Not for publication or presentation

A G E N D A
CIBMTR WORKING COMMITTEE FOR PLASMA CELL DISORDERS WORKING COMMITTEE
Honolulu, HI
Thursday, February 13, 2025, 1:00 – 3:00 PM HST

Co-Chair:	**Heather Landau, MD; Memorial Sloan Kettering Cancer Center, New York, NY; Phone: 212-639-8808; E-mail: landauh@mskcc.org**
Co-Chair:	**Yvonne Efebera, MD, MPH; OhioHealth, Columbus, OH; Telephone: 614-566-2268; E-mail: yvonne.efebera@ohiohealth.com**
Co-Chair:	**Taiga Nishihori, MBBS; Moffitt Cancer Center, Tampa, FL; Phone: 813-745-8156; E-mail: taiga.nishihori@moffitt.org**
Scientific Director:	**Marcelo Pasquini, MD, MS; CIBMTR® (Center for International Blood and Marrow Transplant Research), Milwaukee, WI; Telephone: 414-805-0680; E-mail: mpasquini@mcw.edu**
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Statistician:	**Temitope Oloyede, MPH; CIBMTR® (Center for International Blood and Marrow Transplant Research), Milwaukee, WI; Telephone: 414-805-0673; E-mail: toloyede@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. **MM21-01** Garderet L, Gras L, Koster L, Baaij L, Hamad N, Dsouza A, Estrada-Merly N, Hari P, Saber W, Cowan AJ, Iida M, Okamoto S, Takamatsu H, Mizuno S, Kawamura K, Kodera Y, Ko B, Liam C, Ho KW, Goh Ai Sim, Keat TS, Elhaddad AM, Bazarbachi A, Chaudhry Q, Alfar R, Bekadja M, Benakli M, Frutos C, Riva E, Galeano S, Bass F, Mian HS, McCurdy A, Wang FR, Meng L, Neumann D, Koh M, Snowden JA, Schönland S, McLornan DP, Hayden PJ, Sureda A, Greinix HT, Aljurf M, Atsuta Y, Niederwieser D. Global characteristics and outcomes of autologous hematopoietic stem cell transplantation for newly diagnosed multiple myeloma: A study of the worldwide network for blood and marrow transplantation (WBMT). ***American Journal of Hematology. doi:10.1002/ajh.27451. Epub 2024 Aug 19.***
   b. **MM23-01a** Standard of Care Idecabtagene Vicleucel (Ide-cel) for Relapsed/Refractory Multiple Myeloma: A CIBMTR Analysis. (N Ahmed/ S Ganguly/ B Dhakal/ C Ferreri/ K Patel/ A Afrough/ L Anderson Jr/ H Hashmi/ S Usmani/ S Sidana// D Hansen/ L Gowda/ S Mirza/ C Freeman/ O Akhtar). ***Submitted (Under review). Oral Presentation, ASH 2023. Poster Presentation, EHA 2024.***
   c. **MM23-01b** Akhtar OS, Oloyede T, Brazauskas R, Afrough A, Hashmi H, Sidana S, Ahmed N, Bye M, Hansen D, Ferreri C, Dhakal B. Outcomes of Older Adults and Frail Patients Receiving

Idecabtagene Vicleucel: A CIBMTR Study. ***Blood advances. doi:10.1182/bloodadvances.2024014970. Epub 2025 Jan 2.***

4. Studies in progress (Attachment 3)

a. **MM20-02b** Risk factors for and characteristics of second primary malignancies following autologous hematopoietic cell transplant for multiple myeloma (B Ragon/M Shah/S Usmani). **Data File Preparation.**
b. **MM22-01** Outcomes of autologous hematopoietic cell transplantation for light chain deposition disease (H Hashmi/ B Dhakal). **Protocol Received.**
c. **CT23-02** Prolonged cytopenia following anti-B cell maturation antigen chimeric antigen receptor T-cell therapy for multiple myeloma (J Logue/D Hansen/ M Janakiram/ G Kaur). **Manuscript Preparation.**
d. **MM24-01** Safety and efficacy of ciltacabtagene in patients with relapsed or refractory multiple myeloma (D Hansen/ K Patel/ H Hashmi/ S Usmani/ R Narra/ B Dhakal/ A Afrough/ L Anderson/A Bidikian/ L Gowda/ D Dima/ N Ahmed/ S Sidana/ S Mirza/ T Nishihori/ H Mian/ M Mohan/ M Faisal). **Analysis.**
e. **MM24-02** Real-world comparison of anti-BCMA CAR T-cell therapies in relapsed or refractory multiple myeloma (M Mohan/ C Schinke/ A Bidikian/ L Gowda/ C Freeman/ D Hansen/ S Gupta/ A Afrough/ L Anderson/ M Janakiram/ S Goldsmith/ S Ahmed/ K Patel/ M Krem/ N Ahmed). **Analysis.**

5. Future/proposed studies

a. **PROP 2409-20; 2410-97; 2410-140** Predictors of Early Relapse and Durable Remissions in patients with multiple myeloma treated with BCMA-Targeted CAR T-Cell Therapy (A Ali/M Janakiram/ G Kaur) (Attachment 4)
b. **PROP 2409-30; 2410-69; 2410-172; 2410-213** Comparative effectiveness between 2nd Auto-HCT and CAR T overall and in key subgroups in relapsed / refractory multiple myeloma (L Liu/ M Janakiram/ A Afrough/ L Anderson Jr/ Y Shestovska/ H Fung/ E Biltibo/ K Adetola) (Attachment 5)
c. **PROP 2410-35** Impact of Autologous Stem Cell Transplantation on Outcomes with High-risk Multiple Myeloma (S Zanwar/ S Kumar) (Attachment 6)
d. **PROP 2410-53** An Inflammatory Biomarker Signature Predicts CAR-T Treatment Failure in Patients with Multiple Myeloma (H Hashmi/ S Mailankody/ S Usmani) (Attachment 7)
e. **PROP 2410-58; 2410-143; 2410-161; 2410-187** Impact of Lenalidomide vs. Lenalidomide + CD38 Monoclonal Antibody Maintenance on Outcomes in Post-Autologous Stem Cell Transplant Patients with Multiple Myeloma (M Sanchez/ A Avila/ T Schmidt/ P Rajan Abraham/ A Afrough) (Attachment 8)
f. **PROP 2410-71; 2410-210; 2410-228** Real-World Safety, Efficacy, and Outcomes of Cilta-cel and Ide-cel Treatment in Earlier Lines for Patients with Relapsed or Refractory Multiple Myeloma (H Hashmi/ S Mailankody/ S Usmani/ A Bidikian/ L Gowda/ N Abdallah/ S Gupta) (Attachment 9)
g. **PROP 2410-74** Trends In Utilization of a Delayed Autologous Transplant Approach (ASCT) In Newly Diagnosed Multiple Myeloma (NDMM) (M Mohan/ C Schinke) (Attachment 10)
h. **PROP 2410-91** Treatment Paradigm of Monoclonal Gammopathy of Renal Significance (H Shaikh/ Y Efebera) (Attachment 11)
i. **PROP 2410-93** Outcomes of Out-of-specification BCMA-directed Chimeric antigen receptor (CAR) T-cell therapies in patients with Heavily Pretreated Relapsed/Refractory Multiple Myeloma (D Dima/ D Hansen) (Attachment 12)

Proposed studies; not accepted for consideration at this time

j. **PROP 2403-02** The impact of frailty on the efficacy and safety of CAR T-cell therapy in R/R MM (N Abdallah/ S Kumar). ***Dropped due to overlap with current study/publication.***
k. **PROP 2409-01** Outcomes of patients with Daratumumab, Bortezomib, Cyclophosphamide and Dexathasone followed by Autologous stem cell transplantation (H Parmar/ D Vesole). ***Dropped due to low scientific impact.***
l. **PROP 2409-04** The impact of prior ASCT, either at any point or within **2** years beforehand, on BCMA CAR-T efficacy (R Banerjee). ***Dropped due to overlap with current study/publication.***
m. **PROP 2409-05** The impact of prior belantamab on real-world BCMA CAR-T efficacy (R Banerjee). ***Dropped due to overlap with current study/publication.***
n. **PROP 2409-06** Timing of hematopoietic stem cell boost after BCMA CAR-T therapy (R Banerjee). ***Dropped due to overlap with current study/publication.***
o. **PROP 2409-33** Defining the best hematologic response criteria in AL Amyloidosis post autologous stem cell transplantation (D Bhutani). ***Dropped due to low scientific impact.***
p. **PROP 2410-07** Patient-Reported Outcome (PRO) Assessment of Patients Treated with ABECMA and CARVYKTI, Chimeric Antigen Receptor (CAR) T-Cell Therapies Targeting BCMA in Patients with Multiple Myeloma (MM) (A Afrough/ L Anderson). ***Dropped due to small sample size.***
q. **PROP 2410-30** Machine learning for predicting toxicity and clinical outcomes in patients with relapsed and refractory multiple myeloma who received ciltacabtagene autoleucel, an anti-B-cell maturation antigen chimeric antigen receptor T-cell therapy. (J Cooperrider/ R Shaw). ***Dropped due to low scientific impact.***
r. **PROP 2410-31** Patient-Reported Outcome (PRO) Assessment of Patients Treated with CARVYKTI, Chimeric Antigen Receptor (CAR) T-Cell Therapies Targeting BCMA in Patients with Multiple Myeloma (MM) (A Afrough/ L Anderson). ***Dropped due to small sample size.***
s. **PROP 2410-34** Patient-Reported Outcome (PRO) Assessment of Patients Treated with ABECMA, Chimeric Antigen Receptor (CAR) T-Cell Therapies Targeting BCMA in Patients with Multiple Myeloma (MM) (A Afrough/ L Anderson). ***Dropped due to small sample size.***
t. **PROP 2410-37** Comparison of Non-relapsed Mortality, Toxicity Profile, Infection Patterns, and Impact on Outcomes in patients receiving Two Commercially Available anti-BCMA CAR-T Therapy (M Abid). ***Dropped due to overlap with current study/publication.***
u. **PROP 2410-54** Impact of bridging chemotherapy with bispecific antibodies on outcomes post CAR-T cell therapy for relapsed refractory multiple myeloma (H Hashmi/ S Mailankody/ S Usmani). ***Dropped due to overlap with current study/publication.***
v. **PROP 2410-86** Predictive Modeling for BCMA-Directed CAR-T Therapies in Relapsed/Refractory Multiple Myeloma Using Machine Learning. (N Ahmed/ S Irfan). ***Dropped due to low scientific impact.***
w. **PROP 2410-126** Impact of the emergence of post-transplant oligoclonal bands on autologous stem cell transplant outcomes in patients with multiple myeloma (Z Gahvari/ N Callander). ***Dropped due to supplemental data needed.***
x. **PROP 2410-139** Efficacy of Ciltacabtagene autoleucel (Cilta-cel) compared to Idecabtagene vicleucel (ide-cel) in patients with high-risk Multiple Myeloma (R Kishore Narra/ B Dhakal). ***Dropped due to overlap with current study/publication.***
y. **PROP 2410-175** Investigating the Role of Radiation Therapy Before CAR-T Cell Therapy in Multiple Myeloma (J Kort/ L Shune). ***Dropped due to overlap with current study/publication.***
z. **PROP 2410-181** Investigating the Role of CAR-T Cell Therapy in Multiple Myeloma Patients with CNS Involvement (J Kort/ L Shune). ***Dropped due to supplemental data needed.***

aa. **PROP 2410-221** Real World Impact of Prior BiTE therapy (teclistamab, talquetamab, elranatamab) on BCMA-drected CAR-T Safety and Efficacy in Multiple Myeloma (K Chetlapalli/ L Gowda). ***Dropped due to overlap with current study/publication.***
bb. **PROP 2410-234** Patient Reported Outcomes Following BCMA Directed CAR-T Cell Therapy (S Sidana). ***Dropped due to small sample size.***
cc. **PROP 2410-241** Triplet versus quadruplet induction regimen in RCT-ineligible multiple myeloma patients undergoing autologous transplant (M Krem/ G Hildebrandt). ***Dropped due to low scientific impact.***
dd. **PROP 2410-242** Determine Efficacy Outcomes of Ciltacabtagene Autoleucel (cilta-cel) in Patients with Relapsed Refractory Multiple Myeloma with or without prior exposure to CD**38** directed monoclonal antibody therapy (M Yasir). ***Dropped due to overlap with current study/publication.***

6. Other business

MINUTES AND OVERVIEW PLAN
CIBMTR WORKING COMMITTEE FOR PLASMA CELL DISORDERS
San Antonio, TX
Thursday, February 22, 2024, 1:00 – 3:00 PM CT

Co-Chair:	**Muzaffar Qazilbash, MD; MD Anderson Cancer Center, Houston, TX; Telephone: 713-745-3458; E-mail: mqazilba@mdanderson.org**
Co-Chair:	**Heather Landau, MD; Memorial Sloan Kettering Cancer Center, New York, NY; Phone: 212-639-8808; E-mail: landauh@mskcc.org**
Co-Chair:	**Taiga Nishihori, MD; Moffitt Cancer Center, Tampa, FL; Phone: 813-745-8156; E-mail: taiga.nishihori@moffitt.org**
Scientific Director:	**Marcelo Pasquini, MD, MS; CIBMTR® (Center for International Blood and Marrow Transplant Research), Medical College of Wisconsin, Milwaukee, WI; Telephone: 414-805-0680; E-mail: mpasquini@mcw.edu**
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Statistical Director:	**Ruta Brazauskas, PhD; CIBMTR® (Center for International Blood and Marrow Transplant Research), Medical College of Wisconsin, Milwaukee, WI; Telephone: 414-456-8687; E-mail: ruta@mcw.edu**
Statistician:	**Temitope Oloyede, MPH, CPH; CIBMTR® (Center for International Blood and Marrow Transplant Research), Medical College of Wisconsin, Milwaukee, WI; E-mail: toloyede@mcw.edu**

1. Introduction

The Plasma Cell Disorders Working Committee meeting held on Thursday, February 22, 2024, at 1:00 p.m. The chairs, scientific directors and statisticians were all present at the meeting. All attendees had their name badges scanned at the front gate for attendance purpose and those who attended the meeting virtually were also added to the meeting attendance list.

The meeting started with Dr. Heather Landau – co-chair of the committee – welcoming the attendees on behalf of the working committee leadership and introduced each member of the working committee leadership. The committee announced Dr. Muzaffar Qazilbash's departure, thanking him for his significant contributions, and welcomed Dr. Yvonne Efebera as his successor. CIBMTR's conflict of interest policy was discussed highlighting the importance of disclosing and managing potential conflicts. Dr. Landau presented information about the publicly available research datasets provided by the CIBMTR for secondary research. She discussed the working committee membership process informing the audience that the committee is open to any individual willing to take an active role in study development through completion. Everyone who attends the working committee meeting, in person (with badge scanned) and virtually, will be automatically added to the working committee membership roster. Dr. Landau further discussed the committee's goals of publishing high-impact studies and selecting proposals that will have a significant scientific impact on the field. The proposals will be assessed based on their scientific impact and potential to change the field. Resources for additional information on the CIBMTR and Working Committee was provided as well as information about the CIBMTR Collaborative Session scheduled for Saturday, February

24, 2024 at 1:00 p.m. The committee discussed the sources of CIBMTR data and the different types of data available. Furthermore, Dr. Landau highlighted the availability of Patient Reported Outcome (PRO) data collection and introduced the CIBMTR working committee training and leadership program for early career investigators.

The working committee's portfolio was presented by Dr. Qazilbash. The committee discussed abstract presentations and publications between 2023 – 2024 and provided an update on the status of ongoing studies and future goals. The committee also reviewed the proposals for 2024 PCDWC meeting. Of the 43 proposals submitted to the committee, 14 proposals were dropped, and 29 proposals (multiple proposals combined into 9) were presented at the meeting. The voting process was reiterated with information on how to score each proposal through the Tandem App.

Dr. Taiga Nishihori moderated the online meeting, responding to questions and comments sent via chat by attendees who joined the meeting virtually.

The proposals were introduced by the working committee chairs. Each proposal was allotted 5 minutes for presentation and 5 minutes for questions and discussions.

2. Accrual summary

The accrual summary provides information about the number of patients available in the registration (TED) level and research (CRF) level for potential studies. As of December 2023, 12,5942 plasma cell disorder cases were reported at the TED level – of which 16,827 cases were reported at the research level – to the CIBMTR for first autologous transplant. For first allogeneic transplants, these numbers are 5,280 cases and 2,127 cases at the TED and research level respectively. For CAR T-cell infusion, 2,821 plasma cell disorders cases were reported to the CIBMTR between 2016-2023. The full accrual summary is available online as part of the attachments to the working committee meeting agenda.

