 (0)	0 (0)	23 (0)
Not reported	3565 (26)	80 (26)	3645 (26)
Lymphodepleting regimen - no. (%)			
Fludarabine + Cyclophosphamide	10559 (76)	241 (77)	10800 (76)
Bendamustine only	1032 (7)	19 (6)	1051 (7)
Others	2330 (17)	52 (17)	2382 (17)
None	28 (0)	1 (0)	29 (0)
Not reported	1 (0)	0 (0)	1 (0)
Commercial vs. noncommercial CAR-T product - no. (%)			
Commercial	12988 (93)	294 (94)	13282 (93)
Noncommercial	962 (7)	19 (6)	981 (7)
Product - no. (%)			
Kymriah	2181 (16)	57 (18)	2238 (16)

Characteristic	No	Yes	Total
Yescarta	5508 (39)	91 (29)	5599 (39)
Tecartus	1313 (9)	51 (16)	1364 (10)
Breyanzi	1161 (8)	26 (8)	1187 (8)
Abecma	1516 (11)	16 (5)	1532 (11)
Carvykti	1309 (9)	53 (17)	1362 (10)
Other	962 (7)	19 (6)	981 (7)
Is the recipient participating in a cellular therapy clinical trial? - no. (%)			
No	12610 (90)	282 (90)	12892 (90)
Yes	1338 (10)	31 (10)	1369 (10)
Not reported	2 (0)	0 (0)	2 (0)
2-year product embargo - no. (%)			
No	10664 (76)	221 (71)	10885 (76)
Yes	3286 (24)	92 (29)	3378 (24)
Year of infusion - no. (%)			
Before 2017	24 (0)	0 (0)	24 (0)
2017	22 (0)	0 (0)	22 (0)
2018	302 (2)	1 (0)	303 (2)
2019	578 (4)	1 (0)	579 (4)
2020	1122 (8)	13 (4)	1135 (8)
2021	2218 (16)	47 (15)	2265 (16)
2022	3678 (26)	73 (23)	3751 (26)
2023	4562 (33)	129 (41)	4691 (33)
2024	1444 (10)	49 (16)	1493 (10)
Follow-up of survivors, months - median (range)	13 (0-4880)	12 (2-36)	13 (0-4880)

Field	Response
Proposal Number	2410-249-KULASEKARAN
Proposal Title	Clonal Cytopenia Mutations: The Impact of the Recipient's Underlying Malignant Disease Biology on Posttransplant Engraftment of Donor-derived Clonal Cytopenia (CH) Clones
Key Words	Clonal Cytopenia, Biology, Posttransplant, Engraftment, Donor-derived Clonal Cytopenia
Principal Investigator #1: - First and last name, degree(s)	Monika Kulasekaran, MD,
Principal Investigator #1: - Email address	mky55@health.missouri.edu
Principal Investigator #1: - Institution name	University of Missouri, Columbia
Principal Investigator #1: - Academic rank	Junior Investigator
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):	Gerhard Hildebrandt, MD, FACP
Principal Investigator #2 (If applicable): - Email address:)	gchhrb@health.missouri.edu
Principal Investigator #2 (If applicable): - Institution name:	University of Missouri, Columbia
Principal Investigator #2 (If applicable): - Academic rank:	Professor of Medicine
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:	Dr. Monika Kulasekaran and Dr. Gerhard Hildebrandt
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
Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.	-
Do any of the PI(s) within this proposal have a CIBMTR WC study in manuscript preparation >6 months?	No
PROPOSED WORKING COMMITTEE:	Immunobiology
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:	Dr. Nelli Bejanyan

Field	Response
RESEARCH QUESTION:	Does the underlying disease biology influence the engraftment of donor-derived clonal cytopenias
RESEARCH HYPOTHESIS:	We hypothesize that disease biology influences the engraftment of donor CH clones in posttransplant bone marrow, whether it is directly or indirectly through effects on the bone marrow stroma or on immunosurveillance as the result of disease- or prior chemotherapy-related effects. Specifically, we will compare post-allogeneic donor-derived CH mutations in patients with myeloproliferative neoplasms (MPN), acute myeloid leukemia (AML), acute lymphoblastic lymphoma (ALL), who underwent allogeneic transplantation, with their CH mutations pre-HSCT. In addition, we will assess, whether donor-specific factors, such as gender, degree of HLA matching, and age affect the outgrowth of donor-derived clonal hematopoiesis after allogeneic HSCT.
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	Primary outcome: - To study the differences in the engraftment of donor-derived CH mutations between AML, B- ALL, T-ALL, and MPN patients who undergo allogeneic HSCT. Secondary outcomes: 1) To study the impact of Donor unmodifiable risk factors (age, gender, sex), type of condition regimen, post-transplantation immunosuppression, donor type, donor source, degree of mismatch/match across the diseases AML, MPN, B-ALL, and T-ALLon CH engraftment 2) To study the impact of acute and chronic GVHD in patients on posttransplant clonal hematopoiesis across the diseases AML, MPN, B-ALL, and T-ALL 3) To study disease-free survival and overall survival in patients with or without posttransplant clonal hematopoiesis across the diseases AML, MPN, B-ALL, and T-ALL
SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.	Clonal cytopenias are age-related acquired somatic mutations that may be influenced by the specific disease biology and the unique bone marrow microenvironment. Understanding how these factors affect donor-derived clonal hematopoiesis (CH) engraftment—whether they create a more or less supportive environment for the survival of donor-derived CH clones—could allow us to use particular diseases as models to identify potential treatments for clonal cytopenias. Additionally, external factors, including immunosuppressive agents, may also play a role in this process

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.	The prevalence of clonal hematopoietic (CH) mutations increases with age, reaching as high as 20% in older populations. Studies have shown that donor CH mutations are transferred to recipients during allogeneic hematopoietic stem cell transplantation (HSCT) and can affect graft-versus-host disease (GVHD) and engraftment outcomes. It is unclear whether the underlying malignant disease biology of the recipient has an impact on the engraftment of donor CH clones. We hypothesize that disease biology influences the engraftment of donor CH clones in posttransplant bone marrow, whether it is directly or indirectly through effects on the bone marrow stroma or on immunosurveillance as the result of disease- or prior chemotherapy related effects. Specifically, we will compare post-allogeneic donor derived CH mutations in patients with myeloproliferative neoplasms (MPN), acute myeloid leukemia (AML), acute lymphoblastic lymphoma (ALL), who underwent allogeneic transplantation, with their CH mutations pre-HSCT. In addition, we will assess, whether donor specific factors, such as gender, degree of HLA matching, age affect the outgrowth of donor derived clonal hematopoiesis after allogeneic HSCT. In clonal hematopoiesis genetically altered clones dominantly expand, which can lead to ineffective hematopoiesis and can be considered a premalignant condition. Premalignant clonal cytopenia carries the risk of progression to myeloid neoplasm. Commonly involved pathways are epigenetic regulators (DNMT3A, TET2, IDH1, IDH2), chromatin modifiers (KDM6A, PHF6, ASXL1), RNA splicing (SF3B1, SRSF2, U2AF1, ZRSR2), genes involved in DNA repair (TP53, PPM1D, ATM), signaling (JAK2, GNAS, GNB1, CBL, KIT, PTEN) and transcription regulation (RUNX1, BCOR, BCORL). Among these variants, TP53, IDH1 and, IDH2 carries high risk of progression to myeloid malignancy. DNMT3A mutations are the most commonly noted mutations in individuals over 40 years old. Despite the risk of donor-derived CH clones, HSCT remains a crucial treatment option for conditions such as myeloid neoplasms, lymphoblastic leukemia, and high-risk myelofibrosis. Due to significant differences in treatment types, conditioning regimens, cell of origin and disease courses, there are alterations in the bone marrow microenvironment milieu. For instance, in MPN with myelofibrosis, there are increased levels of inflammatory cytokines, which can have longstanding systemic effects. Likewise, each disease, with its unique biology, affects the engraftment of donor-derived CH mutations. The use of post-transplantation

Field	Response
	cyclophosphamide has expanded the feasibility of using haploidentical and mismatched unrelated donors in addition to matched siblings and matched unrelated donors, benefiting patients who previously faced donor scarcity. Furthermore, finding a suitable donor can be particularly challenging for patients from racial and ethnic minority groups. Therefore, sometimes the ability to select between more than one suitable donor is limited, and additional donor information, such as CH risk is helpful for adequate risk counseling. In this study, we will collect data on molecular mutations from bone marrow biopsies obtained as prior to allogenic transplant, as well as after allogeneic HSCT until day 100 (D-100) after allogeneic HSCT. We will include all patients with MPN, B-ALL, T- ALL, AML , who had a pre-HSCT bone marrow biopsy and molecular mutation testing available. Pre-HSCT mutation prevalence will be compared with post-HSCT mutation prevalence, and we will look for any new mutations acquired during these periods until day 100, not detected in pretransplant molecular studies. As we limit our time period to 100 days after allo HSCT, we assume that new molecular mutations are likely to have been acquired from donor cells. We further will correlate molecular findings with donor chimerism as well as other disease-specific markers (e.g. FLT3, NPM1, etc) to assess for donor-derived CH in the absence of relapsing underlying disease.
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	Inclusion criteria: - Age > 18 years - Patients with MPN, AML, B-ALL, and T-ALL who underwent allogeneic HCT between 2015 – 2024 CR and absence of molecular CH mutations at the time of transplant. - Molecular CH mutation testing results are available prior to allogeneic HCT, as well as at any time point until day 100 after allogeneic HCT. Exclusion criteria: - No molecular CH mutation testing results are available for patients prior to allogeneic HSCT
Does this study include pediatric patients?	No
If this study does not include pediatric patients, please provide justification:	We included studies like Myeloproliferative neoplasm which is common is adults.