3. Publications and Presentations

The published papers and abstracts that were presented at various conferences between 2023 - 2024 are shown below demonstrating that it was a productive year for our committee.

a. **MM20-02A** Ragon BK, Shah MV, D'Souza A, Estrada-Merly N, Gowda L, George G, de Lima M, Hashmi S, Kharfan-Dabaja MA, Majhail NS, Banerjee R, Saad A, Hildebrandt GC, Mian H, Abid MB, Battiwalla M, Lekakis LJ, Patel SS, Murthy HS, Nieto Y, Strouse C, Badawy SM, Al Hadidi S, Dholaria B, Aljurf M, Vesole DH, Lee CH, Pawarode A, Gergis U, Miller KC, Holmberg LA, Afrough A, Solh M, Munshi PN, Nishihori T, Anderson LD Jr, Wirk B, Kaur G, Qazilbash MH, Shah N, Kumar SK, Usmani SZ. Impact of second primary malignancy post-autologous transplantation on outcomes of multiple myeloma: a CIBMTR analysis. ***Blood Advances. 2023 Jun 27;7(12):2746-2757. doi: 10.1182/bloodadvances.2022009138. Epub 2023 Jun 15. PMCID: PMC10275699.***

b. **MM20-03** Bumma N, Dhakal B, Fraser R, Estrada-Merly N, Anderson K, Freytes CO, Hildebrandt GC, Holmberg L, Krem MM, Lee C, Lekakis L, Lazarus HM, Mian H, Murthy HS, Nathan S, Nishihori T, Parrondo R, Patel SS, Solh M, Strouse C, Vesole DH, Kumar S, Qazilbash MH, Shah N, D'Souza A, Sidana S. Impact of bortezomib-based versus lenalidomide maintenance therapy on outcomes of patients with high-risk multiple myeloma. ***Cancer. 2023 Jul 15;129(14):2179-2191. doi: 10.1002/cncr.34778. Epub 2023 Apr 6. PMCID: PMC10516285.***

c. **MM23-01** Sidana S, Ahmed N, Akhtar OS, Heim M, Brazauskas R, Hansen DK, Ferreri C, Freeman CL, Afrough A, Anderson Jr LD, Dhakal B. Real World Outcomes with Idecabtagene Vicleucel (Ide-Cel) CAR-T Cell Therapy for Relapsed/Refractory Multiple Myeloma. ***Oral presentation, ASH 2023.***

d. **MM23-01** Akhtar OS, Hashmi H, Oloyede T, Brazauskas R, Bye M, Sidana S, Hansen DK, Ahmed N, Ferreri C, Afrough A, Anderson L, Dhakal B, Dhanda D, Gowda L, Harrison M, Kitali A, Landau H, Mirza S, Patel J, Patwardhan P, Qazilbash M, Patel K, Nishihori T, Ganguly S, Pasquini MC, Usmani S, Freeman CL. Real World Outcomes of Older Adults and Frail Patients with Relapse/Refractory Multiple Myeloma Receiving Idecabtagene Vicleucel. ***Poster presentation, Tandem 2024.***

4. Studies in progress

The current studies within the working committee and their status are as follows:

a. **MM20-02b** Risk factors for and characteristics of second primary malignancies following autologous hematopoietic cell transplant for multiple myeloma. (B Ragon/ M Shah/ S Zafar Usmani). **Deferred until follow-up data is available.**

b. **MM21-01** Differences in outcomes on myeloma treatment worldwide. (L Garderet). **Manuscript Preparation.**

c. **MM22-01** Outcomes of autologous hematopoietic cell transplantation for light chain deposition disease.(H Hashmi/ B Dhakal). **Protocol Development.**

d. **MM23-01** Real world experience of feasibility, safety, efficacy, and outcomes following anti-BCMA CAR T-cell therapy for patients with relapsed or refractory multiple myeloma. (N Ahmed/ S Ganguly/ B Dhakal/ C Ferreri/ K Patel/ A Afrough/ L Anderson Jr/ H Hashmi/ S Usmani/ S Sidana/ D Hansen/ L Gowda/ S Mirza/ C Freeman/ O Akhtar). **Data Analysis.**

e. **CT23-02** Prolonged cytopenia following anti-B cell maturation antigen chimeric antigen receptor T-cell therapy for multiple myeloma. (J Logue/ D Hansen/ M Janakiram/ G Kaur). **Protocol Development.**

5. Future/proposed studies

The committee thanked all investigators who submitted proposals. Of the 43 proposals submitted to the committee, 14 proposals were dropped, majority due to lack of feasibility or overlap with current studies or existing publication(s). The 29 proposals presented at the meeting were combined based on themes and presented as 9 proposals.

a. **PROP 2309-11/PROP 2310-262 /PROP 2310-01 /PROP 2310-02/PROP 2310-03 /PROP 2310-12 / PROP 2310-14 /PROP 2310-41 /PROP 2310-59 /PROP 2310-71 /PROP 2310-102 /PROP 2310-240**
Combined proposal: Real-world Experience of Safety and Efficacy Outcomes Following Ciltacabtagene Autoleucel for Patients with Relapsed or Refractory Multiple Myeloma (**D Hansen**/ K Patel/ H Hashmi/ S Usmani/ R Narra/ B Dhakal/ A Afrough/ L Anderson/ A Bidikian/ L Gowda/ D Dima/ N Ahmed/ S Sidana/ S Mirza/ T Nishihori)
Submitted proposals:
PROP 2309-11 Safety and Efficacy of Standard of Care Ciltacabtagene Autoleucel for Relapsed/Refractory Multiple Myeloma (D Hansen/K Patel)

PROP 2310-01 Determine Efficacy Outcomes of CAR-T Cell Therapy in Patients with Relapsed Refractory Multiple Myeloma with Extramedullary Disease and High-Risk Cytogenetics (H Hashmi/S Usmani)
PROP 2310-02 Impact of Bridging Chemotherapy on Outcomes Post CAR-T Cell Therapy for Relapsed Refractory Multiple Myeloma (H Hashmi/S Usmani)
PROP 2310-03 Impact of Lymphodepleting Chemotherapy on Outcomes After CAR-T Cell Therapy for Relapsed Refractory Multiple Myeloma (H Hashmi/S Usmani)
PROP 2310-12 Impact of Prior BCMA Exposure on Outcomes Post BCMA Directed CAR-T Cell Therapy for Relapsed Refractory Multiple Myeloma (H Hashmi/S Usmani)
PROP 2310-14 Safety and Efficacy of CAR-T Cell Therapy for Non-Triple Class Exposed Multiple Myeloma (H Hashmi/S Usmani)
PROP 2310-41 Real-World Evidence of Safety and Efficacy of Ciltacabtagene Autoleucel in Patients with Multiple Myeloma (R Narra/B Dhakal)
PROP 2310-59 Real World Experience of CARVYKTI, Chimeric Antigen Receptor (CAR) T-Cells Targeting BCMA in Patients with Multiple Myeloma (MM) (A Afrough/L Anderson)
PROP 2310-71 Real-World Experience of Safety, Efficacy, and Outcomes Following Cilta-cel Therapy for Patients with Relapsed or Refractory Multiple Myeloma (A Bidikian/L Gowda)
PROP 2310-102 Real-World Experience and Utilization of Ciltacabtagene Autoleucel (cilta-cel) in Patients with Relapsed-Refractory Multiple Myeloma (D Dima/N Ahmed)
PROP 2310-240 Real World Experience of Feasibility, Safety, Efficacy, and Outcomes Following Ciltacabtagene Vicleucel CAR T-Cell Therapy for Patients with Relapsed or Refractory Multiple Myeloma (S Sidana)
PROP 2310-262 Impact of Prior Line of Therapy on on Post BCMA-CAR-T Outcomes for Multiple Myeloma (S Mirza/T Nishihori)

Dr. Hansen presented this combined proposal on behalf of the group. The goal of this study is to assess the safety and efficacy of ciltacabtagene autoleucel (cilta-cel) in a large and comprehensive real-world patient cohort across the United States. This study hypothesizes that standard of care cilta-cel has a similar safety and efficacy profile as that observed with investigational cilta-cel in a highly selected population of patients treated on clinical trial. The primary objective is to determine the overall response rate (ORR) and progression-free survival (PFS) of patients receiving cilta-cel in the real-world setting. The secondary objectives are to assess overall survival (OS) and safety - incidence, severity, and factors associated with CRS, ICANS, delayed neurologic toxicities, IEC-HLH, cytopenias, infections, and second primary malignancies. The cohort of interest includes about 570 patients with multiple myeloma treated with cilta-cel between 2022-2023.

Comments from the Audience:
Dr. Nishihori thanked Dr. Hansen for the presentation and welcomed comments, contributions, and questions from the audience.

The first question was about duration of follow-up for assessing outcomes. To this, Dr. Hansen responded saying this depends on the amount of follow-up available if the proposal is selected to move forward. The committee's Scientific Directors, Drs. Akhtar and Pasquini provided further information on the current duration of follow-up and future projections.

Another question was about the possibility of assessing additional outcomes such as secondary malignancies. Drs. Pasquini and Hansen responded saying the analysis will explore these additional outcomes and decision on whether or not to include them in the study will be dependent of number of events and follow-up duration.

One of the attendees asked about the study design to which Drs. Hansen and Akhtar mentioned that it will likely be descriptive with univariable and multivariable analyses.

Dr. Nishihori read out the questions submitted via online chat. There was a question about the follow-up period for delayed neurotoxicity. Another question was asking if there is detailed data on patients who received non-conforming product. Drs. Hansen, Pasquini and Akhtar responded by providing information on the data available for neurotoxicity and patients who received non-conforming product. CIBMTR forms were recently revised to include more information about neurotoxicity.

b. **PROP 2309-15/PROP 2310-119/PROP 2310-121/PROP 2310-123/PROP 2310-157/PROP 2310-200/PROP 2310-235/PROP 2310-242**

Combined proposal: Real-world comparison of anti-BCMA CAR T-cell therapies in relapsed or refractory multiple myeloma (M Mohan/ C Schinke/ A Bidikian/ L Gowda/ C Freeman/ D Hansen/ S Gupta/ **A Afrough**/ L Anderson/ M Janakiram/ S Goldsmith/ S Ahmed/ K Patel/ M Krem/ N Ahmed)

Submitted proposals:

PROP 2309-15 Non-Relapse Mortality with BCMA Directed Chimeric Antigen Receptor T Cell Therapy for Multiple Myeloma (M Mohan/C Schinke)

PROP 2310-119 Real-World Comparison of Safety, Efficacy, and Outcomes of treatment Cilta-cel vs Ide-cel in Patients with Relapsed or Refractory Multiple Myeloma (A Bidikian/L Gowda)

PROP 2310-121 Real-World Comparison of Idecabtagene Vicleucel (ide-cel) and Ciltacabtagene Autoleucel (cilta-cel) Chimeric Antigen Receptor (CAR) T-Cells versus Clinical Trial Outcomes Achieved by Patients with Relapsed/Refractory Multiple Myeloma (C Freeman/D Hansen)

PROP 2310-123 Comparative Analysis of Ciltacabtagene Autoleucel and Idecabtagene Vicleucel CAR-T Cell Therapies in Multiple Myeloma. (S Gupta)

PROP 2310-157 Comparing Real World Outcome of Patients Treated with ABECMA and CARVYKTI, Chimeric Antigen Receptor (CAR) T-Cell Therapies Targeting BCMA in Patients with Multiple Myeloma (MM) (A Afrough/L Anderson)

PROP 2310-200 Comparative Effectiveness of Short-Term Clinical Outcomes of Ide-Cel versus Cilta-Cel in Multiple Myeloma (M Janakiram/S Goldsmith)

PROP 2310-235 Outcomes of Vulnerable Patients with Multiple Myeloma and Chronic Kidney Disease who have Been Treated with Idecabtagene Vicleucel vs Ciltacabtagene Autoleucel (S Ahmed/K Patel)

PROP 2310-242 Comparison of Commercial BCMA-Directed CAR T Cells for Relapsed or Refractory Multiple Myeloma (M Krem/N Ahmed)

Dr. Afrough represented the group by presenting this proposal centered around the comparison of two FDA-approved CAR T-cell therapies in treating relapsed or refractory multiple myeloma, ide-cel and cilta-cel, with a focus on efficacy and safety. Regarding the hypothesis, cilta-cel is anticipated to have superior efficacy but higher toxicity in R/R MM patients treated with anti-BCMA CAR T-cell therapies. The endpoints to compare include:

Primary:

- *Progression-free survival*

Secondary:

- *Efficacy: Response rate per IMWG; Duration of response; Time to progression; Early progression (<6 months); Overall survival*
- *Safety: CRS and ICANS incidence and severity; Non ICANS related neurotoxicity; Non-relapse mortality (3- and 6-month); HLH-like; ICAHT; Infections*

Of the patients who received anti-BCMA CAR T-cell therapies for R/R MM between 2021 – 2023 and reported to the CIBMTR, 1,256 patients received ide-cel and 570 patients received cilta-cel.

Comments from the Audience:
Dr. Nishihori thanked Dr. Afrough for the presentation and opened the floor for questions and discussion.

Members of the audience emphasized the importance of this study. One of the attendees wanted to know if the CIBMTR database is sufficient to adequately answer the research question, especially as it relates to center preference for one CAR-T product over the other. Another question was how the study will account for patient- and treatment-specific differences between the two products being compared especially when the follow-up durations are still relatively short. Drs. Afrough and Pasquini, and members of the audience provided information to address these questions. The reason for the differences is mostly due to difference in FDA approval dates for the products. The accrual of patients receiving these CAR-T products is projected to increase rapidly and it is expected that over time, some of these differences will narrow down, especially as it relates to follow-up interval, between the two products. Information on statistical methods that can be used for the analysis was also provided.

c. **PROP 2309-19/2310-09** Combined proposal: Characterization, Prognostic impact, and Management of cytopenias in patients receiving BCMA directed CAR-T cell therapy for Relapsed Refractory Multiple Myeloma (R Banerjee/ **H Hashmi**/ S Usmani)
Submitted proposals:
PROP 2309-19 Timing and Dosing of Hematopoietic Stem Cell Boosts After BCMA CAR-T Therapy (R Banerjee)
PROP 2310-09 Incidence, Risk Factors, and Management of Post CAR-T Cytopenias for Relapsed Refractory Multiple Myeloma (H Hashmi/S Usmani)

This proposal was presented by Dr. Hashmi. The study hypothesized that:
- *Incidence and severity of post CAR-T cytopenia is similar to what has been reported in clinical trials*
- *CAR-HEMATOTOX score is predictive of safety and efficacy outcomes post CAR-T for RRMM*
- *Patients who receive Hematopoietic stem cell boost (HSCB) have higher rates of resolution of cytopenias and infections compared to patients who do not receive HSCB*
- *Earlier administration of HSCB relative to CAR-T (e.g., ≤Day +30) is associated with better outcomes versus administration at later timepoints*
- *Lower HSCB doses (≤ 2 million cells /kg) will perform similarly to higher doses in terms of cytopenia resolutions and prevention of infections*

The endpoints to be assessed are:
- *Response by IMWG Criteria*
- *Survival - Overall survival (OS), Progression-free survival (PFS), Relapse/Progression, and Non-relapse mortality (NRM)*
- *Toxicity - CRS (all grades/grade ≥3); Neurotoxicity/ICANS (all grades/grade ≥3)*
- *Infections; Cytopenia (all grades, grade ≥3).*

The cohort of interest are patients who received anti-BCMA CAR T-cell therapies for R/R MM between 2021 – 2023 and reported to the CIBMTR. This includes 1,256 patients received ide-cel and 570 patients received cilta-cel.

Comments from the Audience:
Dr. Nishihori thanked Dr. Hashmi for the presentation and moderated the discussion.

One of the questions asked if the newly propose ICAT score may have any impact on this study. Dr. Hashmi differed to the committee to provide information on data availability from the CIBMTR registry, to which Drs. Akhtar and Pasquini confirmed availability of data needed to calculate CAR-HEMATOTOX score.

An attendee wanted to know if there is sufficient data to assess stem cell boost. Dr. Hashmi explained the different methods that can be used extract the data from CIBMTR database. Dr. Akhtar who recently reviewed this data provided the current numbers.

Another attendee asked if this proposal has considered bridging therapy and other tumor burden reduction techniques which can reduce development of toxicity and impact the HEMATOTOX score. Dr. Hashmi confirmed that the CIBMTR data can be used to analyze bridging therapy but may be challenging to analyze tumor burden.

Regarding early vs late stem cell boost, there was a question about how the investigators plan to identify patients who would have recovered cell counts on their own without a boost as opposed to patients who really needed stem cell boost. Dr. Hashmi mentioned that patients who have not received stem cell boost will be the comparison group. He also provided the assessment timepoints and data that will be used for the analysis.

In response to a question asking if there is any added information this study will provide over an ongoing CIBMTR study, Dr. Hashmi mentioned that this study included information on two CR-T products as opposed to one product in the other study.

Responding to a recommendation to adjust for potential bias in the analysis, Dr. Hashmi described some methods that will be employed to minimize confounders and bias.

Other questions about availability of data on GCSF use and transfusion need was addressed by Dr. Akhtar with confirmation on timeframe for which this data is collected.

d. **PROP 2310-05** Outcomes of autologous stem cell transplantation in double-hit multiple myeloma (B Wirk)

This proposal was presented by Dr. Wirk. This study hypothesizes that the outcomes of autologous stem cell transplantation in double-hit multiple myeloma are poorer than in single-hit or standard-risk multiple myeloma, despite using novel agents. The objective is to assess Progression-free survival, Relapse/Progression, and Overall survival. The study population is patients with multiple myeloma between 2008 and 2020 who had autologous HCT within 12 months of diagnosis. This includes 388 patients with double hit, 1,188 with single hit, and 4,327 with no hit.

Comments from the Audience:
Dr. Landau moderated the discussions after thanking Dr. Wirk for the presentation.

In response to a question about data availability, Dr. Akhtar confirmed provided information about data on novel therapies such as Quads.
Dr. Wirk responded to the question about the study design and how covariates will be adjusted, providing information on patient selection and study design. Dr. Wirk welcomed a suggestion to use publicly available dataset with appropriately matched cohort for comparison.

Addressing other suggestions to use publicly available datasets for this study, Dr. Wirk provided justification for why conducting this study as a CIBMTR working committee study is the best way to answer the research question. Dr. Akhtar added that currently no publicly available datasets have contemporary information required to carry out this study and a new dataset will need to be created.

e. **PROP 2310-11** Development of Comorbidity Scores that Could Impact the Treatment Related Mortality and Survival in Patients Receiving BCMA Directed Chimeric Antigen Receptor (CAR) T-Cell Therapy for Relapsed Refractory Multiple Myeloma (**H Hashmi**/S Usmani)

Dr. Hashmi presented this proposal hypothesizing that pre-treatment comorbidities are predictive of CAR T-cell therapy related toxicities and survival outcomes. The objectives of this study are to evaluate the impact of individual comorbidities on development of severe toxicities (CRS, neurotoxicity, organ toxicity) and survival outcomes (PFS, OS, relapse) after CAR-T for RRMM, and design and validate a CAR-T specific -comorbidity index (CAR-T-CI) for RRMM.

The study population will comprise all CAR T recipients with RRMM in the CIBMTR database (N=1826 as of 2023). The study endpoints are Response by IMWG Criteria; Survival - Overall survival (OS), Progression-free survival (PFS), Relapse/Progression, Non-relapse mortality (NRM); and Toxicity - CRS (all grades/grade ≥3), Neurotoxicity/ICANS (all grades/grade ≥3), Infections, Cytopenia (all grades, grade ≥3).

Comments from the Audience:
Dr. Landau thanked Dr. Hashmi for the presentation and welcomed comments, contributions, and questions from the audience.

To the question asking how differences in toxicity between the two CAR-T products will be addressed, Dr. Hashmi provided information on how covariates will be adjusted in the modelling.
For a suggestion to expand this question to other studies instead of restricting to Multiple myeloma, Drs. Hashmi and Pasquini provided information on studies addressing this in other diseases such as lymphoma.

Drs. Hashmi and Pasquini further addressed a question asking how to different disease-related outcomes from those that are co-morbidity related, and welcomed suggestions.

An attendee raised concerns over the timeliness and application of the Comorbidity index in this era of rapidly changing intervention techniques especially as it relates to lines of therapy which is an important covariate.

f. **PROP 2310-27** Defining the Best Hematologic Response Criteria in AL Amyloidosis Post Autologous Stem Cell Transplantation (**D Bhutani**/R Chakraborty)

Dr. Bhutani presented this proposal with the following hypotheses:

- *Persistent of even low abnormal levels of involved free light chain level leads to poor outcomes in patients with systemic AL Amyloidosis post ASCT.*
- *A low iFLC level (≤2 mg/dl) and dFLC (≤1 mg/dl) are the best predictor of improved long term outcomes in patients with systemic AL Amyloidosis post ASCT.*
-

The primary objective of this study is to evaluate the impact of achieving a deep light chain response in patients with AL Amyloidosis post ASCT by comparing different iFLC and dFLC levels for overall survival (OS) and time to next treatment (TTNT). The secondary objectives are to evaluate the impact of achieving a deep light chain response among patients who achieve a CR post ACST amongst different iFLC and dFLC groups by comparing OS and TTNT; and evaluate the incidence and impact of deep light chain response among patients with low eGFR <30 ml/min (Incidence of iFLC ≤ 2mg/dl and dFLC <1 mg/dl among patients with eGFR <30 vs >30 ml/min; Define the ideal iFLC and dFLC among these patients).

The CIBMTR dataset contains over 1000 patients who underwent ASCT for AL Amyloidosis between 2000-2020 with CRF level data available.

Comments from the Audience:
This presentation was followed by questions and comments from attendees. Dr. Bhutani addressed questions about the study design and best method of addressing the research question.

There was another question asking if the study will take into consideration the presence of abnormal protein and how this correlates with the outcome. This was followed by recommendation to consider adding supplemental data from external sources to address this. Drs. Bhutani and Landau mentioned that there is paucity of data on abnormal light chain even from external sources.

g. PROP 2310-72 Effects of Using Autologous Stem Cells That Have Been Cryopreserved Long Term in Myeloma Autografts (A Masurekar/R Vasudevan Nampoothiri)

This proposal was presented by Dr. Masurekar. The study hypothesizes that auto HSC result in appropriate engraftment despite long term cryopreservation. The population of interest are myeloma patients who had autologous transplant using cell that are cryopreserved after initial therapy. Any concurrent hematological condition that may impact engraftment of cryopreserved autologous HSC will be excluded.

The CIBMTR registry contains about 4688 patients with stem cells that have been cryopreserved less than 5years, 215 patients with stem cells that have been cryopreserved for over 5 years, and 76 patients with stem cells that have been cryopreserved over 8 years. The primary endpoint to be assessed is Cumulative Incidence of engraftment. Secondary Endpoints are 100 - day mortality, Secondary graft failure, Secondary Myeloid Malignancy.

Comments from the Audience:
Dr. Qazilbash thanked Dr. Masurekar for the presentation and opened the proposal to contributions, and questions from the audience.

In response to a concern about the suitability of the CIBMTR data in answering this research question, Dr. Masurekar reiterated the rationale and goals of the study.

h. **PROP 2310-237 /2310-73** Combined proposal: Safety and efficacy of ciltacabtagene autoleucel in older patients with relapsed multiple myeloma (H Mian/ M Mohan/ **M Faisal**)
Submitted proposals:
PROP 2310-237 Outcomes of CAR-T treatment for Myeloma Patients >65 Years of Age (M Salman Faisal)
PROP 2310-73 Outcomes of Cilta-cel Therapy for Older Adults with Multiple Myeloma (H Mian/M Mohan)

Dr. Faisal delivered presentation for this proposal which is aimed at assessing the efficacy and safety of standard of care Cilta-cel among older adults (≥65) versus younger adults (<65) with R/R MM. The research hypothesis is that cilta-cel therapy is associated with comparable safety and efficacy outcomes among both younger (<65) and older adults (age ≥ 65) with R/R MM. This study will include patients who received commercial cilta-cel therapy for R/R MM and have atleast 3 months of follow up after cellular therapy infusion. Outcomes will be compared between the patients ≥ 65 years and <65 years.

The investigators also plan to conduct a subset analysis for patients ≥ 70 years vs <70 and for patients defined as non-frail vs frail (simplified frailty score). The outcomes to be assessed are:

Primary Outcome:
- *Progression free survival (time from cilta-cel infusion to relapse, disease progression, or death from any cause)*
-

Secondary outcomes:
- *Overall response rate (ORR) per IMWG criteria.*
- *Incidence and cause of non-relapse mortality (within 100 days of CART infusion)*
- *Overall survival (defined as the time from cilta-cel infusion to death from any cause)*
- *Toxicity (grade ≥3: CRS, ICANS, infections and cytopenia).*

Of the 570 patients that meet the study's inclusion criteria, about 255 patients were aged 65 and above with about half of the patients older than 70 years.

Comments from the Audience:
Dr. Qazilbash moderated the discussions after thanking Dr. Salman for the presentation.

In response to a comment about ongoing study with similar research questions, Dr. Faisal provided information on the differences between that study and the proposed study.

Dr. Faisal reiterated in response to another attendee that frailty score will be adopted in the analysis.

i. **PROP 2310-103** Machine Learning in Predicting the Factors Associated with Early Relapse After Autologous Stem Cell Transplant in Multiple Myeloma Patients (**L Gonzalez Mosquera**/S Farhan/S Vuyyala/A Mosquera Orgeira/M Mateos)

Dr. Gonzalez Mosquera presented this proposal on behalf of the investigators. The hypothesis and objectives of this study are as follows:

Hypothesis: Data routinely collected for patients with multiple myeloma who undergo autologous stem cell transplant as part of the CIBMTR reporting contain predictive information which can be

used to build predictive machine learning models that can provide physician and providers with more precise information regarding the risk of early relapse after autologous transplant for multiple myeloma.

Primary objective: To create a new personalized prognostic model to predict early relapse at the 18-month landmark post auto SCT using ML algorithm.

Secondary objectives: Predict PFS, OS after autologous transplant, identify which patients benefit the most from SCT especially high risk, to compare this model with established risk scores.

The CIBMTR registry has over 4000 Multiple Myeloma patients, transplanted from 2008 to 2020, with CRF level data that can be used for this research.

Comments from the Audience:
Dr. Qazilbash thanked Dr. Gonzalez Mosquera for the presentation and welcomed comments, contributions, and questions from the audience.

Given that the one of the benefits of machine learning is to analyze thousands of variables and provide information on which variables are important, some attendees had concerns that this study may not provide much advantage using the CIBMTR data which collects select variables that are considered significant. Dr. Gonzales Mosquera responded saying that this study can provide additional information on disease prognostication.

In response to another question, Dr. Gonzales Mosquera mentioned that there are studies that have applied this technique in other diseases.

Proposed studies; not accepted for consideration at this time

j. **PROP 2308-01** Optimum Timing for PBSC Infusion Following High Dose Melphalan in Multiple Myeloma (R Kamble). *Dropped for low scientific impact.*
k. **PROP 2308-06** Outcomes with Commercial CAR-T Therapy in Plasma Cell Leukemia (R Banerjee). *Dropped for small sample size.*
l. **PROP 2309-01** Pre-Transplant Treatment Patterns and Post-Transplant Outcomes in Myeloma Patients with Partial Responses to First-Line Therapy (R Banerjee/L Williams). *Dropped for small sample size; Supplemental data needed.*
m. **PROP 2310-36** Autologous Stem Cell Transplantation Affect on Extramedullary Plasmocytoma (M Pamukcuoglu). *Dropped for low scientific impact.*
n. **PROP 2310-37** Autologous Stem Cell Transplantation or Daratumumab in Extramedullary Plasmacytoma? (M Pamukcuoglu). *Dropped - Supplemental data needed.*
o. **PROP 2310-78** Optimal Monitoring Period for Lymphoma Pts who are Recipients of Commercial BCMA CAR-T Therapy (A Britt/N Ahmed). *Dropped for low scientific impact.*
P. **PROP 2310-94** Outcomes in Patients with HIV Infection and Multiple Myeloma Post Autologous Stem Cell Transplant (U Yadav/S Chhabra). *Dropped for small sample size.*
q. **PROP 2310-125** Impact of Prior Autologous Stem Cell Transplant on CAR-T Cell Therapy Outcomes in Patients with Multiple Myeloma (U Yadav/S Chhabra). *Dropped for low scientific impact.*
r. **PROP 2310-152** Patient-Reported Outcome (PRO) Assessment of Patients Treated with ABECMA and CARVYKTI, Chimeric Antigen Receptor (CAR) T-Cell Therapies Targeting BCMA in Patients with Multiple Myeloma (MM) (A Afrough/L Anderson). *Dropped for small sample size.*

s. **PROP 2310-169** Retrospective Analysis Comparing Outcomes of Relapsed/Refractory Multiple Myeloma That Have Received Chimeric Antigen Receptor T Cell Therapy or Bispecific Antibody Therapy. (J Wiedmeier-Nutor/S Chhabra). *Dropped - Supplemental data needed.*

t. **PROP 2310-192** Risk Factors and Outcomes of Patients with Multiple Myeloma Receiving Out of Specification Autologous Cell Therapy Products (S Ivanov/J Logue). *Supplemental data needed.*

u. **PROP 2310-198** Outcomes of Pomalidomide-Based Post-Transplant Maintenance in Comparison to Lenalidomide-Based Maintenance for Multiple Myeloma Patients (S Manjappa/L Holmberg). *Dropped for low scientific impact.*

v **PROP 2310-208** Outcomes of allogeneic hematopoietic stem cell transplant in multiple myeloma patient (Y Yang/U Gergis). *Dropped for low scientific impact.*

w. **PROP 2310-246** Melphalan Dose Choice Stratified by Depth of Response or Quadruplet Induction Regimen in Multiple Myeloma Patients Undergoing Autologous Transplant (M Krem/A Suvannasankha). *Dropped for low scientific impact.*

*The instructions for voting through the Tandem2024 App was reiterated and attendees were thanked for participating in the meeting. The meeting was adjourned on at **3:00** p.m. The Chairs, Scientific Directors, and Statisticians stayed behind for extra time to meet and interact one on one with attendees.*

6. Other Business

The chairs of the working committee, scientific directors and statisticians had a post-WC meeting afterwards to discuss proposals. After the proposal presentations, each attendee had the opportunity to score the presented proposals using the provided scoring sheet.

Based on the voting results, current scientific merit, and impact of the studies on the field, the following studies were accepted to move forward as the committee's new research projects for the upcoming year:

a. Combined study: Safety and Efficacy of Ciltacabtagene Autoleucel in Patients with Relapsed or Refractory Multiple Myeloma (D Hansen/ K Patel/ H Hashmi/ S Usmani/ R Narra/ B Dhakal/ A Afrough/ L Anderson/ A Bidikian/ L Gowda/ D Dima/ N Ahmed/ S Sidana/ S Mirza/ T Nishihori/ H Mian/ M Mohan/ M Faisal**)**

Proposals:

PROP 2309-11/PROP 2310-01/PROP 2310-02/PROP 2310-03/PROP 2310-12/PROP 2310-14 /PROP 2310-41/PROP 2310-59/PROP 2310-71/PROP 2310-102/PROP 2310-240/PROP 2310-262

Combined proposal: Real-world Experience of Safety and Efficacy Outcomes Following Ciltacabtagene Autoleucel for Patients with Relapsed or Refractory Multiple Myeloma (D Hansen/ K Patel/ H Hashmi/ S Usmani/ R Narra/ B Dhakal/ A Afrough/ L Anderson/ A Bidikian/ L Gowda/ D Dima/ N Ahmed/ S Sidana/ S Mirza/ T Nishihori)

Submitted proposals:

PROP 2309-11 Safety and Efficacy of Standard of Care Ciltacabtagene Autoleucel for Relapsed/Refractory Multiple Myeloma (D Hansen/K Patel)

PROP 2310-01 Determine Efficacy Outcomes of CAR-T Cell Therapy in Patients with Relapsed Refractory Multiple Myeloma with Extramedullary Disease and High-Risk Cytogenetics (H Hashmi/S Usmani)

PROP 2310-02 Impact of Bridging Chemotherapy on Outcomes Post CAR-T Cell Therapy for Relapsed Refractory Multiple Myeloma (H Hashmi/S Usmani)

PROP 2310-03 Impact of Lymphodepleting Chemotherapy on Outcomes After CAR-T Cell Therapy for Relapsed Refractory Multiple Myeloma (H Hashmi/S Usmani)

PROP 2310-12 Impact of Prior BCMA Exposure on Outcomes Post BCMA Directed CAR-T Cell Therapy for Relapsed Refractory Multiple Myeloma (H Hashmi/S Usmani)
PROP 2310-14 Safety and Efficacy of CAR-T Cell Therapy for Non-Triple Class Exposed Multiple Myeloma (H Hashmi/S Usmani)
PROP 2310-41 Real-World Evidence of Safety and Efficacy of Ciltacabtagene Autoleucel in Patients with Multiple Myeloma (R Narra/B Dhakal)
PROP 2310-59 Real World Experience of CARVYKTI, Chimeric Antigen Receptor (CAR) T-Cells Targeting BCMA in Patients with Multiple Myeloma (MM) (A Afrough/L Anderson)
PROP 2310-71 Real-World Experience of Safety, Efficacy, and Outcomes Following Cilta-cel Therapy for Patients with Relapsed or Refractory Multiple Myeloma (A Bidikian/L Gowda)
PROP 2310-102 Real-World Experience and Utilization of Ciltacabtagene Autoleucel (cilta-cel) in Patients with Relapsed-Refractory Multiple Myeloma (D Dima/N Ahmed)
PROP 2310-240 Real World Experience of Feasibility, Safety, Efficacy, and Outcomes Following Ciltacabtagene Vicleucel CAR T-Cell Therapy for Patients with Relapsed or Refractory Multiple Myeloma (S Sidana)
PROP 2310-262 Impact of Prior Line of Therapy on on Post BCMA-CAR-T Outcomes for Multiple Myeloma (S Mirza/T Nishihori)

PROP 2310-73/ 2310-237
Combined proposal: Safety and efficacy of ciltacabtagene autoleucel in older patients with relapsed multiple myeloma (H Mian/ M Mohan/ M Faisal)
Submitted proposals:
PROP 2310-237 Outcomes of CAR-T treatment for Myeloma Patients >65 Years of Age (M Salman Faisal)
PROP 2310-73 Outcomes of Cilta-cel Therapy for Older Adults with Multiple Myeloma (H Mian/M Mohan)

b. PROP 2309-15/PROP 2310-119/PROP 2310-121/PROP 2310-123/PROP 2310-157/PROP 2310-200/PROP 2310-235/PROP 2310-242
Combined proposal: Real-world comparison of anti-BCMA CAR T-cell therapies in relapsed or refractory multiple myeloma (M Mohan/ C Schinke/ A Bidikian/ L Gowda/ C Freeman/ D Hansen/ S Gupta/ **A Afrough**/ L Anderson/ M Janakiram/ S Goldsmith/ S Ahmed/ K Patel/ M Krem/ N Ahmed)
Submitted proposals:
PROP 2309-15 Non-Relapse Mortality with BCMA Directed Chimeric Antigen Receptor T Cell Therapy for Multiple Myeloma (M Mohan/C Schinke)
PROP 2310-119 Real-World Comparison of Safety, Efficacy, and Outcomes of treatment Cilta-cel vs Ide-cel in Patients with Relapsed or Refractory Multiple Myeloma (A Bidikian/L Gowda)
PROP 2310-121 Real-World Comparison of Idecabtagene Vicleucel (ide-cel) and Ciltacabtagene Autoleucel (cilta-cel) Chimeric Antigen Receptor (CAR) T-Cells versus Clinical Trial Outcomes Achieved by Patients with Relapsed/Refractory Multiple Myeloma (C Freeman/D Hansen)
PROP 2310-123 Comparative Analysis of Ciltacabtagene Autoleucel and Idecabtagene Vicleucel CAR-T Cell Therapies in Multiple Myeloma. (S Gupta)
PROP 2310-157 Comparing Real World Outcome of Patients Treated with ABECMA and CARVYKTI, Chimeric Antigen Receptor (CAR) T-Cell Therapies Targeting BCMA in Patients with Multiple Myeloma (MM) (A Afrough/L Anderson)
PROP 2310-200 Comparative Effectiveness of Short-Term Clinical Outcomes of Ide-Cel versus Cilta-Cel in Multiple Myeloma (M Janakiram/S Goldsmith)