Field	Response
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.	Recipient related - Age at allogeneic HCT - Gender: Male vs. Female - Ethnicity: Caucasian, Hispanic, African American, Asian Pacific Islander - Performance Status: Karnofsky score (³90% vs. 80-80% vs. <80%) for adults HSCT variables: Type of HCT (allogenic related HCT, allogenic unrelated HCT, alternative donor source (haplo / cord blood)) - Product type (bone marrow, peripheral blood stem cell, cord blood) - Degree of donor/recipient match (8/8 matched sibling, 8/8 matched unrelated donor, 7/8 or less mismatched unrelated donor, haploidentical donor, cord blood donor - Conditioning regimen (myeloablative, RIC, non-myeloablative (mini) and regimen type/drugs) - GVHD prophylaxis: - Calcineurin inhibitor (CNI) plus mini MTX - CNI plus MMF - Post-transplant cyclophosphamide plus CNI plus MMF - ATG yes/no - Campath yes/no - TBI yes/no - TBI dose - Donor gender - Donor age - Donor and Patient CMV serostatus - Donor blood group - If available, molecular CH mutation testing will be done on donor CIBMTR samples based on availabilityDonor / Patient gender mismatch: male into female/female into female/female into male/male into male) - Presence of donor HLA-directed antibodies for HLA mismatched donor/recipient pairs - Post-allo transplant maintenance y/n - Post-allo transplant donor lymphocyte infusion y/n Disease-related: - Pre-transplant molecular mutations - Post-transplant molecular mutations D30 and D100 - MF risk - DIPPSI - AML cytogenetics - AML risk stratification - ALL subtype - Blast count in blood - Blast in bone marrow - Prior lines of chemotherapy - Prior chemotherapy regimens Post HSCT: - Acute GvHD >/= grade 2 - Acute GVHD grade 3 or grade 4 - Chronic GVHD -Limited versus extensive - NIH consensus grading criteria - mild - moderate - severe - Time to platelet engraftment - Time to neutrophil engraftment - Engraftment failure yes/no - Donor chimerism. - Date of last contact - Alive or dead
Types of cellular therapy data this proposal includes:	Hematopoietic Cell Transplantation (HCT)

Field	Response
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	-
MACHINE LEARNING: Please indicate if the study requires methodology related to machine-learning and clinical predictions.	-
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	One way to access the donor CH mutations are by evaluating the acquisition of new molecular mutations in the post-transplant period at day 30 and at day 100. While our assumption about the evolution of CH likely being donor-derived within the first 100 days is logical, a major limitation is the lack of donor sample testing, which is necessary to accurately reflect the prevalence of donor CH mutations and determine how many recipients within each disease group (AML, ALL, and MPN) were exposed to and engrafted with donor-derived CH mutations. To address this, we will collaborate with the Center for International Blood and Marrow Transplant Research (CIBMTR) Immunobiology working group to test blood samples for CH mutations of donors based on availability, that have provided blood samples to the CIBMTR biorepository, using Next Generation Sequencing for myeloid mutations. The University of Missouri will arrange funding for this donor testing, and as a sequencing platform we at this point plan to utilize using FoundationOne or Illumina platform, which is available at the University of Missouri for research-grade testing. This proposal serves as an initial step toward understanding which disease types have an increased propensity for donor CH mutations to engraft. My mentor and primary investigator, Dr. Hildebrant, will guide and supervise sample testing. He is a member of national and international committees, such as the Center for International Blood and Marrow Transplant Research as well as a good-standing member of the American Society of Hematology, American Society of Stem Cell Transplant and Cellular Therapy, American College of Physicians, American Society of Clinical Oncology and American Association for Cancer Research. He is actively involved in multiple preclinical studies for graft versus host disease, with a primary focus on Graft versus host disease involving lungs.
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.	-

Field	Response
REFERENCES:	1. Gibson CJ, Kim HT, Zhao L, Murdock HM, Hambley B, Ogata A, Madero-Marroquin R, Wang S, Green L, Fleharty M, Dougan T. Donor clonal hematopoiesis and recipient outcomes after transplantation. Journal of Clinical Oncology. 2022 Jan 10;40(2):189-201. 2. Gillis N, Padron E, Wang T, Chen K, DeVos JD, Spellman SR, Lee SJ, Kitko CL, MacMillan ML, West J, Tang YH. Pilot Study of Donor-Engrafted Clonal Hematopoiesis Evolution and Clinical Outcomes in Allogeneic Hematopoietic Cell Transplantation Recipients Using a National Registry. Transplantation and Cellular Therapy. 2023 Oct 1;29(10):640-e1. 3. Jan M, Ebert BL, Jaiswal S. Clonal hematopoiesis. InSeminars in hematology 2017 Jan 1 (Vol. 54, No. 1, pp. 43-50). WB Saunders. 4. Jaiswal S, Ebert BL. Clonal hematopoiesis in human aging and disease. Science. 2019 Nov 1;366(6465):eaan4673. 5.Bowman RL, Busque L, Levine RL. Clonal hematopoiesis and evolution to hematopoietic malignancies. Cell stem cell. 2018 Feb 1;22(2):157-70. 6. Jaiswal S, Fontanillas P, Flannick J, Manning A, Grauman PV, Mar BG, Lindsley RC, Mermel CH, Burtt N, Chavez A, Higgins JM. Age-related clonal hematopoiesis associated with adverse outcomes. New England Journal of Medicine. 2014 Dec 25;371(26):2488-98.
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
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.	-

Characteristics of adults with AML, B-ALL, T-ALL, and MPN who undergo allogeneic HCT reported to the CIBMTR between 2015 and 2024

Characteristic	AML	ALL	MPN	Total
No. of patients	30956	10757	4515	46228
No. of centers	327	312	228	339
Patient-Related Characteristics				
Samples in biorepository - no. (%)				
Samples available for recipient and donor	9142 (30)	3071 (29)	1285 (28)	13498 (29)
Samples available for recipient only	5942 (19)	1713 (16)	1064 (24)	8719 (19)
Samples available for donor only	1501 (5)	488 (5)	192 (4)	2181 (5)
No sample	14371 (46)	5485 (51)	1974 (44)	21830 (47)
Were tests for molecular markers performed anytime before HCT - no. (%)				
No	2445 (8)	2113 (20)	642 (14)	5200 (11)
Yes	28083 (91)	8416 (78)	2069 (46)	38568 (83)
Not reported	428 (1)	228 (2)	1804 (40)	2460 (5)
TED or RES (RF) track determined for this event - no. (%)				
TED	25719 (83)	8984 (84)	1721 (38)	36424 (79)
CRF (RES)	5237 (17)	1773 (16)	2794 (62)	9804 (21)
Age, by decades - no. (%)				
Median (min-max)	57 (18-88)	41 (18-79)	62 (18-81)	55 (18-88)
10-19	436 (1)	572 (5)	4 (0)	1012 (2)
20-29	2451 (8)	2581 (24)	44 (1)	5076 (11)
30-39	3173 (10)	2023 (19)	110 (2)	5306 (11)
40-49	4349 (14)	1955 (18)	384 (9)	6688 (14)
50-59	7312 (24)	2031 (19)	1242 (28)	10585 (23)
60-69	10125 (33)	1411 (13)	2194 (49)	13730 (30)
70+	3110 (10)	184 (2)	537 (12)	3831 (8)
Sex - no. (%)				
Male	16726 (54)	6253 (58)	2652 (59)	25631 (55)
Female	14230 (46)	4504 (42)	1863 (41)	20597 (45)
Race - no. (%)				
White	22252 (72)	7204 (67)	3402 (75)	32858 (71)
Black or African American	1722 (6)	566 (5)	221 (5)	2509 (5)
Asian	1730 (6)	691 (6)	192 (4)	2613 (6)
Native Hawaiian or other Pacific Islander	114 (0)	50 (0)	26 (1)	190 (0)
American Indian or Alaska Native	92 (0)	78 (1)	10 (0)	180 (0)

Characteristic	AML	ALL	MPN	Total
More than one race	247 (1)	132 (1)	29 (1)	408 (1)
Not reported	4799 (16)	2036 (19)	635 (14)	7470 (16)
Ethnicity - no. (%)				
Hispanic or Latino	2482 (8)	2394 (22)	247 (5)	5123 (11)
Non-Hispanic or Latino	20820 (67)	5554 (52)	3190 (71)	29564 (64)
Non-resident of the U.S.	6983 (23)	2579 (24)	958 (21)	10520 (23)
Not reported	671 (2)	230 (2)	120 (3)	1021 (2)
Current CCN region of patient - no. (%)				
US	23297 (75)	7897 (73)	3454 (77)	34648 (75)
Canada	2076 (7)	552 (5)	318 (7)	2946 (6)
Europe	1439 (5)	372 (3)	231 (5)	2042 (4)
Asia	684 (2)	385 (4)	70 (2)	1139 (2)
Australia/New Zealand	1633 (5)	550 (5)	259 (6)	2442 (5)
Mideast/Africa	524 (2)	211 (2)	34 (1)	769 (2)
Central/South America	1303 (4)	790 (7)	149 (3)	2242 (5)
Karnofsky score prior to HCT - no. (%)				
90-100%	17731 (57)	6725 (63)	2405 (53)	26861 (58)
< 90%	12696 (41)	3852 (36)	2021 (45)	18569 (40)
Not reported	529 (2)	180 (2)	89 (2)	798 (2)
HCT-CI - no. (%)				
0	7432 (24)	3101 (29)	1101 (24)	11634 (25)
1	4934 (16)	1739 (16)	668 (15)	7341 (16)
2	4612 (15)	1699 (16)	707 (16)	7018 (15)
3	5326 (17)	1743 (16)	822 (18)	7891 (17)
4	3614 (12)	1180 (11)	535 (12)	5329 (12)
5+	4849 (16)	1260 (12)	660 (15)	6769 (15)
Not reported	189 (1)	35 (0)	22 (0)	246 (1)
Disease-Related Characteristics				
Interval from diagnosis to HCT, months - median (min-max)	5 (0-1208)	7 (1-542)	28 (1-630)	6 (0-1208)
Disease Status				
AML pre-HCT disease stage - no. (%)				
Disease is not AML	0 (0)	10757 (100)	4515 (100)	15272 (33)
CR1	22116 (71)	0 (0)	0 (0)	22116 (48)
CR2	4422 (14)	0 (0)	0 (0)	4422 (10)
CR3+	268 (1)	0 (0)	0 (0)	268 (1)
Advanced or active disease	3999 (13)	0 (0)	0 (0)	3999 (9)
Not reported	151 (0)	0 (0)	0 (0)	151 (0)