PROP 2310-235 Outcomes of Vulnerable Patients with Multiple Myeloma and Chronic Kidney Disease who have Been Treated with Idecabtagene Vicleucel vs Ciltacabtagene Autoleucel (S Ahmed/K Patel)
PROP 2310-242 Comparison of Commercial BCMA-Directed CAR T Cells for Relapsed or Refractory Multiple Myeloma (M Krem/N Ahmed)

Working Committee Overview Plan for 2024-2025		
Study Number and Title	**Current Status**	**Chairs Priority**
MM20-02B: Risk factors for and characteristics of secondary primary malignancies following autologous hematopoietic cell transplant for multiple myeloma	Deferred	2
MM21-01: Differences in outcomes on myeloma treatment worldwide	Manuscript preparation	1
MM22-01: Outcomes of autologous hematopoietic cell transplantation for light chain deposition disease	Protocol received	2
MM23-01: Real world experience of Feasibility, Safety, Efficacy, and Outcomes Following anti-BCMA CAR T-cell Therapy for Patients with Relapsed or Refractory Multiple Myeloma	Manuscript preparation	1
CT23-02: Prolonged cytopenia following anti-B cell maturation antigen chimeric antigen receptor T-cell therapy for multiple myeloma	Datafile preparation	1
MM24-01: Safety and Efficacy of Ciltacabtagene Autoleucel in Patients with Relapsed or Refractory Multiple Myeloma	Protocol pending	1
MM24-02: Real-world comparison of anti-BCMA CAR T-cell therapies in relapsed or refractory multiple myeloma	Protocol pending	1

Working Assignments for Working Committee Leadership (2024-2025)	
Yvonne Efebera, MD:	**MM20-02B:** Risk factors for and characteristics of secondary primary malignancies following autologous hematopoietic cell transplant for multiple myeloma **MM24-02:** Real-world comparison of anti-BCMA CAR T-cell therapies in relapsed or refractory multiple myeloma
Heather Landau, MD:	**MM22-01:** Outcomes of autologous hematopoietic cell transplantation for light chain deposition disease **MM24-01:** Safety and Efficacy of Ciltacabtagene Autoleucel in Patients with Relapsed or Refractory Multiple Myeloma
Taiga Nishihori, MD:	**MM23-01:** Real world experience of Feasibility, Safety, Efficacy, and Outcomes Following anti-BCMA CAR T-cell Therapy for Patients with Relapsed or Refractory Multiple Myeloma **CT23-02:** Prolonged cytopenia following anti-B cell maturation antigen chimeric antigen receptor T-cell therapy for multiple myeloma

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	952	300	211
Source of data			
CRF	508 (53)	139 (46)	88 (42)
TED	444 (47)	161 (54)	123 (58)
Number of centers	125	80	86
Disease at transplant			
Plasma cell disorder/Multiple Myeloma	952 (100)	300 (100)	211 (100)
Recipient age at transplant			
10-17 years	3 (<1)	0	0
18-29 years	7 (1)	3 (1)	3 (1)
30-39 years	86 (9)	31 (10)	23 (11)
40-49 years	277 (29)	77 (26)	52 (25)
50-59 years	396 (42)	128 (43)	93 (44)
60-69 years	177 (19)	60 (20)	39 (18)
70+ years	6 (1)	1 (<1)	1 (<1)
Median (Range)	53 (10-77)	53 (22-72)	53 (18-74)
Recipient race			
White	841 (91)	267 (90)	170 (96)
Black or African American	62 (7)	19 (6)	5 (3)
Asian	17 (2)	6 (2)	2 (1)
Native Hawaiian or other Pacific Islander	1 (<1)	1 (<1)	0
American Indian or Alaska Native	3 (<1)	1 (<1)	0
More than one race	2 (<1)	3 (1)	0
Unknown	26 (N/A)	3 (N/A)	34 (N/A)
Recipient ethnicity			
Hispanic or Latino	52 (6)	11 (4)	10 (5)
Non Hispanic or non-Latino	756 (90)	244 (93)	132 (71)
Non-resident of the U.S.	32 (4)	8 (3)	44 (24)
Unknown	112 (N/A)	37 (N/A)	25 (N/A)
Recipient sex			
Male	600 (63)	197 (66)	141 (67)
Female	352 (37)	103 (34)	70 (33)
Karnofsky score			
10-80	390 (41)	139 (46)	82 (39)
90-100	523 (55)	154 (51)	122 (58)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Missing	39 (4)	7 (2)	7 (3)
HLA-A B DRB1 groups - low resolution			
4/6	1 (<1)	0	0
5/6	109 (12)	29 (10)	19 (10)
6/6	803 (88)	249 (90)	175 (90)
Unknown	39 (N/A)	22 (N/A)	17 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	9 (1)	0	1 (1)
6/8	33 (4)	1 (<1)	3 (2)
7/8	141 (17)	30 (14)	26 (18)
8/8	652 (78)	180 (85)	114 (79)
Unknown	117 (N/A)	89 (N/A)	67 (N/A)
HLA-DPB1 Match			
Double allele mismatch	161 (30)	27 (23)	20 (33)
Single allele mismatch	305 (56)	62 (53)	30 (49)
Full allele matched	79 (14)	29 (25)	11 (18)
Unknown	407 (N/A)	182 (N/A)	150 (N/A)
High resolution release score			
No	572 (60)	300 (100)	209 (99)
Yes	380 (40)	0	2 (1)
KIR typing available			
No	884 (93)	300 (100)	210 (>99)
Yes	68 (7)	0	1 (<1)
Graft type			
Marrow	160 (17)	37 (12)	32 (15)
PBSC	789 (83)	263 (88)	179 (85)
BM+PBSC	2 (<1)	0	0
PBSC+UCB	1 (<1)	0	0
Conditioning regimen			
Myeloablative	328 (34)	111 (37)	84 (40)
RIC/Nonmyeloablative	611 (64)	185 (62)	118 (56)
TBD	13 (1)	4 (1)	9 (4)
Donor age at donation			
To Be Determined/NA	18 (2)	13 (4)	5 (2)
18-29 years	427 (45)	149 (50)	88 (42)
30-39 years	255 (27)	79 (26)	58 (27)
40-49 years	177 (19)	42 (14)	48 (23)
50+ years	75 (8)	17 (6)	12 (6)
Median (Range)	31 (18-61)	29 (18-58)	33 (19-58)
Donor/Recipient CMV serostatus			
+/+	221 (23)	76 (25)	49 (23)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
+/-	104 (11)	39 (13)	27 (13)
-/+	288 (30)	90 (30)	57 (27)
-/-	326 (34)	87 (29)	72 (34)
CB - recipient +	1 (<1)	0	0
Missing	12 (1)	8 (3)	6 (3)
GvHD Prophylaxis			
No GvHD Prophylaxis	7 (1)	2 (1)	5 (2)
TDEPLETION alone	3 (<1)	3 (1)	2 (1)
TDEPLETION +- other	15 (2)	5 (2)	5 (2)
CD34 select alone	43 (5)	18 (6)	10 (5)
CD34 select +- other	15 (2)	3 (1)	2 (1)
Cyclophosphamide alone	3 (<1)	1 (<1)	1 (<1)
Cyclophosphamide +- others	52 (5)	24 (8)	10 (5)
FK506 + MMF +- others	158 (17)	33 (11)	28 (13)
FK506 + MTX +- others(not MMF)	310 (33)	119 (40)	40 (19)
FK506 +- others(not MMF,MTX)	46 (5)	13 (4)	10 (5)
FK506 alone	22 (2)	5 (2)	4 (2)
CSA + MMF +- others(not FK506)	166 (17)	32 (11)	45 (21)
CSA + MTX +- others(not MMF,FK506)	51 (5)	21 (7)	25 (12)
CSA +- others(not FK506,MMF,MTX)	13 (1)	6 (2)	9 (4)
CSA alone	12 (1)	4 (1)	4 (2)
Other GVHD Prophylaxis	31 (3)	11 (4)	7 (3)
Missing	5 (1)	0	4 (2)
Donor/Recipient sex match			
Male-Male	416 (44)	123 (41)	92 (44)
Male-Female	208 (22)	58 (19)	42 (20)
Female-Male	182 (19)	72 (24)	47 (22)
Female-Female	142 (15)	45 (15)	26 (12)
CB - recipient M	1 (<1)	0	0
Missing	3 (<1)	2 (1)	4 (2)
Year of transplant			
1986-1990	1 (<1)	0	0
1991-1995	18 (2)	4 (1)	7 (3)
1996-2000	59 (6)	19 (6)	11 (5)
2001-2005	144 (15)	23 (8)	39 (18)
2006-2010	271 (28)	45 (15)	48 (23)
2011-2015	285 (30)	82 (27)	62 (29)
2016-2020	135 (14)	104 (35)	36 (17)
2021-2024	39 (4)	23 (8)	8 (4)
Follow-up among survivors, Months			
N Eval	217	107	54

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Median (Range)	60 (0-288)	37 (0-194)	38 (0-216)

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

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Number of patients	38	12	13
Source of data			
CRF	30 (79)	6 (50)	6 (46)
TED	8 (21)	6 (50)	7 (54)
Number of centers	19	8	7
Disease at transplant			
Plasma cell disorder/Multiple Myeloma	38 (100)	12 (100)	13 (100)
Recipient age at transplant			
18-29 years	1 (3)	0	1 (8)
30-39 years	2 (5)	0	0
40-49 years	9 (24)	1 (8)	4 (31)
50-59 years	24 (63)	7 (58)	4 (31)
60-69 years	2 (5)	4 (33)	4 (31)
Median (Range)	52 (22-64)	58 (48-67)	52 (19-70)
Recipient race			
White	23 (68)	8 (73)	4 (57)
Black or African American	10 (29)	3 (27)	2 (29)
Asian	1 (3)	0	1 (14)
Unknown	4 (N/A)	1 (N/A)	6 (N/A)
Recipient ethnicity			
Hispanic or Latino	6 (16)	1 (10)	0
Non Hispanic or non-Latino	30 (81)	9 (90)	7 (54)
Non-resident of the U.S.	1 (3)	0	6 (46)
Unknown	1 (N/A)	2 (N/A)	0 (N/A)
Recipient sex			
Male	20 (53)	7 (58)	8 (62)
Female	18 (47)	5 (42)	5 (38)
Karnofsky score			
10-80	13 (34)	3 (25)	5 (38)
90-100	25 (66)	7 (58)	8 (62)
Missing	0	2 (17)	0
HLA-A B DRB1 groups - low resolution			
4/6	23 (64)	7 (78)	8 (80)
5/6	10 (28)	1 (11)	1 (10)
6/6	3 (8)	1 (11)	1 (10)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Unknown	2 (N/A)	3 (N/A)	3 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	16 (73)	6 (86)	4 (50)
6/8	4 (18)	1 (14)	3 (38)
7/8	2 (9)	0	0
8/8	0	0	1 (13)
Unknown	16 (N/A)	5 (N/A)	5 (N/A)
HLA-DPB1 Match			
Double allele mismatch	2 (20)	1 (100)	2 (40)
Single allele mismatch	8 (80)	0	2 (40)
Full allele matched	0	0	1 (20)
Unknown	28 (N/A)	11 (N/A)	8 (N/A)
High resolution release score			
No	34 (89)	12 (100)	13 (100)
Yes	4 (11)	0	0
KIR typing available			
No	35 (92)	12 (100)	13 (100)
Yes	3 (8)	0	0
Graft type			
UCB	36 (95)	12 (100)	11 (85)
PBSC+UCB	2 (5)	0	2 (15)
Number of cord units			
1	29 (76)	0	8 (62)
2	9 (24)	0	5 (38)
Unknown	0 (N/A)	12 (N/A)	0 (N/A)
Conditioning regimen			
Myeloablative	12 (32)	4 (33)	4 (31)
RIC/Nonmyeloablative	24 (63)	7 (58)	9 (69)
TBD	2 (5)	1 (8)	0
Donor/Recipient CMV serostatus			
CB - recipient +	25 (66)	5 (42)	8 (62)
CB - recipient -	13 (34)	5 (42)	5 (38)
CB - recipient CMV unknown	0	2 (17)	0
GvHD Prophylaxis			
CD34 select +- other	1 (3)	0	0
FK506 + MMF +- others	11 (29)	3 (25)	4 (31)
FK506 + MTX +- others(not MMF)	1 (3)	0	2 (15)
FK506 +- others(not MMF,MTX)	1 (3)	0	0
FK506 alone	0	2 (17)	0
CSA + MMF +- others(not FK506)	17 (45)	6 (50)	4 (31)
CSA + MTX +- others(not MMF,FK506)	0	1 (8)	0

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
CSA +- others(not FK506,MMF,MTX)	0	0	1 (8)
CSA alone	0	0	2 (15)
Other GVHD Prophylaxis	6 (16)	0	0
Missing	1 (3)	0	0
Donor/Recipient sex match			
CB - recipient M	20 (53)	7 (58)	8 (62)
CB - recipient F	18 (47)	5 (42)	5 (38)
Year of transplant			
2006-2010	8 (21)	4 (33)	4 (31)
2011-2015	25 (66)	4 (33)	5 (38)
2016-2020	4 (11)	3 (25)	3 (23)
2021-2024	1 (3)	1 (8)	1 (8)
Follow-up among survivors, Months			
N Eval	4	2	4
Median (Range)	59 (48-72)	68 (64-72)	37 (15-50)

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, recipient only 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	265	41	22
Source of data			
CRF	92 (35)	8 (20)	10 (45)
TED	173 (65)	33 (80)	12 (55)
Number of centers	31	13	8
Disease at transplant			
Plasma cell disorder/Multiple Myeloma	265 (100)	41 (100)	22 (100)
Recipient age at transplant			
18-29 years	4 (2)	0	0
30-39 years	13 (5)	2 (5)	0
40-49 years	65 (25)	10 (24)	4 (18)
50-59 years	111 (42)	20 (49)	10 (45)
60-69 years	66 (25)	9 (22)	6 (27)
70+ years	6 (2)	0	2 (9)
Median (Range)	55 (26-75)	55 (35-69)	56 (40-72)
Recipient race			
White	217 (84)	34 (83)	17 (81)
Black or African American	26 (10)	5 (12)	3 (14)
Asian	12 (5)	2 (5)	1 (5)
Native Hawaiian or other Pacific Islander	1 (<1)	0	0
American Indian or Alaska Native	1 (<1)	0	0
More than one race	2 (1)	0	0
Unknown	6 (N/A)	0 (N/A)	1 (N/A)
Recipient ethnicity			
Hispanic or Latino	47 (18)	8 (20)	3 (14)
Non Hispanic or non-Latino	215 (81)	33 (80)	19 (86)
Non-resident of the U.S.	2 (1)	0	0
White	1 (N/A)	0 (N/A)	0 (N/A)
Recipient sex			
Male	153 (58)	32 (78)	15 (68)
Female	112 (42)	9 (22)	7 (32)
Karnofsky score			
10-80	105 (40)	15 (37)	6 (27)
90-100	155 (58)	26 (63)	15 (68)
Missing	5 (2)	0	1 (5)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
HLA-A B DRB1 groups - low resolution			
<=3/6	43 (18)	1 (3)	2 (14)
4/6	6 (3)	0	1 (7)
5/6	7 (3)	0	0
6/6	182 (76)	30 (97)	11 (79)
Unknown	27 (N/A)	10 (N/A)	8 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	47 (24)	1 (4)	1 (13)
6/8	1 (1)	0	0
7/8	4 (2)	0	0
8/8	145 (74)	26 (96)	7 (88)
Unknown	68 (N/A)	14 (N/A)	14 (N/A)
HLA-DPB1 Match			
Single allele mismatch	37 (27)	0	1 (20)
Full allele matched	98 (73)	10 (100)	4 (80)
Unknown	130 (N/A)	31 (N/A)	17 (N/A)
High resolution release score			
No	184 (69)	40 (98)	22 (100)
Yes	81 (31)	1 (2)	0
Graft type			
Marrow	22 (8)	1 (2)	2 (9)
PBSC	243 (92)	40 (98)	19 (86)
PBSC+UCB	0	0	1 (5)
Number of cord units			
Unknown	265 (N/A)	41 (N/A)	22 (N/A)
Conditioning regimen			
Myeloablative	93 (35)	20 (49)	12 (55)
RIC/Nonmyeloablative	172 (65)	21 (51)	10 (45)
Donor age at donation			
To Be Determined/NA	0	0	1 (5)
0-9 years	1 (<1)	0	0
10-17 years	3 (1)	0	0
18-29 years	30 (11)	1 (2)	1 (5)
30-39 years	25 (9)	4 (10)	4 (18)
40-49 years	63 (24)	10 (24)	1 (5)
50+ years	143 (54)	26 (63)	15 (68)
Median (Range)	51 (0-76)	54 (27-69)	58 (29-74)
Donor/Recipient CMV serostatus			
+/+	104 (39)	18 (44)	5 (23)
+/-	27 (10)	5 (12)	3 (14)
-/+	56 (21)	9 (22)	5 (23)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
-/-	76 (29)	9 (22)	8 (36)
CB - recipient +	0	0	1 (5)
Missing	2 (1)	0	0
GvHD Prophylaxis			
No GvHD Prophylaxis	27 (10)	4 (10)	6 (27)
TDEPLETION +- other	2 (1)	0	0
CD34 select alone	0	1 (2)	0
Cyclophosphamide alone	2 (1)	0	0
Cyclophosphamide +- others	58 (22)	4 (10)	4 (18)
FK506 + MMF +- others	26 (10)	2 (5)	0
FK506 + MTX +- others(not MMF)	107 (40)	24 (59)	10 (45)
FK506 +- others(not MMF,MTX)	10 (4)	5 (12)	1 (5)
FK506 alone	2 (1)	1 (2)	0
CSA + MMF +- others(not FK506)	6 (2)	0	0
CSA + MTX +- others(not MMF,FK506)	5 (2)	0	0
CSA +- others(not FK506,MMF,MTX)	2 (1)	0	0
CSA alone	1 (<1)	0	0
Other GVHD Prophylaxis	15 (6)	0	1 (5)
Missing	2 (1)	0	0
Donor/Recipient sex match			
Male-Male	96 (36)	20 (49)	11 (50)
Male-Female	48 (18)	4 (10)	3 (14)
Female-Male	57 (22)	12 (29)	3 (14)
Female-Female	64 (24)	5 (12)	4 (18)
CB - recipient M	0	0	1 (5)
Year of transplant			
2006-2010	27 (10)	7 (17)	5 (23)
2011-2015	117 (44)	20 (49)	8 (36)
2016-2020	105 (40)	11 (27)	5 (23)
2021-2024	16 (6)	3 (7)	4 (18)
Follow-up among survivors, Months			
N Eval	123	16	12
Median (Range)	49 (0-146)	36 (4-96)	37 (6-122)

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TO: Plasma Cell Disorders Working Committee Members

FROM: Marcelo Pasquini, MD and Othman Akhtar, MD; Scientific Directors for the Plasma Cell Disorders Working Committee

RE: 2024-2025 Studies in Progress Summary

MM20-02b Risk factors for and characteristics of second primary malignancies following autologous hematopoietic cell transplant for multiple myeloma (B Ragon/M Shah/S Usmani). This study looks to identify patient, disease, and therapy-related characteristics that predict an increased risk of developing SPM and SHM.