Characteristic	AML	ALL	MPN	Total
ALL pre-HCT disease stage - no. (%)				
Disease is not ALL	30956 (100)	0 (0)	4515 (100)	35471 (77)
CR1	0 (0)	7636 (71)	0 (0)	7636 (17)
CR2	0 (0)	2225 (21)	0 (0)	2225 (5)
CR3+	0 (0)	407 (4)	0 (0)	407 (1)
Advanced or active disease	0 (0)	478 (4)	0 (0)	478 (1)
Not reported	0 (0)	11 (0)	0 (0)	11 (0)
MDS pre-HCT disease stage - no. (%)				
Disease is not MDS/MPN	30956 (100)	10757 (100)	36 (1)	41749 (90)
Early	0 (0)	0 (0)	91 (2)	91 (0)
Advanced	0 (0)	0 (0)	3765 (83)	3765 (8)
Not reported	0 (0)	0 (0)	623 (14)	623 (1)
Transplant-Related Characteristics				
Conditioning intensity reported by center - no. (%)				
MAC	15656 (51)	7588 (71)	1550 (34)	24794 (54)
NMA	4029 (13)	816 (8)	590 (13)	5435 (12)
RIC	11023 (36)	2292 (21)	2340 (52)	15655 (34)
Not MAC, either RIC or NMA	17 (0)	0 (0)	3 (0)	20 (0)
Not reported	231 (1)	61 (1)	32 (1)	324 (1)
Conditioning regimen - no. (%)				
TBI/Cy	921 (3)	2924 (27)	35 (1)	3880 (8)
TBI/Cy/Flu	3460 (11)	1033 (10)	356 (8)	4849 (10)
TBI/Cy/Flu/TT	263 (1)	84 (1)	6 (0)	353 (1)
TBI/Cy/TT	8 (0)	115 (1)	0 (0)	123 (0)
TBI/Cy/VP	72 (0)	109 (1)	0 (0)	181 (0)
TBI/VP	119 (0)	792 (7)	2 (0)	913 (2)
TBI/Mel	1158 (4)	354 (3)	197 (4)	1709 (4)
TBI/Flu	2861 (9)	1900 (18)	394 (9)	5155 (11)
TBI/other(s)	214 (1)	217 (2)	9 (0)	440 (1)
Bu/Cy/Mel	4 (0)	2 (0)	0 (0)	6 (0)
Bu/Cy	4120 (13)	427 (4)	306 (7)	4853 (10)
Bu/Mel	198 (1)	33 (0)	12 (0)	243 (1)
Flu/Bu/TT	872 (3)	170 (2)	242 (5)	1284 (3)
Flu/Bu	10217 (33)	1079 (10)	1404 (31)	12700 (27)
Flu/Mel/TT	264 (1)	131 (1)	32 (1)	427 (1)
Flu/Mel	4946 (16)	1007 (9)	1319 (29)	7272 (16)
FCR	0 (0)	1 (0)	0 (0)	1 (0)

Characteristic	AML	ALL	MPN	Total
Cy/Flu	170 (1)	42 (0)	24 (1)	236 (1)
Cy alone	8 (0)	52 (0)	1 (0)	61 (0)
BEAM	0 (0)	2 (0)	0 (0)	2 (0)
Mel alone	43 (0)	7 (0)	4 (0)	54 (0)
Mel/other(s)	50 (0)	12 (0)	4 (0)	66 (0)
Treosulfan	299 (1)	37 (0)	28 (1)	364 (1)
Carb/other(s)	1 (0)	0 (0)	0 (0)	1 (0)
TLI	69 (0)	8 (0)	5 (0)	82 (0)
Other(s)	469 (2)	161 (1)	73 (2)	703 (2)
None	7 (0)	6 (0)	5 (0)	18 (0)
Missing	143 (0)	52 (0)	57 (1)	252 (1)
TBI usage - no. (%)				
TBI (single dose > 500 cGy or fractionated > 800 cGy)	2079 (7)	5504 (51)	60 (1)	7643 (17)
TBI (single dose <= 500 cGy or fractionated <= 800 cGy), other agents delivered at MA doses	407 (1)	138 (1)	36 (1)	581 (1)
TBI (single dose > 200 and <= 500 cGy, or fractionated > 200 and <= 800 cGy)	2118 (7)	709 (7)	388 (9)	3215 (7)
TBI = 200 cGy	4273 (14)	1068 (10)	506 (11)	5847 (13)
TBI, dose unknown	275 (1)	126 (1)	10 (0)	411 (1)
Non-TBI regimen	17645 (57)	2341 (22)	3029 (67)	23015 (50)
Not reported	4159 (13)	871 (8)	486 (11)	5516 (12)
Donor type - no. (%)				
HLA identical sibling	7401 (24)	3105 (29)	1074 (24)	11580 (25)
Twin	1 (0)	0 (0)	2 (0)	3 (0)
Haploidentical donor	5446 (18)	2216 (21)	633 (14)	8295 (18)
Other related	626 (2)	230 (2)	64 (1)	920 (2)
Well-matched unrelated (8/8)	12852 (42)	3598 (33)	2176 (48)	18626 (40)
Partially-matched unrelated (7/8)	1963 (6)	671 (6)	297 (7)	2931 (6)
Mismatched unrelated (<= 6/8)	165 (1)	38 (0)	13 (0)	216 (0)
Multi-donor	202 (1)	92 (1)	20 (0)	314 (1)
Unrelated (matching cannot be determined)	1317 (4)	392 (4)	209 (5)	1918 (4)
Cord blood	983 (3)	415 (4)	27 (1)	1425 (3)
Donor/recipient sex match - no. (%)				
M-M	10723 (35)	3800 (35)	1755 (39)	16278 (35)
M-F	7803 (25)	2453 (23)	1079 (24)	11335 (25)
F-M	5478 (18)	2190 (20)	866 (19)	8534 (18)