Status: This study is in Data File Preparation phase. The goal is to complete data analysis by June 2025.

MM22-01 Outcomes of autologous hematopoietic cell transplantation for light chain deposition disease (H Hashmi/ B Dhakal). This study looks to determine overall survival (OS), disease response [hematological, clinical], progression-free survival (PFS), transplant-related mortality (TRM), cumulative incidence of relapse after autologous HCT for Light Chain Deposition Disease.

Status: The preliminary protocol has been received, with the goal of proceeding to data analysis by June 2025.

CT23-02 Prolonged cytopenia following anti-B cell maturation antigen chimeric antigen receptor T-cell therapy for multiple myeloma (J Logue/D Hansen/ M Janakiram/ G Kaur). The aims of this study are:

1. To quantify the incidence of prolonged cytopenia defined as ANC <500/mm3 and Platelets <20 $x10^9$/L at D+30 and D+100 after BCMA CAR T-cell therapy.
2. To conduct a multivariate analysis to identify patient baseline characteristics associated with prolonged cytopenia (D+30 and D+100) defined as ANC <500/mm3 and Platelets <20 $x10^9$/L from BCMA CAR T-cell therapy.
3. To validate the CAR-HEMATOTOX score in RRMM in a large, multicenter group of patients.

Status: This study is in Manuscript Preparation phase. The goal is to submit for publication by March 2025.

MM24-01 Safety and efficacy of ciltacabtagene in patients with relapsed or refractory multiple myeloma (D Hansen/ K Patel/ H Hashmi/ S Usmani/ R Narra/ B Dhakal/ A Afrough/ L Anderson/ A Bidikian/ L Gowda/ D Dima/ N Ahmed/ S Sidana/ S Mirza/ T Nishihori/ H Mian/ M Mohan/ M Faisal). The primary objectives are to describe the demographic and clinical characteristics of patients receiving cilta-cel in the real-world setting and to evaluate safety and efficacy outcomes of cilta-cel CAR T-cell therapy as intended standard of care therapy for relapsed/refractory multiple myeloma.

Status: This study is in Analysis phase. The goal is to submit for presentation at EHA in March 2025 and Publication by June 2025.

MM24-02 Real-world comparison of anti-BCMA CAR T-cell therapies in relapsed or refractory multiple myeloma (M Mohan/ C Schinke/ A Bidikian/ L Gowda/ C Freeman/ D Hansen/ S Gupta/ A Afrough/ L Anderson/ M Janakiram/ S Goldsmith/ S Ahmed/ K Patel/ M Krem/ N Ahmed). The objective of this study is to compare efficacy and safety outcomes of ide-cel and cilta-cel in relapsed/refractory multiple myeloma.

Status: This study is in Analysis stage, with the goal of submitting for presentation at EHA in March 2025 and Publication by June 2025.

Title: Predictors of Early Relapse and Durable Remissions in patients with multiple myeloma treated with BCMA-Targeted CAR T-Cell Therapy

Research question: What are the key predictors of early relapse (defined as occurring within 6 months) versus late relapse (defined as occurring more than 2 years post-treatment) in patients with relapsed/refractory multiple myeloma treated with BCMA-targeted CAR T-cell therapy, specifically ide-cel and cilta-cel?

Early Relapse:
Early relapse is defined as the absence of response to CAR T-cell therapy at Day 100, progressive disease **within 3 and 6 months of** CAR T-cell therapy, or the need for subsequent treatment within 3 and 6 months of CAR T-cell therapy (excluding radiotherapy). Predictive factors for early relapse will be evaluated using baseline patient characteristics, regardless of the line of therapy, with treatment-related mortality (TRM) excluded from this analysis.

Long-Term Responders:

Long-term responders are patients who achieve sustained clinical remission or disease control: ABECMA- 20 months and CARVKTY – 48 months following CAR T-cell therapy without additional systemic treatments (excluding maintenance therapy). This includes patients who maintain durable minimal residual disease (MRD) negativity or stable complete or partial responses over this time frame

Key words: BCMA-targeted CAR T-cell therapy, relapsed/refractory multiple myeloma, ide-cel, cilta-cel, progression-free survival (PFS).

Research hypothesis: Specific patient-related factors, disease-related factors, product-related factors, treatment-related factors, and the initial response after treatment are significant predictors of response durability in patients with relapsed/refractory multiple myeloma treated with BCMA-targeted CAR T-cell therapy.

Specific objectives/outcomes to be investigated (include Primary, Secondary, etc). Suggested word limit of 200 words

Primary: Identify the key clinical factors associated with longer progression-free survival (PFS) in patients with relapsed/refractory multiple myeloma treated with BCMA-targeted CAR T-cell therapy, including:

- Initial response to CAR T cell therapy.
- Patient-related factors (e.g., age, ECOG performance status, comorbidities, and prior therapies).
- Disease-related factors (e.g., cytogenetic risk, disease burden, and presence of extramedullary disease).
- Product-related factors (e.g., CAR T-cell type and dose).
- Treatment-related factors (e.g., lymphodepletion regimen, bridging therapy, and toxicity grades)

Secondary:

- OS

- Treatment related mortality

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

The findings of this CIBMTR study will help enhance understanding of the clinical, biological, and treatment-related factors that predict response durability and relapse timing in relapsed/refractory multiple myeloma patients treated with BCMA-targeted CAR T-cell therapy, including ide-cel and cilta-cel. It will lead to informed clinical decision-making and personalized care through the integration of patient-specific characteristics, disease attributes, and treatment-related factors for patients with RRMM. Furthermore, it will help advance the development of more effective CAR T-cell therapies and post-treatment strategies by identifying key markers influencing outcomes, including those associated with sustained deep responses and long-term remission durability.

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.

Relapsed, refractory multiple myeloma (RRMM) remains a challenging entity to treat even with the advent of chimeric antigen receptor T-cell therapy (CAR T). Some A percentage of patients can achieve deep and durable responses with both approved B-cell maturation antigen (BCMA)-directed CAR T therapies (Ide- cel and cilta-cel) , and while a portion of patients experience early relapse. There is a significant gap in data regarding long-term outcomes and the predictors of early versus late relapse in patients with relapsed/refractory multiple myeloma treated with BCMA-targeted CAR T cells. This gap exists primarily due to the more recent development and approval of BCMA-directed CAR T cell therapies.[1, 2]

Clinical trials with median follow-up of at least one year (range: 13–48 months) have started to provide insights into the long-term outcomes of these patients. [3-11] However, the median progression-free survival (PFS) reported in these trials has varied significantly, ranging from 5.2 months to not reached, indicating significant heterogeneity in the durability of patient responses. Notably, a subset of patients has demonstrated prolonged remissions lasting several years without the need for consolidative or maintenance therapies. [3-7] Key factors associated with long-term remission include lower disease burden, better performance status, absence of high-risk cytogenetics, sustained MRD negativity, lower ferritin levels, and reduced disease refractoriness. Additionally, some patients develop deep minimal residual disease (MRD)-negative complete remissions (CRs) but still experience relapse later. This highlights the need for a deeper understanding of the factors contributing to these extended remissions.

To date, the predictors of durable remissions remain insufficiently characterized in large patient cohorts and real-world settings. In clinical practice, identifying these factors is essential to support clinicians in making more informed decisions about the benefit-risk ratio, long-term prognosis, and subsequent therapeutic strategies. Furthermore, given the high cost of CAR T-cell therapies, research that focuses on identifying patients most likely to experience durable responses is crucial for optimizing resource allocation and improving patient selection.

PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.

Inclusion criteria:

- Patients with relapsed/refractory multiple myeloma who received BCMA-targeted CAR T-cell therapy (e.g., ide-cel or ciltacel).
- Available follow-up data for at least one-year post-CAR T-cell therapy.

Exclusion criteria:

- Patients who have received prior CAR T-cell therapy targeting BCMA.

DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Data collection forms available at: http://www.cibmtr.org/DataManagement/DataCollectionForms/Pages/index.aspx Outline any supplementary data required. Additional data collection is extremely difficult and will make your proposal less feasible.

Patient-Related Variables:

- Age at the time of CAR T-cell therapy.
- Gender.
- ECOG performance status prior to CAR T-cell infusion.
- Comorbidities (e.g., cardiovascular disease, diabetes).
- Prior therapies (number and types, including autologous stem cell transplant, immunomodulatory drugs, proteasome inhibitors).
- Time since diagnosis of multiple myeloma.
- MRD (Minimal Residual Disease) status post-treatment.

Disease-Related Variables:

- Cytogenetic risk profile (e.g., del(17p), t(4;14)).
- Plasma cell burden (percentage of bone marrow involvement), LDH, B2M, stage
- Presence of extramedullary disease.
- Disease status pre-CAR T-cell therapy (refractory or relapsed).
- Serum free light chains and M-protein levels

Infusion-Related Variables:

- Type of CAR T-cell product (ide-cel, ciltacel).
- CAR T-cell dose administered.
- Lymphodepletion regimen prior to CAR T-cell infusion.
- T-cell expansion and persistence (surrogate: low absolute lymphocyte count [ALC] post-infusion).

- Bridging therapy received prior to CAR T-cell infusion.
- Toxicity grades (e.g., CRS, ICANS severity).
- Time to neutrophil and platelet recovery post-infusion.

Outcome Variables:

- Response to therapy (CR, PR, stable disease, progressive disease).
- Time to relapse (early vs. late relapse, with late relapse defined as more than 1 year post-therapy).
- Progression-free survival (PFS).
- Overall survival (OS).
- MRD disease negativity s

Supplementary Data:

No supplementary data collection is required at this time. All necessary variables can be derived from the existing CIBMTR data collection forms.

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PROP 2409-20/2410-97/2410-140: Predictors of Early Relapse and Durable Remissions in patients with multiple myeloma treated with BCMA-Targeted CAR T-Cell Therapy (A Ali/M Janakiram/ G Kaur)

Table: Characteristics of patients with multiple myeloma treated with BCMA-Targeted CAR T-Cell Therapy and reported to the CIBMTR

Characteristic	Idecabtagene vicleucel	Ciltacabtagene autoleucel	Total
No. of patients	1464	1176	2640
No. of centers	81	68	97
Patient Related			
Age, by decades - no. (%)			
Median (min-max)	67 (29-90)	65 (33-84)	66 (29-90)
20-29	1 (0)	0 (0)	1 (0)
30-39	7 (0)	12 (1)	19 (1)
40-49	69 (5)	80 (7)	149 (6)
50-59	287 (20)	268 (23)	555 (21)
60-69	580 (40)	502 (43)	1082 (41)
70+	520 (36)	314 (27)	834 (32)
Recipient Sex - no. (%)			
Male	855 (58)	657 (56)	1512 (57)
Female	609 (42)	519 (44)	1128 (43)
Recipient race - no. (%)			
White	1131 (77)	903 (77)	2034 (77)
African-American	245 (17)	164 (14)	409 (15)
Asian	31 (2)	39 (3)	70 (3)
Pacific Islander	3 (0)	3 (0)	6 (0)
Native American	7 (0)	1 (0)	8 (0)
More than one race	4 (0)	5 (0)	9 (0)
Not reported	43 (3)	61 (5)	104 (4)
Ethnicity - no. (%)			
Hispanic or Latino	106 (7)	105 (9)	211 (8)
Non-Hispanic or non-Latino	1329 (91)	1028 (87)	2357 (89)
N/A - Not a resident of the U.S.	0 (0)	9 (1)	9 (0)
Not reported	29 (2)	34 (3)	63 (2)
Karnofsky performance score prior to CT - no. (%)			
90-100	472 (32)	513 (44)	985 (37)
80	565 (39)	373 (32)	938 (36)
< 80	307 (21)	166 (14)	473 (18)
Not reported	120 (8)	124 (11)	244 (9)
HCT-CI Score - no. (%)			
0	323 (22)	341 (29)	664 (25)

Characteristic	Idecabtagene vicleucel	Ciltacabtagene autoleucel	Total
1	243 (17)	227 (19)	470 (18)
2	225 (15)	180 (15)	405 (15)
3	263 (18)	175 (15)	438 (17)
4	171 (12)	117 (10)	288 (11)
5+	233 (16)	128 (11)	361 (14)
Not reported	6 (0)	8 (1)	14 (1)
Disease-related			
Sub-disease - no. (%)			
Multiple myeloma, NOS	1073 (73)	893 (76)	1966 (74)
Multiple myeloma - light chain only	359 (25)	265 (23)	624 (24)
Multiple myeloma - non-secretory	32 (2)	18 (2)	50 (2)
Disease status prior to CT - no. (%)			
Stringent complete remission (sCR)	9 (1)	12 (1)	21 (1)
Complete remission (CR)	16 (1)	25 (2)	41 (2)
Very good partial remission (VGPR)	122 (8)	122 (10)	244 (9)
Partial response (PR) / Not Complete Remission	187 (13)	145 (12)	332 (13)
Stable disease (SD)	233 (16)	214 (18)	447 (17)
Progressive disease (PD)	878 (60)	625 (53)	1503 (57)
Relapse from CR (Rel) (untreated)	16 (1)	30 (3)	46 (2)
Not reported	3 (0)	3 (0)	6 (0)
Treatment-related			
No. of lines of prior therapies (including HCT and CT) - no. (%)			
1	6 (0)	5 (0)	11 (0)
2	38 (3)	17 (1)	55 (2)
3	50 (3)	54 (5)	104 (4)
4+ Lines	935 (64)	988 (84)	1923 (73)
Not reported	435 (30)	112 (10)	547 (21)
Year of CT - no. (%)			
2021	284 (19)	0 (0)	284 (11)
2022	529 (36)	203 (17)	732 (28)
2023	564 (39)	689 (59)	1253 (47)
2024	87 (6)	284 (24)	371 (14)
Follow up interval for all patients, months - no. (%)			
0-12 months	645 (44)	746 (63)	1391 (53)
>12-24 months	598 (41)	401 (34)	999 (38)
>24 months	221 (15)	29 (2)	250 (9)
Follow-up interval of survivors, months - no. (%)			
0-12 months	333 (23)	615 (52)	948 (36)
>12-24 months	506 (35)	376 (32)	882 (33)
>24 months	197 (13)	27 (2)	224 (8)

Characteristic	Idecabtagene vicleucel	Ciltacabtagene autoleucel	Total
Not applicable - Dead	428 (29)	158 (13)	586 (22)
Follow-up of survivors, months - median (range)	13 (1-37)	7 (1-28)	12 (1-37)

**Data source: CT Extract November 2024*

Study Title: Comparative effectiveness between 2nd autoHCT and CAR T overall and in key subgroups in relapsed / refractory multiple myeloma.

Key Words: Salvage Autologous Stem Cell Transplant (ASCT), second autologous stem cell transplant, CAR-T, Ide-cel, ABECMA, Cilta-cel, CARVYKTI, Real-world data, autoHCT, autoSCT.

Research Question:

Are B-cell maturation antigen (BCMA) Chimeric antigen receptor (CAR) T-cell therapies superior to second high dose therapy (HDT)/autologous stem cell transplantation (ASCT) in relapsed refractory multiple myeloma (RRMM) overall and in key subgroups?

Research Hypothesis: We hypothesize that BCMA-directed CAR T cell therapy will be associated with longer progression free survival overall and in key subgroups with RRMM.

SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED:

Primary Outcome:

Progression free survival (PFS)

Secondary Outcomes:

Overall Survival (OS) / 1-year OS

1-year PFS

Complete Response (CR) rate

Duration of response (mDOR)

30-day mortality

Secondary primary malignancy

SCIENTIFIC IMPACT:

I. Prior studies of second autoHCT compared to standard of care (SOC) demonstrated conflicting efficacy results. With chimeric antigen receptor T cell (CAR T) therapy becoming SOC in earlier lines of therapy, it is important to have a large population-based study to report on the efficacy and safety of either therapy. It will also be important to study these therapies in key subgroups.

II. Racial and ethnic minorities are historically underrepresented in clinical trials, limiting understanding of safety and efficacy profiles of new treatment interventions in this unique population. This study will bridge this critical knowledge gap using real world data from the CIBMTR database.

III. Multiple myeloma (MM) with t(11;14) have unique clinicopathologic characteristics which has been noted in countless prior studies. It will be important to determine which cellular therapy is more effective in this population.

SCIENTIFIC JUSTIFICATION:

Although prior prospective studies of second autoHCT versus standard of care (SOC) have been conducted, they were largely in the older era of myeloma treatment with weaker SOC options compared to the CAR T cell therapy products which have moved into earlier lines of

therapy. The most recent was the GMMG ReLApsE trial (conducted during 2010-2016) comparing continuous lenalidomide and dexamethasone (Len-Dex) to Len-Dex re-induction followed by salvage autoHCT and lenalidomide maintenance. This study was an ITT analysis showing a possible benefit after multivariate, landmark analysis at time of HCT; although, the final analysis demonstrated a non-significant trend towards OS benefit by 10 months favoring autoHCT. It is difficult to extrapolate these results, and those of earlier similar studies, to our modern myeloma patient for a few reasons: 1) the SOC now includes cellular therapies in earlier lines of therapy, 2) there are much better triplet/quadruplet salvage therapy options, 3) this was an IIT analysis that randomized at baseline so it had a high drop out rate due to progression (likely related to doublet salvage [Len-Dex]). The earlier study of salvage autoHCT versus SOC (NCRI Myeloma X Relapse [Intensive trial]) demonstrated a PFS benefit and had key differences from the GMMR ReLApse trial: 1) triplet salvage regimen, 2) randomization after stem cell collection to reduce drop out from progression. A recent multicenter cohort study comparing CAR T to second autoHCT demonstrated that the 1-year PFS favored CAR T after propensity score matching: 1-year PFS favored CAR T (68% versus 44%, P=0.048) and 1-year OS was 81% versus 68% (P=0.059). However, they had low sample size (CAR T, N=59). Given the challenges with studying second autoHCT versus SOC via a prospective study (for the previously mentioned reasons) and that the SOC options in myeloma are rapidly expanding and improving, it is essential to study this on the population-level with a large database.

Just as important as it is to understand the efficacy of these cellular therapies overall is the need to understand key subgroups that may benefit from specific therapies. Despite many governmental and industry-sponsored efforts to improve clinical trial participation among racial and ethnic minorities, this still remains low despite the fact that multiple myeloma disproportionately affects non-Hispanic Black (NHB) patients. Given that this effort to racially diversify clinical trial participants still faces significant setbacks, real world databases, like the CIBMTR database, become a key source of information to bridge the gap in the understanding of safety and efficacy of newer therapies like CAR T cell therapy.

Other key subgroups are the MM with t(11;14). Many studies have demonstrated that t(11;14) is a very different from other MM in its response to certain therapies. Additionally, prior studies have demonstrated that it can have improved outcomes with first-line autoHCT. As such, it will be important to understand the efficacy of second autoHCT versus CAR T to better sequence these powerful therapies.

PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.

Inclusion Criteria:

Inclusion:

-Patients with MM who have history of one prior autoHCT (or one prior tandem autoHCT) and now have received idecabtagene vicleucel (ide-cel) or ciltacabtagene autoleucel (cilta-cel) or have received a second salvage autoHCT in the 2nd-line or later setting.

-Patients receiving the cellular therapy of interest in 2010 or afterwards.

-Patients with at least 1 year of follow-up data from the date of cellular therapy infusion.

Exclusion Criteria:

Exclude:

-Patients who did not have first-line autoHCT (“delayed autoHCT”).

-Patients who received allogeneic SCT before cellular therapy of interest.

-Patients with amyloidosis.

Exposure:

-second autoHCT versus cilta-cel versus ide-cel.

Stratification:

- Stratification by key subgroups: race/ethnicity and t(11;14).

Variables of interest:

- For the overall analysis covariates: HRCA (del 1p, gain/amp1q, t[4;14], t[14;16], t[14;20], del17p) – single/double/triple HRCAs, t(11;14), karnofsky score, RISS, ISS, age, sex, race/ethnicity, HCTCI, year of cellular therapy.

Data Requirements

Data element	CIBMTR Forms source							
	2400	4000	2402	2016	2450	4100	2116	3500
Baseline: Demographic characteristics at the salvage auto-HCT or BCMA-directed CAR-T therapy								
Age at the time of cells infusion	X	X						
Sex	X	X						
Race	X	X						
Ethnicity	X	X						
Karnofsky performance status	X	X						
HCT-CI Score (as calculated from standard comorbidities)	X	X						
Conditioning regimen/lymphodepletion prior to 2ndHCT/CAR-T	X							
CAR-T product (for CAR-t patients)		X						
Year of salvage auto-HCT or BCMA-directed CAR-T therapy	X	X						
Baseline: Primary diagnosis at the salvage auto-HCT or BCMA-directed CAR-T therapy								
History of prior HCT or other cellular therapy *(for incl/excl criteria assessment only)*	X	X		X				
Myeloma subtype (Myeloma vs myeloma light chain only vs non secretory myeloma)			X	X				
Heavy and light chain type			X	X				
ISS stage			X					
R-ISS stage			X					

Time from Diagnosis to 2ndHCT/CAR-T infusion (mon)	**X**		**X**					
Time from 1st Auto HCT to 2ndHCT/CAR-T infusion (mon)	**X**	**X**						
Time from 1st Auto HCT to 1st post-HCT relapse/PD	**X**	**X**		**X**	**X**		**X**	
Disease response prior to salvage auto-HCT or BCMA-directed CAR-T therapy (sCR, CR, VGPR, PR, SD, PD)			**X**	**X**				
Baseline: Cytogenetic								
t(11;14)			**X**	**X**				
t(14;14)			**X**	**X**				
t(14;16)			**X**	**X**				
t(14;20)			**X**	**X**				
1q gain/amplification			**X**	**X**				
Monosomy 17 / del 17p			**X**	**X**				
Baseline: Planned Maintenance/Consolidation after the salvage auto-HCT or BCMA-directed CAR-T therapy (exclude new line of therapy given for relapsed/progressive/persisting disease)								
Maintenance therapy (Yes/No)					**X**		**X**	
Time from salvage auto-HCT or BCMA-directed CAR-T infusion to maintenance start					**X**		**X**	
Maintenance regimen agents					**X**		**X**	
Outcomes after the salvage auto-HCT or BCMA-directed CAR-T therapy								
Survival status at the time of most recent Fup					**X**	**X**		
Time from salvage auto-HCT or BCMA-directed CAR-T infusion to death or most recent follow up (mon)					**X**	**X**		
Complete remission(CR) achieved as a result of salvage auto-HCT or BCMA-directed CAR-T (Yes/No)					**X**		**X**	
Time from salvage auto-HCT or BCMA-directed CAR-T infusion to CR (if applicable) (mon)					**X**		**X**	
1st Relapse/PD after 2nd HCT/CAR-T: Yes/No					**X**		**X**	
Time from salvage auto-HCT or BCMA-directed CAR-T					**X**		**X**	

infusion to relapse/PD or most recent disease assessment (mon)								
New malignancy post salvage auto-HCT or BCMA-directed CAR-T infusion					**X**	**X**		
Time from salvage auto-HCT or BCMA-directed CAR-T infusion to new malignancy					**X**	**X**		**X**
Type of new malignancy (myeloid, non-myeloud, BCC/SCC of skin)					**X**	**X**		**X**

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PROP 2409-30; 2410-69; 2410-172; 2410-213: Comparative effectiveness between 2nd Auto-HCT and CAR T overall and in key subgroups in relapsed / refractory multiple myeloma (L Liu/ M Janakiram/ A Afrough/ L Anderson Jr/ Y Shestovska/ H Fung/ E Biltibo/ K Adetola)

Table: Characteristics of adult patients who underwent 2nd autologous HCT or 1st CAR-T infusion for multiple myeloma between 2021-2024, and reported to the CIBMTR

Characteristic	Second autoHCT	Idecabtagene vicleucel	Ciltacabtagene autoleucel	Total
No. of patients	1306	1182	957	3445
No. of centers	184	77	66	193
Patient-related				
Patient age - median (min-max)	63.3 (28.5-81.0)	67.1 (35.0-90.3)	65.1 (33.0-84.3)	65.2 (28.5-90.3)
Age, by decades - no. (%)				
20-29	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.0)
30-39	10 (0.8)	7 (0.6)	10 (1.0)	27 (0.8)
40-49	92 (7.0)	53 (4.5)	65 (6.8)	210 (6.1)
50-59	352 (27.0)	212 (17.9)	210 (21.9)	774 (22.5)
60-69	612 (46.9)	472 (39.9)	410 (42.8)	1494 (43.4)
70+	239 (18.3)	438 (37.1)	262 (27.4)	939 (27.3)
Sex - no. (%)				
Male	759 (58.1)	685 (58.0)	533 (55.7)	1977 (57.4)
Female	547 (41.9)	497 (42.0)	424 (44.3)	1468 (42.6)
Race - no. (%)				
White	825 (63.2)	914 (77.3)	736 (76.9)	2475 (71.8)
Black or African American	232 (17.8)	194 (16.4)	133 (13.9)	559 (16.2)
Asian	30 (2.3)	26 (2.2)	34 (3.6)	90 (2.6)
Native Hawaiian or other Pacific Islander	3 (0.2)	2 (0.2)	3 (0.3)	8 (0.2)
American Indian or Alaska Native	9 (0.7)	5 (0.4)	1 (0.1)	15 (0.4)
Other	0 (0.0)	2 (0.2)	2 (0.2)	4 (0.1)
More than one race	13 (1.0)	26 (2.2)	31 (3.2)	70 (2.0)
Not reported	194 (14.9)	13 (1.1)	17 (1.8)	224 (6.5)
Ethnicity - no. (%)				
Hispanic or Latino	132 (10.1)	88 (7.4)	84 (8.8)	304 (8.8)
Not Hispanic or Latino	895 (68.5)	1066 (90.2)	836 (87.4)	2797 (81.2)
Non-resident of the U.S.	258 (19.8)	0 (0.0)	8 (0.8)	266 (7.7)
Not reported	21 (1.6)	28 (2.4)	29 (3.0)	78 (2.3)
Research Track - no. (%)				
HCT - TED	1192 (91.3)	0 (0.0)	0 (0.0)	1192 (34.6)
HCT - CRF	114 (8.7)	0 (0.0)	0 (0.0)	114 (3.3)
CT	0 (0.0)	1182 (100)	957 (100)	2139 (62.1)

Characteristic	Second autoHCT	Idecabtagene vicleucel	Ciltacabtagene autoleucel	Total
HCT - Comorbidity Index - no. (%)				
0	0 (0.0)	255 (21.6)	275 (28.7)	530 (15.4)
1	0 (0.0)	193 (16.3)	190 (19.9)	383 (11.1)
2	0 (0.0)	179 (15.1)	150 (15.7)	329 (9.6)
3	0 (0.0)	221 (18.7)	134 (14.0)	355 (10.3)
4	0 (0.0)	135 (11.4)	93 (9.7)	228 (6.6)
5+	0 (0.0)	193 (16.3)	108 (11.3)	301 (8.7)
Not reported	1306 (100)	6 (0.5)	7 (0.7)	1319 (38.3)
Karnofsky score prior to HCT - no. (%)				
90-100	623 (47.7)	371 (31.4)	436 (45.6)	1430 (41.5)
80	408 (31.2)	461 (39.0)	301 (31.5)	1170 (34.0)
< 80	239 (18.3)	246 (20.8)	118 (12.3)	603 (17.5)
Not reported	36 (2.8)	104 (8.8)	102 (10.7)	242 (7.0)
Disease-related				
MM classification - no. (%)				
Multiple myeloma, NOS	1043 (79.9)	865 (73.2)	736 (76.9)	2644 (76.7)
Multiple myeloma - light chain only	249 (19.1)	294 (24.9)	211 (22.0)	754 (21.9)
Multiple myeloma - non-secretory	14 (1.1)	23 (1.9)	10 (1.0)	47 (1.4)
Disease status prior to transplant - no. (%)				
sCR/CR	172 (13.2)	22 (1.9)	31 (3.2)	225 (6.5)
VGPR	485 (37.1)	99 (8.4)	101 (10.6)	685 (19.9)
PR	332 (25.4)	159 (13.5)	125 (13.1)	616 (17.9)
SD	98 (7.5)	188 (15.9)	166 (17.3)	452 (13.1)
PD/Relapse	205 (15.7)	712 (60.2)	533 (55.7)	1450 (42.1)
Not reported	14 (1.1)	2 (0.2)	1 (0.1)	17 (0.5)
Treatment-related				
Prior HCTs - no. (%)				
No				
CAR-T only	0 (0.0)	260 (22.0)	215 (22.5)	475 (13.8)
Yes				
Prior allo-HCT	0 (0.0)	8 (0.7)	4 (0.4)	12 (0.3)
Prior auto-HCT	1306 (100)	899 (76.1)	724 (75.7)	2929 (85.0)
Prior auto and allo-HCT	0 (0.0)	15 (1.3)	14 (1.5)	29 (0.8)
Subsequent CAR-T - no. (%)				
No	1232 (94.3)	1072 (90.7)	744 (77.7)	3048 (88.5)
Yes	74 (5.7)	16 (1.4)	4 (0.4)	94 (2.7)
Not reported	0 (0.0)	94 (8.0)	209 (21.8)	303 (8.8)
Year of current HCT/CAR-T - no. (%)				
2021	393 (30.1)	214 (18.1)	0 (0.0)	607 (17.6)

Characteristic	Second autoHCT	Idecabtagene vicleucel	Ciltacabtagene autoleucel	Total
2022	398 (30.5)	420 (35.5)	154 (16.1)	972 (28.2)
2023	328 (25.1)	471 (39.8)	564 (58.9)	1363 (39.6)
2024	187 (14.3)	77 (6.5)	239 (25.0)	503 (14.6)
Follow-up of survivors - median (range)	12.9 (0.0-43.3)	12.7 (1.0-37.4)	6.7 (1.7-25.7)	12.3 (0.0-43.3)

**Data source: HCT Essentials November 2024, CT Extract November 2024*

Field	Response
Proposal Number	2410-35-ZANWAR
Proposal Title	Impact of Autologous Stem Cell Transplantation on Outcomes with High-risk Multiple Myeloma
Key Words	consolidation, melphalan, high-risk, deletion 17p, Overall Survival, MRD
Principal Investigator #1: - First and last name, degree(s)	Saurabh Zanwar, MBBS, MD
Principal Investigator #1: - Email address	zanwar.saurabh@mayo.edu
Principal Investigator #1: - Institution name	Mayo Clinic, Rochester, MN
Principal Investigator #1: - Academic rank	Assistant Professor
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):	Shaji Kumar, MD
Principal Investigator #2 (If applicable): - Email address:)	kumar.shaji@mayo.edu
Principal Investigator #2 (If applicable): - Institution name:	Mayo Clinic
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:	-
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:	Plasma Cell Disorders
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:	To investigate the impact of autologous stem cell transplantation on the survival outcomes for patients with multiple myeloma harboring two or more high-risk cytogenetic abnormalities.
RESEARCH HYPOTHESIS:	We hypothesize that utilization of autologous stem cell transplantation (ASCT) as a consolidation strategy after induction therapy improves the outcomes for patients with multiple myeloma (MM) with 2 or more high-risk cytogenetic abnormalities and confers similar survival outcomes compared to patients with 1 high-risk cytogenetic abnormality.
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	Primary objective: To assess the progression-free survival (OS) from autologous stem cell transplant (ASCT) for patients with multiple myeloma harboring 1 and ≥2 high-risk cytogenetic abnormalities (HRCAs) as defined by the presence of 17p deletion, 1q gain/amplification, 1p deletion, t(4;14), t(14;16), t(14;20) by fluorescence in-situ hybridization at diagnosis of MM. Secondary objectives: 1. Compare the overall survival (OS) for patients with 1 and ≥2 HRCA from the time of ASCT. 2. Compare the rates of minimal residual disease negativity [MRD, measured with either next generation flow cytometry or next generation sequence with at least at a sensitivity of 1x10-5] post ASCT for patients with 1 and ≥2 HRCAs versus no HRCAs. 3. Compare the PFS, MRD negativity rates and OS in the various subgroups of HRCAs from the time of ASCT.
SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.	Patients with 'double hit' multiple myeloma [≥2 high-risk cytogenetic abnormalities (HRCA)] have significantly inferior outcomes even the era of novel therapies.(1) The utility of ASCT in this cohort of patients remains to be well-established. Our study will provide information on the impact of ASCT as a consolidation strategy for patients with 1 versus ≥2 HRCAs. Additionally, as the prognostic impact of various cytogenetic abnormalities continues to evolve, our study will establish the utility of ASCT in the individual high-risk cytogenetic subgroups to further assist in optimal patient selection for ASCT. These data will enable physicians to make a nuanced and personalized decision regarding upfront versus delayed autologous stem cell transplant based on the cytogenetic profile.