Characteristic	AML	ALL	MPN	Total
F-F	5816 (19)	1871 (17)	769 (17)	8456 (18)
CB - recipient M	497 (2)	257 (2)	24 (1)	778 (2)
CB - recipient F	578 (2)	178 (2)	14 (0)	770 (2)
Not reported	61 (0)	8 (0)	8 (0)	77 (0)
GVHD prophylaxis - no. (%)				
None	223 (1)	78 (1)	86 (2)	387 (1)
Ex-vivo T-cell depletion	163 (1)	110 (1)	6 (0)	279 (1)
CD34 selection	388 (1)	169 (2)	52 (1)	609 (1)
PtCy + other(s)	10361 (33)	3589 (33)	1333 (30)	15283 (33)
PtCy alone	163 (1)	59 (1)	10 (0)	232 (1)
TAC + MMF +- other(s) (except PtCy)	2488 (8)	659 (6)	353 (8)	3500 (8)
TAC + MTX +- other(s) (except MMF, PtCy)	9486 (31)	3230 (30)	1622 (36)	14338 (31)
TAC + other(s) (except MMF, MTX, PtCy)	1291 (4)	438 (4)	229 (5)	1958 (4)
TAC alone	666 (2)	227 (2)	59 (1)	952 (2)
CSA + MMF +- other(s) (except PtCy,TAC)	1601 (5)	390 (4)	203 (4)	2194 (5)
CSA + MTX +- other(s) (except PtCy,TAC,MMF)	3572 (12)	1622 (15)	489 (11)	5683 (12)
CSA + other(s) (except PtCy,TAC,MMF,MTX)	16 (0)	5 (0)	3 (0)	24 (0)
CSA alone	249 (1)	93 (1)	23 (1)	365 (1)
Other(s)	271 (1)	80 (1)	41 (1)	392 (1)
Missing	18 (0)	8 (0)	6 (0)	32 (0)
Product type - no. (%)				
BM	3099 (10)	1542 (14)	183 (4)	4824 (10)
PBSC	26780 (87)	8779 (82)	4293 (95)	39852 (86)
UCB	1075 (3)	435 (4)	38 (1)	1548 (3)
Other	1 (0)	1 (0)	1 (0)	3 (0)
Not reported	1 (0)	0 (0)	0 (0)	1 (0)
Year of HCT - no. (%)				
2006-2010	2962 (10)	966 (9)	291 (6)	4219 (9)
2011-2015	13333 (43)	4631 (43)	1819 (40)	19783 (43)
2016-2020	13819 (45)	4889 (45)	2244 (50)	20952 (45)
2021+	842 (3)	271 (3)	161 (4)	1274 (3)
Follow-up of survivors - median (range)	36.5 (0.0-113.8)	36.3 (0.0-108.9)	36.0 (0.0-104.6)	36.4 (0.0-113.8)

Field	Response
Proposal Number	2410-258-HOLTER
Proposal Title	The Risk of Engraftment Syndrome in Multiple Myeloma Patients Undergoing Autologous Stem Cell Transplantation: A Comparison of Plerixafor + G-CSF vs. G-CSF Alone
Key Words	-
Principal Investigator #1: - First and last name, degree(s)	Holter Chakrabarty, Jennifer
Principal Investigator #1: - Email address	jennifer-holter@ouhsc.edu
Principal Investigator #1: - Institution name	University Of Oklahoma Health Sciences Centre
Principal Investigator #1: - Academic rank	Professor
Junior investigator status (defined as ≤5 years from fellowship)	No
Do you identify as an underrepresented/minority?	No
Principal Investigator #2 (If applicable): - First and last name, degree(s):	Nishant Tawari
Principal Investigator #2 (If applicable): - Email address:)	
Principal Investigator #2 (If applicable): - Institution name:	University Of Oklahoma Health Sciences Centre
Principal Investigator #2 (If applicable): - Academic rank:	
Junior investigator status (defined as ≤5 years from fellowship)	
Do you identify as an underrepresented/minority?	
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:	
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
Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.	-
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
If you have already spoken with a scientific director or working committee chair regarding this study, then please specify who:	-

Field	Response
RESEARCH QUESTION:	Is the risk of engraftment syndrome higher in patients who have received plerixafor for hematopoietic cell mobilization in multiple myeloma patients undergoing autologous stem cell transplant?
RESEARCH HYPOTHESIS:	Plerixafor-based mobilization is associated with an increased risk of developing engraftment syndrome in multiple myeloma patients undergoing autologous stem cell transplantation, likely due to the higher number of mononuclear cells in the mobilized graft.
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	Primary Objective To evaluate the incidence of engraftment syndrome in multiple myeloma patients who receive plerixafor + G-CSF for stem cell mobilization compared to those who receive G-CSF alone. Secondary Objectives 1.To assess whether higher mononuclear cell counts in the graft are associated with an increased risk of engraftment syndrome. 2.To analyze patient and disease-specific factors that may contribute to an increased risk of engraftment syndrome in the plerixafor group.
SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.	Identifying a potential link between plerixafor use and increased risk of ES will help clinicians make more informed decisions regarding mobilization strategies. If confirmed, adjustments in pre-transplant protocols or close monitoring for ES may reduce morbidity, improve post-transplant recovery, and prevent severe complications in MM patients.

Field	Response
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.	Multiple myeloma (MM) is a clonal plasma cell neoplasm for which autologous stem cell transplantation remains a key therapeutic strategy for eligible patients. The reported incidence of engraftment syndrome in patients with MM undergoing ASCT varies between 7% and 17%. Engraftment syndrome is a severe systemic inflammatory response that typically manifests during the neutrophil recovery phase following hematopoietic stem cell transplantation. Clinically, Engraftment syndrome is characterized by a spectrum of signs and symptoms ranging from fever, rash, pulmonary edema to organ dysfunction with renal or hepatic dysfunction. Engraftment syndrome is a notable cause of morbidity, following ASCT in patients with Lymphoma and Multiple myeloma Plerixafor is a CXCR4 antagonist that mobilizes hematopoietic stem cells from the bone marrow into the peripheral blood for collection prior to transplantation. It is often used in combination with G-CSF or patients who fail to mobilize sufficient stem cells with G-CSF alone. While plerixafor has significantly enhanced stem cell mobilization and contributed to better engraftment outcomes. Our institutional observations have suggested a potential association between plerixafor use and an increased incidence of engraftment syndrome in MM patients undergoing ASCT. A review of the literature revealed limited data addressing this association. However, a key study by Le-Qing Cao et al., titled "Plerixafor-based mobilization and mononuclear cell counts in graft increased the risk of engraftment syndrome after autologous hematopoietic stem cell transplantation," demonstrated a higher incidence of ES in patients mobilized with plerixafor. Multivariate analysis highlighted that in the total cohort, factors like age ≥60, receiving ASCT during complete remission , and a higher number of mononuclear cells in the graft were significantly associated with ES. In sub group analysis, patients with plasma cell diseases, plerixafor use was also a notable risk factor. Given the extensive use of plerixafor for stem cell mobilization in MM, further investigation is warranted to determine whether its use inherently increases the risk of ES and to elucidate the mechanisms underlying this association.
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	Inclusion Criteria 1.Patients diagnosed with multiple myeloma. 2. Patients who underwent autologous stem cell transplantation. 3.Patients who received either plerixafor + G-CSF or G-CSF alone for stem cell mobilization.

Field	Response
Does this study include pediatric patients?	No
If this study does not include pediatric patients, please provide justification:	This study focuses on multiple myeloma (MM), a clonal plasma cell neoplasm that predominantly affects older adults. MM is exceedingly rare in the pediatric population, with the majority of cases occurring in individuals over the age of 65.
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.	Variables to Be Collected Patient-Related Variables Age at Transplant Sex Pre-transplant Performance Status: ECOG Co-morbidities: Soroor score Prior Therapies: Chemotherapy, Radiation Disease-Related Variables R-ISS stage at diagnosis. Disease Status Prior to Transplant: Complete Response Partial Response Very Good Partial Response No Response or Stable Disease Progressive Disease Relapsed/Refractory Cytogenetics and Molecular Markers: Pre-transplant labs: Hemoglobin, serum calcium, creatinine, serum albumin M spike Type of M spike, serum free light chains Levels of IgG, IgA, IgM Plasma cells in bone marrow aspirate by flow cytometry Plasma cells in bone marrow aspirate by morphologic assessment Plasma cells in bone marrow biopsy Cytogenetics by FISH Cytogenetics via karyotype Transplant-Related Variables Volume of product infused Total number of cells administered Concomitant therapy with GM-CSF Conditioning regimen Outcome Variables Engraftment: Incidence of engraftment syndrome Time to neutrophil and platelet engraftment. Post-Transplant Disease Status Duration of hospital stay post-transplant.
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	N/A
MACHINE LEARNING: Please indicate if the study requires methodology related to machine-learning and clinical predictions.	N/A
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	N/A

Field	Response
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.	N/A
REFERENCES:	Plerixafor and G-CSF versus placebo and G-CSF to mobilize hematopoietic stem cells for autologous stem cell transplantation in patients with multiple myeloma. Authors: John F. DiPersio, Edward A. Stadtmauer, Auayporn Nademanee, Ivana N. M. Micallef, Patrick J. Stiff, Jonathan L. Kaufman, Richard T. Maziarz, Chitra Hosing, Stefan Früehauf, Mitchell Horwitz, Dennis Cooper, Gary Bridger, Gary Calandra, for the 3102 Investigators. Engraftment Syndrome after Autologous Stem Cell Transplantation: An Update Unifying the Definition and Management Approach. Authors: Cornell, Robert Frank et al. Source: Biology of Blood and Marrow Transplantation, Volume 21, Issue 12, 2061 - 2068. Engraftment Syndrome: Clinical Features and Predictive Factors in Autologous Stem Cell Transplant. Authors: Sheth, V., Jain, R., Gore, A. et al. Source: Indian Journal of Hematology and Blood Transfusion, Volume 34, 448–453 (2018).
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
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.	-

Population of adults with multiple myeloma who received an autoHCT with either plerixafor + G-CSF or G-CSF alone