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.	Randomized controlled trial data from the DETERMINATIION(2) and IFM-2009 study(3), demonstrate an improvement in the progression-free survival but no difference in the overall survival for patients undergoing an early versus deferred ASCT. As a result, upfront ASCT or deferring ASCT are both considered reasonable strategies for patients with MM. However, the majority of patients enrolled in these clinical trials harbored standard-risk cytogenetics.(2, 3) These studies were not powered to assess the impact of ASCT in HRCA subgroups and do not present data on the differential outcomes for patients with 1 versus ≥2 HRCAs versus no HRCAs. Recently, four single -arm phase 2 clinical trials enrolling high-risk patients were reported, and most of them incorporated ASCT as part of the treatment regimen, demonstrating improved outcomes compared to historical data.(4-7) However, the lack of randomization and small sample sizes limit the evaluation of the impact of ASCT in patients with 1 versus 2 or more HRCA. The impact of ASCT in improving the MRD negativity rates and survival outcomes of patients with 2 or more HRCAs is becoming an especially relevant question, with long term results from the MASTER trial demonstrating treatment de-escalation as a feasible option in patients with no or 1 HRCA achieving a sustained MRD negativity (but not in ≥2 HRCAs).(8) It is likely that ASCT continues to plays an important role in achieving a deep and durable response in these ultra-high risk patients and this merits further study. We hypothesize that utilizing an autologous stem cell transplant abrogates the inferior outcomes associated with patient's having 2 or more HRCA and imparts PFS outcomes similar to those with 1 HRCA. Additionally, limited data exists on the differential outcomes with ASCT in individual high-risk cytogenetic abnormalities, and the different combinations of high-risk features that can exist in patients with MM. Findings from this study will enable us to answer questions regarding the utility of autologous stem cell transplant in patients with ultra high-risk disease as well as the differential impact of cytogenetic abnormalities on outcomes post ASCT.

Field	Response
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	Inclusion criteria: 1. Patients with active multiple myeloma diagnosed between 01/01/2013 and 06/15/2023 and undergoing ASCT within 12 months of initiation of induction therapy. 2. Presence of fluorescence in-situ hybridization data diagnosis for classifying high-risk cytogenetic abnormalities [deletion 17p, t(4;14), t(14;16), t(14;20), 1q gain/amplification classified as high-risk]. 3. Melphalan-based conditioning regimens utilized for ASCT, including tandem autologous transplants. 4. Age at diagnosis of multiple myeloma between 18 and 75 years. 5. Patients with plasma cell leukemia (>5% plasma cells on peripheral smear) to be included. Exclusion Criteria: 1. Patients undergoing ASCT beyond 12 months from the diagnosis of Multiple Myeloma. 2. Patients without fluorescence in situ hybridization data available at diagnosis.
Does this study include pediatric patients?	No
If this study does not include pediatric patients, please provide justification:	Multiple myeloma is a diagnosis of adults.
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.	1. Response prior to ASCT (stratified as very good partial response or better) 2. Minimal residual disease negativity prior to ASCT 2. Age at ASCT (>65 years) 3. Presence of extramedullary plasmacytoma at diagnosis 4. Beta-2 microglobulin >5.5 µg/dL (or >5.5 mg/L) at diagnosis of multiple myeloma 5. Elevated serum lactate dehydrogenase (LDH) above the upper limit of normal (if data is available) 6. High-risk cytogenetics (none versus 1 versus ≥2)
Types of cellular therapy data this proposal includes:	Hematopoietic Cell Transplantation (HCT)
PATIENT REPORTED OUTCOME (PRO) REQUIREMENTS: If the study requires PRO data collected by CIBMTR, the proposal should include: 1) A detailed description of the PRO domains, timepoints, and proposed analysis of PROs; 2) A description of the hypothesis speci	Not required
MACHINE LEARNING: Please indicate if the study requires methodology related to machine-learning and clinical predictions.	Not required
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	Not required

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.	Not required
REFERENCES:	References: 1. Walker BA, Mavrommatis K, Wardell CP, Ashby TC, Bauer M, Davies F, et al. A high-risk, Double-Hit, group of newly diagnosed myeloma identified by genomic analysis. Leukemia. 2019;33(1):159-70. 2. Richardson PG, Jacobus SJ, Weller EA, Hassoun H, Lonial S, Raje NS, et al. Triplet Therapy, Transplantation, and Maintenance until Progression in Myeloma. New England Journal of Medicine. 2022;387(2):132-47. 3. Perrot A, Lauwers-Cances V, Cazaubiel T, Facon T, Caillot D, Clement-Filliatre L, et al. Early Versus Late Autologous Stem Cell Transplant in Newly Diagnosed Multiple Myeloma: Long-Term Follow-up Analysis of the IFM 2009 Trial. Blood. 2020;136:39. 4. Kaiser MF, Hall A, Walker K, Sherborne A, De Tute RM, Newnham N, et al. Daratumumab, Cyclophosphamide, Bortezomib, Lenalidomide, and Dexamethasone as Induction and Extended Consolidation Improves Outcome in Ultra-High-Risk Multiple Myeloma. Journal of Clinical Oncology. 2023:JCO.22.02567. 5. van de Donk N, Minnema MC, van der Holt B, Schjesvold F, Wu KL, Broijl A, et al. Treatment of primary plasma cell leukaemia with carfilzomib and lenalidomide-based therapy (EMN12/HOVON-129): final analysis of a non-randomised, multicentre, phase 2 study. Lancet Oncol. 2023;24(10):1119-33. 6. Leypoldt LB, Tichy D, Besemer B, Hänel M, Raab MS, Mann C, et al. Isatuximab, Carfilzomib, Lenalidomide, and Dexamethasone for the Treatment of High-Risk Newly Diagnosed Multiple Myeloma. Journal of Clinical Oncology.0(0):JCO.23.01696. 7. Leleu X, Hulin C, Lambert J, Bobin A, Perrot A, Karlin L, et al. Isatuximab, lenalidomide, dexamethasone and bortezomib in transplant-ineligible multiple myeloma: the randomized phase 3 BENEFIT trial. Nature Medicine. 2024. 8. Costa LJ, Chhabra S, Medvedova E, Dholaria BR, Schmidt TM, Godby KN, et al. Minimal residual disease response-adapted therapy in newly diagnosed multiple myeloma (MASTER): final report of the multicentre, single-arm, phase 2 trial. Lancet Haematol. 2023;10(11):e890-e901.
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

Field	Response
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.	-

PROP 2410-35: Impact of Autologous Stem Cell Transplantation on Outcomes with High-risk Multiple Myeloma (S Zanwar/ S Kumar)

Table: Characteristics of adult patients who underwent autologous HCT between 2008-2020 for multiple myeloma within 12 months of diagnosis, and reported to the CIBMTR

Characteristic	No high risk	Single high risk	>=2 high risk
No. of patients	4327	1188	388
No. of centers	162	115	81
Patient-related			
Age at HCT - no. (%)			
20-29	11 (0.3)	5 (0.4)	0 (0.0)
30-39	138 (3.2)	28 (2.4)	8 (2.1)
40-49	596 (13.8)	136 (11.4)	41 (10.6)
50-59	1430 (33.0)	358 (30.1)	125 (32.2)
60-69	1784 (41.2)	526 (44.3)	167 (43.0)
70+	368 (8.5)	135 (11.4)	47 (12.1)
Age at HCT - no. (%)			
<65	3160 (73.0)	800 (67.3)	266 (68.6)
65+	1167 (27.0)	388 (32.7)	122 (31.4)
Gender - no. (%)			
Male	2456 (56.8)	644 (54.2)	200 (51.5)
Female	1871 (43.2)	544 (45.8)	188 (48.5)
Center region - no. (%)			
US	4099 (94.7)	1169 (98.4)	386 (99.5)
Canada	63 (1.5)	5 (0.4)	1 (0.3)
Europe	19 (0.4)	2 (0.2)	0 (0.0)
Asia	50 (1.2)	10 (0.8)	1 (0.3)
Australia/New Zealand	8 (0.2)	0 (0.0)	0 (0.0)
Mideast/Africa	11 (0.3)	1 (0.1)	0 (0.0)
Central/South America	77 (1.8)	1 (0.1)	0 (0.0)
Race - no. (%)			
White	2683 (62.0)	670 (56.4)	234 (60.3)
Black or African American	1264 (29.2)	407 (34.3)	113 (29.1)
Asian	185 (4.3)	59 (5.0)	20 (5.2)
Native Hawaiian or other Pacific Islander	10 (0.2)	2 (0.2)	3 (0.8)
American Indian or Alaska Native	42 (1.0)	12 (1.0)	5 (1.3)
More than one race	18 (0.4)	8 (0.7)	5 (1.3)
Not reported	35 (0.8)	3 (0.3)	0 (0.0)
Not reported	90 (2.1)	27 (2.3)	8 (2.1)
Karnofsky score prior to HCT - no. (%)			

Characteristic	No high risk	Single high risk	>=2 high risk
90-100%	2320 (53.6)	596 (50.2)	217 (55.9)
< 90%	1888 (43.6)	564 (47.5)	162 (41.8)
Not reported	119 (2.8)	28 (2.4)	9 (2.3)
HCT-CI - no. (%)			
0	1370 (31.7)	309 (26.0)	106 (27.3)
1	657 (15.2)	160 (13.5)	61 (15.7)
2	689 (15.9)	210 (17.7)	71 (18.3)
3+	1540 (35.6)	495 (41.7)	146 (37.6)
Not reported	71(1.7)	14 (1.2)	4(1.0)
Disease-related			
ISS stage at diagnosis - no. (%)			
ISS stage I	1362 (31.5)	324 (27.3)	97 (25.0)
ISS stage II	1219 (28.2)	364 (30.6)	119 (30.7)
ISS stage III	888 (20.5)	277 (23.3)	98 (25.3)
Not reported	858 (19.8)	223 (18.8)	74 (19.1)
Durie-Salmon - no. (%)			
Stage III	2142 (49.5)	628 (52.9)	193 (49.7)
Stage I-II	1625 (37.6)	465 (39.1)	151 (38.9)
Not reported	560 (12.9)	95 (8.0)	44 (11.3)
Beta-2 microglobulin at diagnosis - no. (%)			
0- 3.5 mg/l	1915 (44.3)	480 (40.4)	154 (39.7)
3.5-5.5 mg/l	659 (15.2)	210 (17.7)	65 (16.8)
>=5.5mg/l	777 (18.0)	270 (22.7)	95 (24.5)
Not reported	976 (22.6)	228 (19.2)	74 (19.1)
Serum albumin at diagnosis - no. (%)			
< 3.5 g/dl	1363 (31.5)	476 (40.1)	152 (39.2)
>= 3.5 g/dl	2442 (56.4)	636 (53.5)	210 (54.1)
Not reported	522 (12.1)	76 (6.4)	26 (6.7)
Serum creatinine at diagnosis - no. (%)			
< 2 mg/dl	3014 (69.7)	899 (75.7)	277 (71.4)
>= 2 mg/dl	613 (14.2)	167 (14.1)	68 (17.5)
Not reported	700 (16.2)	122 (10.3)	43 (11.1)
High-risk cytogenetics by FISH or conventional - no. (%)			
No high risk	4327 (100)	0 (0.0)	0 (0.0)
Single high risk			
t(4;14)	0 (0.0)	179 (15.1)	0 (0.0)
t(14;16)	0 (0.0)	50 (4.2)	0 (0.0)
t(14;20)	0 (0.0)	12 (1.0)	0 (0.0)
del(17p)	0 (0.0)	233 (19.6)	0 (0.0)
abnormal 1q	0 (0.0)	714 (60.1)	0 (0.0)

Characteristic	No high risk	Single high risk	>=2 high risk
>=2 high risk			388 (100)
t(4;14)	0 (0.0)	0 (0.0)	204(52.6)
t(14;16)	0 (0.0)	0 (0.0)	90(23.2)
t(14;20)	0 (0.0)	0 (0.0)	21(5.4)
del(17p)	0 (0.0)	0 (0.0)	199(51.3)
abnormal 1q	0 (0.0)	0 (0.0)	327(84.3)
Disease status prior to HCT - no. (%)			
sCR/CR	733 (16.9)	172 (14.5)	58 (14.9)
VGPR	1607 (37.1)	513 (43.2)	163 (42.0)
PR	1684 (38.9)	443 (37.3)	149 (38.4)
SD	224 (5.2)	39 (3.3)	7 (1.8)
PD/Relapse	60 (1.4)	13 (1.1)	7 (1.8)
Not reported	19 (0.4)	8 (0.7)	4 (1.0)
Time from diagnosis to HCT - no. (%)			
< 6 months	1614 (37.3)	524 (44.1)	188 (48.5)
6 - 12 months	2713 (62.7)	664 (55.9)	200 (51.5)
Treatment-related			
Prior lines of therapy - no. (%)			
0	3 (0.1)	0 (0.0)	0 (0.0)
1	3360 (77.7)	932 (78.5)	284 (73.2)
2	727 (16.8)	196 (16.5)	87 (22.4)
Not reported	237 (5.5)	60 (5.1)	17 (4.4)
Type of induction chemotherapy - no. (%)			
VTD	147 (3.4)	19 (1.6)	5 (1.3)
VRD	2054 (47.5)	710 (59.8)	236 (60.8)
VCD	643 (14.9)	189 (15.9)	61 (15.7)
VD	400 (9.2)	75 (6.3)	21 (5.4)
RD	446 (10.3)	60 (5.1)	23 (5.9)
TD	160 (3.7)	4 (0.3)	1 (0.3)
Carfilzomib	11 (0.3)	2 (0.2)	0 (0.0)
VAD/similar	52 (1.2)	6 (0.5)	0 (0.0)
Others	80 (1.8)	10 (0.8)	0 (0.0)
KRD	35 (0.8)	20 (1.7)	9 (2.3)
Daratumumab	59 (1.4)	33 (2.8)	15 (3.9)
Not reported	240 (5.5)	60 (5.1)	17 (4.4)
Daratumumab-based induction chemotherapy - no. (%)			
No	4268 (98.6)	1155 (97.2)	373 (96.1)
Yes	59 (1.4)	33 (2.8)	15 (3.9)
Conditioning regimen - no. (%)			
MEL 140	1238 (28.6)	332 (27.9)	98 (25.3)

Characteristic	No high risk	Single high risk	>=2 high risk
MEL 200	3082 (71.2)	855 (72.0)	290 (74.7)
Unknown dose	7 (0.2)	1 (0.1)	0 (0.0)
Year of transplant - no. (%)			
2008	584 (13.5)	32 (2.7)	4 (1.0)
2009	191 (4.4)	19 (1.6)	4 (1.0)
2010	150 (3.5)	18 (1.5)	6 (1.5)
2011	224 (5.2)	39 (3.3)	8 (2.1)
2012	244 (5.6)	39 (3.3)	4 (1.0)
2013	415 (9.6)	81 (6.8)	25 (6.4)
2014	307 (7.1)	81 (6.8)	22 (5.7)
2015	370 (8.6)	122 (10.3)	30 (7.7)
2016	412 (9.5)	137 (11.5)	41 (10.6)
2017	363 (8.4)	144 (12.1)	55 (14.2)
2018	712 (16.5)	325 (27.4)	132 (34.0)
2019	300 (6.9)	120 (10.1)	46 (11.9)
2020[a]	55 (1.3)	31 (2.6)	11 (2.8)

**Data source: CRF retrieval January 2022*

[a]Data from 2020 and after not complete

Field	Response
Proposal Number	2410-53-HASHMI
Proposal Title	An Inflammatory Biomarker Signature Predicts CAR-T Treatment Failure in Patients with Multiple Myeloma
Key Words	Inflammatory, Biomarker, CAR-T, Multiple Myeloma
Principal Investigator #1: - First and last name, degree(s)	Hamza Hashmi, M.D.
Principal Investigator #1: - Email address	hashmih1@mskcc.org
Principal Investigator #1: - Institution name	Memorial Sloan Kettering Cancer Center
Principal Investigator #1: - Academic rank	Assistant Professor
Junior investigator status (defined as ≤5 years from fellowship)	Yes
Do you identify as an underrepresented/minority?	Yes
Principal Investigator #2 (If applicable): - First and last name, degree(s):	Sham Mailankody, MBBS; Saad Z Usmani
Principal Investigator #2 (If applicable): - Email address:)	mailanks@mskcc.org; usmanis@mskcc.org
Principal Investigator #2 (If applicable): - Institution name:	Memorial Sloan Kettering Cancer Center
Principal Investigator #2 (If applicable): - Academic rank:	Associate Professor; Professor
Junior investigator status (defined as ≤5 years from fellowship)	No
Do you identify as an underrepresented/minority?	Yes
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:	Hamza Hashmi
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.	-
Do any of the PI(s) within this proposal have a CIBMTR WC study in manuscript preparation >6 months?	No
PROPOSED WORKING COMMITTEE:	Plasma Cell Disorders
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:	-
RESEARCH QUESTION:	Can simple biomarkers prior to CAR T predict toxicities and efficacy for patients with RRMM