Characteristic	G-CSF alone	G-CSF + plerixafor	Total
No. of patients	24087	40734	64821
No. of centers	257	241	273
Patient-Related Characteristics			
TED or RES (RF) track determined for this event - no. (%)			
TED	21933 (91)	37461 (92)	59394 (92)
CRF (RES)	2154 (9)	3273 (8)	5427 (8)
Age, by decades - no. (%)			
Median (min-max)	61 (19-86)	63 (24-85)	62 (19-86)
18-19	1 (0)	0 (0)	1 (0)
20-29	51 (0)	52 (0)	103 (0)
30-39	565 (2)	560 (1)	1125 (2)
40-49	2833 (12)	3250 (8)	6083 (9)
50-59	7743 (32)	10777 (26)	18520 (29)
60-69	10105 (42)	18776 (46)	28881 (45)
70+	2789 (12)	7319 (18)	10108 (16)
Sex - no. (%)			
Male	13926 (58)	23397 (57)	37323 (58)
Female	10161 (42)	17337 (43)	27498 (42)
Race - no. (%)			
White	14897 (62)	29285 (72)	44182 (68)
Black or African American	3765 (16)	6651 (16)	10416 (16)
Asian	949 (4)	1163 (3)	2112 (3)
Native Hawaiian or other Pacific Islander	54 (0)	66 (0)	120 (0)
American Indian or Alaska Native	112 (0)	231 (1)	343 (1)
More than one race	252 (1)	166 (0)	418 (1)
Not reported	4058 (17)	3172 (8)	7230 (11)
Ethnicity - no. (%)			
Hispanic or Latino	2316 (10)	3964 (10)	6280 (10)
Non-Hispanic or Latino	15689 (65)	33660 (83)	49349 (76)
Non-resident of the U.S.	5556 (23)	1831 (4)	7387 (11)
Not reported	526 (2)	1279 (3)	1805 (3)
Current CCN region of patient - no. (%)			
US	17553 (73)	38681 (95)	56234 (87)

Characteristic	G-CSF alone	G-CSF + plerixafor	Total
Canada	2734 (11)	1152 (3)	3886 (6)
Europe	215 (1)	16 (0)	231 (0)
Asia	719 (3)	267 (1)	986 (2)
Australia/New Zealand	387 (2)	72 (0)	459 (1)
Mideast/Africa	407 (2)	81 (0)	488 (1)
Central/South America	2071 (9)	463 (1)	2534 (4)
Not reported	1 (0)	2 (0)	3 (0)
Karnofsky score prior to HCT - no. (%)			
90-100%	13330 (55)	21019 (52)	34349 (53)
< 90%	10242 (43)	19101 (47)	29343 (45)
Not reported	515 (2)	614 (2)	1129 (2)
HCT-CI - no. (%)			
0	7869 (33)	9597 (24)	17466 (27)
1	3678 (15)	5541 (14)	9219 (14)
2	3854 (16)	6898 (17)	10752 (17)
3	3787 (16)	7497 (18)	11284 (17)
4	2260 (9)	4741 (12)	7001 (11)
5+	2563 (11)	6315 (16)	8878 (14)
Not reported	76 (0)	145 (0)	221 (0)
Disease-Related Characteristics			
Interval from diagnosis to HCT, months - median (min-max)	7 (0-688)	7 (0-657)	7 (0-688)
Disease Status			
MM pre-HCT disease stage - no. (%)			
CR	3598 (15)	6406 (16)	10004 (15)
PR	18463 (77)	31725 (78)	50188 (77)
Advanced/active	1767 (7)	2433 (6)	4200 (6)
Not reported	259 (1)	170 (0)	429 (1)
Transplant-Related Characteristics			
Conditioning regimen - no. (%)			
TBI/Mel	8 (0)	11 (0)	19 (0)
Bu/Cy	1 (0)	0 (0)	1 (0)
Bu/Mel	123 (1)	182 (0)	305 (0)
Flu/Bu	4 (0)	2 (0)	6 (0)
Flu/Mel	1 (0)	2 (0)	3 (0)
Cy alone	2 (0)	0 (0)	2 (0)
BEAM	29 (0)	59 (0)	88 (0)

Characteristic	G-CSF alone	G-CSF + plerixafor	Total
BEAM like	45 (0)	22 (0)	67 (0)
Mel alone	22950 (95)	39849 (98)	62799 (97)
Mel/other(s)	685 (3)	320 (1)	1005 (2)
Other(s)	27 (0)	35 (0)	62 (0)
None	11 (0)	9 (0)	20 (0)
Missing	201 (1)	243 (1)	444 (1)
Product type - no. (%)			
BM	21 (0)	19 (0)	40 (0)
PBSC	24065 (100)	40713 (100)	64778 (100)
UCB	1 (0)	0 (0)	1 (0)
Other	0 (0)	1 (0)	1 (0)
Not reported	0 (0)	1 (0)	1 (0)
Year of HCT - no. (%)			
2008-2011	19 (0)	3 (0)	22 (0)
2012-2015	5468 (23)	4851 (12)	10319 (16)
2016-2019	9954 (41)	14715 (36)	24669 (38)
2020-2023	8189 (34)	19992 (49)	28181 (43)
2024	457 (2)	1173 (3)	1630 (3)
Follow-up of survivors - median (range)	48.8 (0.0-186.8)	36.8 (0.2-170.2)	44.1 (0.0-186.8)