Field	Response
RESEARCH HYPOTHESIS:	Inflammatory signature at time of infusion stratifies patients with RRMM by risk for CAR-T treatment failure and severe toxicities
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	- Determine overall response, complete response, progression free survival, overall survival in patients receiving CAR-T cell therapy stratified by high and low inflammatory signal at time of infusion -Determine the incidence and severity of cytokine release syndrome, immune effector cell associated neurotoxicity syndrome, cytopenias, infections, non-relapse mortality stratified by high and low inflammatory signal at time of infusion
SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.	Potential clinical applications of identifying patients with inflammatory signal include prognostication and informed design of clinical trials to target high-risk populations
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.	For large cell lymphoma patient population, inflammatory signal was evaluated and applied using pre-infusion, day 0 laboratory data (hemoglobin, platelets, white blood cells, CRP, ferritin, aspartate transaminase, alkaline phosphatase, total bilirubin, LDH, albumin) measurements and was strongly associated with safety and efficacy outcomes. Such inflammatory signal can be readily developed (training cohort) using CIBMTR data set and validated (validation cohort) internally.
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	All RRMM treated with standard-of-care idecabtagene viculeucel and ciltacabtagene autoleucel
Does this study include pediatric patients?	No
If this study does not include pediatric patients, please provide justification:	MM is not a disease of the pediatric patient population

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.	Data to be collected:- Patient related: •Age at CAR T-cell therapy•Gender: male vs. female •Race:Caucasian vs. African American vs. vs. Hispanic •Ethnicity: Hispanic or Latino vs. Non-Hispanic or non-Latino vs. non-resident of the U.S. •ECOG Performance status -Disease-related: •Myeloma subtype: IgG versus IgA versus IgM versus light chain [kappa versus lambda] •High risk disease [del 17, 4;14, 14; 16] •Presence of 1q abnormalities (gain of 1q versus amplification 1q) •R-ISS at CAR-T infusion •Number of prior lines of chemotherapy •Response to prior therapy [lenalidomide, pomalidomide, bortezomib, carfilzomib, daratumumab]: Exposed versus refractory •Prior autologous transplant •History of extramedullary disease •Extramedullary disease prior to infusion •Bone marrow plasma cell percentage prior to infusion •Disease status at referral •Disease status prior to infusion •Baseline markers ((hemoglobin, platelets, white blood cells, CRP, ferritin, aspartate transaminase, alkaline phosphatase, total bilirubin, LDH, albumin) prior to infusion •Exposure to BCMA agent (commercial versus trial) -CAR T-cell therapy related: •CAR T product:ide-cel versus cilta-cel •Time from diagnosis to infusion •Time from leukapheresis to infusion •Use of bridging therapy •Type of bridging therapy:Chemotherapy versus radiotherapy versus both chemo and radiotherapy •Bridging chemotherapy regimen •CAR-T cell dose •CRS: grade, onset,duration •ICANS: grade, onset, duration •Use of tocilizumab •Use of corticosteroids •Persistent cytopenias at day +30 and day +90 •Use of G-CSF •Use of TPO agonists •Response at 1 month,3-month, 6 months, 9 months, 12 months •Time from infusion to progression •Date of Death •Cause of death •Date of last contact
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.	yes

Field	Response
SAMPLE REQUIREMENTS: If the study requires biologic samples from the CIBMTR Repository, the proposal should also include: 1) A detailed description of the proposed testing methodology and sample requirements; 2) A summary of the investigator's previous e	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.	NA
REFERENCES:	Faramand RG, Lee SB, Jain MD, Cao B, Wang X, Rejeski K, Subklewe M, Fahrmann JF, Saini NY, Hanash SM, Kang YP, Chang D, Rodriguez PC, Dean EA, Nishihori T, Shah BD, Lazaryan A, Chavez J, Khimani F, Pinilla-Ibarz JA, Dam M, Reid KM, Corallo SA, Menges M, Hidalgo Vargas M, Mandula JK, Holliday BA, Bachmeier CA, Speth K, Song Q, Mattie M, Locke FL, Davila ML. Baseline Serum Inflammatory Proteins Predict Poor CAR T Outcomes in Diffuse Large B-cell Lymphoma. Blood Cancer Discov. 2024 Mar 1;5(2):106-113. doi: 10.1158/2643-3230.BCD-23-0056. PMID: 38194367; PMCID: PMC10905320. Sandeep Raj, Jin Xie, Teng Fei, Qinghua Song, Jenny J. Kim, Christina To, Marcel R.M. van den Brink, Miguel-Angel Perales, Mike Mattie, Roni Shouval; An Inflammatory Biomarker Signature Reproducibly Predicts CAR-T Treatment Failure in Patients with Aggressive Lymphoma across the Zuma Trials Cohorts. Blood 2023; 142 (Supplement 1): 224. doi: https://doi.org/10.1182/blood-2023-173798
CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning?	-
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.	-

PROP 2410-53: An Inflammatory Biomarker Signature Predicts CAR-T Treatment Failure in Patients with Multiple Myeloma (H Hashmi/ S Mailankody/ S Usmani)

Table: Characteristics of patients with multiple myeloma who received CAR-T Treatment and reported to the CIBMTR

Characteristic	Idecabtagene vicleucel	Ciltacabtagene autoleucel	Total
No. of patients	1464	1176	2640
No. of centers	81	68	97
Patient-related			
Age, by decades - no. (%)			
Median (min-max)	67 (29-90)	65 (33-84)	66 (29-90)
20-29	1 (0)	0 (0)	1 (0)
30-39	7 (0)	12 (1)	19 (1)
40-49	69 (5)	80 (7)	149 (6)
50-59	287 (20)	268 (23)	555 (21)
60-69	580 (40)	502 (43)	1082 (41)
70+	520 (36)	314 (27)	834 (32)
Recipient Sex - no. (%)			
Male	855 (58)	657 (56)	1512 (57)
Female	609 (42)	519 (44)	1128 (43)
Recipient race - no. (%)			
White	1131 (77)	903 (77)	2034 (77)
African-American	245 (17)	164 (14)	409 (15)
Asian	31 (2)	39 (3)	70 (3)
Pacific Islander	3 (0)	3 (0)	6 (0)
Native American	7 (0)	1 (0)	8 (0)
More than one race	4 (0)	5 (0)	9 (0)
Not reported	43 (3)	61 (5)	104 (4)
Ethnicity - no. (%)			
Hispanic or Latino	106 (7)	105 (9)	211 (8)
Non-Hispanic or Latino	1329 (91)	1028 (87)	2357 (89)
Non-resident of the U.S.	0 (0)	9 (1)	9 (0)
Not reported	29 (2)	34 (3)	63 (2)
Karnofsky performance score prior to CT - no. (%)			
90-100	472 (32)	513 (44)	985 (37)
80	565 (39)	373 (32)	938 (36)
< 80	307 (21)	166 (14)	473 (18)
Not reported	120 (8)	124 (11)	244 (9)
HCT-CI Score - no. (%)			

Characteristic	Idecabtagene vicleucel	Ciltacabtagene autoleucel	Total
0	323 (22)	341 (29)	664 (25)
1	243 (17)	227 (19)	470 (18)
2	225 (15)	180 (15)	405 (15)
3	263 (18)	175 (15)	438 (17)
4	171 (12)	117 (10)	288 (11)
5+	233 (16)	128 (11)	361 (14)
Not reported	6 (0)	8 (1)	14 (1)
Disease-related			
Sub-disease - no. (%)			
Multiple myeloma, NOS	1073 (73)	893 (76)	1966 (74)
Multiple myeloma - light chain only	359 (25)	265 (23)	624 (24)
Multiple myeloma - non-secretory	32 (2)	18 (2)	50 (2)
Disease status prior to CT - no. (%)			
Stringent complete remission (sCR)	9 (1)	12 (1)	21 (1)
Complete remission (CR)	16 (1)	25 (2)	41 (2)
Very good partial remission (VGPR)	122 (8)	122 (10)	244 (9)
Partial response (PR)/ Not Complete Remission	187 (13)	145 (12)	332 (13)
Stable disease (SD)	233 (16)	214 (18)	447 (17)
Progressive disease (PD)	878 (60)	625 (53)	1503 (57)
Relapse from CR (Rel) (untreated)	16 (1)	30 (3)	46 (2)
Not reported	3 (0)	3 (0)	6 (0)
C-Reactive protein, mg/dL - no. (%)			
Median (Q1 – Q3)	0.5 (0.3-1.4)	0.5 (0.2-1.2)	0.5 (0.3-1.2)
Data available	432 (29.5)	720 (61.2)	1152 (43.6)
Data not reported	1032 (70.5)	456 (38.8)	1488 (56.4)
Serum ferritin, ng/mL - no. (%)			
Median (Q1 – Q3)	201.0 (71.0-601.0)	160.0 (56.0-490.0)	174.0 (62.0-524.0)
Data available	419 (28.6)	671 (57.1)	1090 (41.3)
Data not reported	1045 (71.4)	505 (42.9)	1550 (58.7)
Serum Albumin, g/dl - no. (%)			
Median (Q1 – Q3)	3.8 (3.4-4.1)	3.9 (3.5-4.2)	3.8 (3.5-4.1)
Data available	1011 (69.1)	1051 (89.4)	2062 (78.1)
Data not reported	453 (30.9)	125 (10.6)	578 (21.9)
Hemoglobin, g/dL - no. (%)			
Median (Q1 – Q3)	10.3 (8.9-11.8)	10.9 (9.4-12.2)	10.6 (9.1-12.0)
Data available	1108 (75.7)	1144 (97.3)	2252 (85.3)
Data not reported	356 (24.3)	32 (2.7)	388 (14.7)
Platelets, x 10^9 /L - no. (%)			

Characteristic	Idecabtagene vicleucel	Ciltacabtagene autoleucel	Total
Median (Q1 – Q3)	150.0 (94.0-200.0)	165.0 (118.0-214.0)	157.5 (105.0-208.0)
Data available	1105 (75.5)	1145 (97.4)	2250 (85.2)
Data not reported	359 (24.5)	31 (2.6)	390 (14.8)
Neutrophil x 10^9 /L - no. (%)			
Median (Q1 – Q3)	2.5 (1.7-3.6)	2.7 (1.8-3.6)	2.6 (1.8-3.6)
Data available	1079 (73.7)	1121 (95.3)	2200 (83.3)
Data not reported	385 (26.3)	55 (4.7)	440 (16.7)
ANC x 10^6 /L - no. (%)			
< 750 x 10^6 /L	26 (2)	36 (3)	62 (2)
>=750 x 10^6 /L	1053 (72)	1085 (92)	2138 (81)
Data not reported	385 (26)	55 (5)	440 (17)
LDH, U/L - no. (%)			
Median (Q1 – Q3)	196.5 (165.0-243.0)	188.5 (161.0-235.0)	192.0 (163.0-239.0)
Data available	1276 (87.2)	1058 (90.0)	2334 (88.4)
Data not reported	188 (12.8)	118 (10.0)	306 (11.6)
Treatment-related			
No. of lines of prior therapies (including HCT and CT) - no. (%)			
1	6 (0)	5 (0)	11 (0)
2	38 (3)	17 (1)	55 (2)
3	50 (3)	54 (5)	104 (4)
4+ Lines	935 (64)	988 (84)	1923 (73)
Not reported	435 (30)	112 (10)	547 (21)
Year of CT - no. (%)			
2021	284 (19)	0 (0)	284 (11)
2022	529 (36)	203 (17)	732 (28)
2023	564 (39)	689 (59)	1253 (47)
2024	87 (6)	284 (24)	371 (14)
Follow-up of survivors, months - median (range)	13 (1-37)	7 (1-28)	12 (1-37)

**Data source: CT Extract November 2024*

UNIFIED TABLE	
Field	**Response**
Proposal Title	Outcomes of lenalidomide alone vs daratumumab + lenalidomide maintenance regimen in post autologous transplant multiple myeloma patients
RESEARCH QUESTION:	Safety and efficacy data of daratumumab + lenalidomide vs lenalidomide alone maintenance therapy in multiple myeloma patients who have received either a triplet or a quadruplet induction treatment and then undergone an autologous stem cell transplant
RESEARCH HYPOTHESIS:	The primary hypothesis of this study is that daratumumab + lenalidomide maintenance is superior to lenalidomide alone maintenance in extending the progression free survival in multiple myeloma patients after autologous stem cell transplant
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	Primary endpoint: progression free survival Secondary endpoints: 1. Sub-group analyses for progression free survival and overall survival o Triplet vs quadruplet induction therapy o CD38 naive vs CD38 exposed o Non-secretory disease o High risk characteristics (Can characterize as having >/= 2 high risk features) o Those with suboptimal response to induction and transplant (i.e. did not achieve CR post transplant, and those who were MRD positive post transplant) 2. Response rates o Duration of response o Time to progression o Time to next treatment 3. Toxicity profiles o Hematologic toxicities o Non-relapse mortality o Discontinuation rates not due to progression
SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.	If a PFS benefit of adding a CD38 antibody to lenalidomide is demonstrated in this retrospective study, it will provide further evidence to include an anti-CD38 antibody as a continuous treatment for multiple myeloma before results of ongoing randomized trials using this strategy are available. The data obtained from this study will also help guide if certain subgroups would benefit from doublet maintenance therapy.
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.	Until recently, treatment strategies for newly diagnosed multiple myeloma primarily involved triple-drug regimens, typically combining a proteasome inhibitor (PI), an immunomodulatory drug (IMiD), and a steroid, followed by autologous stem cell transplant (ASCT) for eligible patients, along with maintenance therapy. However, recent data from several quadruplet induction trials have shifted the approach, with a growing number of patients receiving four-drug regimens. The phase 2 GRIFFIN trial evaluated quadruplet induction therapy (DaraRVD) followed by ASCT and maintenance therapy with daratumumab + lenalidomide for two years, demonstrating the efficacy and tolerability of these regimens in transplant-eligible patients with newly diagnosed multiple myeloma (NDMM). Building on these findings, the phase 3 PERSEUS study reinforced the results observed in GRIFFIN, showing that a maintenance strategy using daratumumab for 24 months, in combination with lenalidomide until disease progression, yielded positive outcomes. In the GMMG-HD7 trial, the addition of isatuximab (Isa) was also shown to improve depth of response when added to VRd induction and transplant, with more patients achieving MRD negativity in the isa-VRD arm compared to the VRD arm, and this being reflected in longer PFS.

	Moreover, long-term results from the CASSIOPEIA study demonstrated that adding daratumumab to both induction and consolidation therapy, followed by daratumumab maintenance, led to high and sustained MRD-negativity rates, alongside superior progression-free survival (PFS). Together, these findings highlight the advantages of daratumumab-containing quadruplets for induction and consolidation, followed by daratumumab-based maintenance, in transplant-eligible NDMM patients. However, due to trial design, it remains unclear whether there is a benefit to using a CD38 antibody with both induction therapy and maintenance. More recently, the AURIGA trial further supported this approach by showing improved MRD-negativity conversion rates with doublet maintenance therapy (daratumumab + lenalidomide) in patients who remained MRD-positive post-transplant. However, this trial excluded patients who had previously received a CD38 antibody, limiting its applicability to patients receiving quadruplet induction. The relative impact of CD38 antibodies in combination with lenalidomide will likely be determined by the second randomization of the GMMG-HD7 trial (Isa-R versus lenalidomide), and the SWOG 1803 (DRAMMATIC) trial (Dara-R vs lenalidomide). However, these trials are unlikely to report their outcomes for many years, leaving clinicians today with a difficult decision of whether to incorporate a CD38 antibody into maintenance. In the real world landscape, CD38 antibodies have been incorporated into initial therapy for myeloma since publication of the CASSIOPEIA and GRIFFIN trials in 2019. CD38 antibody usage during induction has increased over time, and incorporation into maintenance therapy is variable. This proposal aims to evaluate whether there is a difference in outcomes for patients based on the use of a CD38 antibody in maintenance along with lenalidomide. The study will also help quantify if certain patient populations will benefit from doublet maintenance therapy.
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	Inclusion criteria: 1. Patient with newly diagnosed MM who received autologous transplant within 1 year of initiation of induction therapy between January 1, 2014 – December 31, 2024 2. At least 3 months post-autologous stem cell transplant therapy 3. Initiated maintenance regimen which included lenalidomide within 180 days of ASCT 4. Age greater than or equal to 18 years 5. Both genders 6. All races Exclusion criteria: 1. Participant in ongoing trials 2. prior allogeneic stem cell transplantation 3. Concurrent diagnosis of plasma cell leukemia, AL amyloidosis, or POEMS syndrome 4. Patients with disease progression prior to transplantation will be excluded 5. Patient with second autologous transplant 6. Lenalidomide not included in maintenance regimen
Does this study include pediatric patients?	No
If this study does not include pediatric patients, please provide justification:	N/a to disease state
DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease-	1. Baseline patient characteristics a. Age at diagnosis b. Age at maintenance therapy initiation c. Gender

and infusion- variables to be considered in the multivariate analyses. Outline any supplementary data required.	d. Weight e. Race/Ethnicity f. Date of multiple myeloma diagnosis g. Disease type (IgG, IgA, IgM, IgD, IgE, light chain only, non-secretory) h. Light chain type (kappa, lambda, ...) i. Disease status at the time of infusion j. Comorbidities/comorbidity Index score k. Renal function l. Cytogenetic by karyotype (conventional) m. Cytogenetic by FISH n. International Staging System (ISS) o. Revised ISS p. Date of HCT q. Time from diagnosis to HCT r. Extramedullary plasmacytoma(s) 2. Treatments prior to maintenance therapy a. Drug class exposure during induction i. IMiD ii. PI iii. CD38 iv. IMiD + PI (no CD38) v. CD38 + PI (no IMiD) vi. CD38 + IMiD (no PI) vii. CD38 + IMiD + PI viii. Other (eg VTD-PACE) b. Melphalan dose (140mg/m2 vs 200mg/m2) c. Duration of induction treatment d. Date of autologous transplant e. Date of maintenance therapy initiation f. Best response after autologous transplant g. MRD status after transplant (if known) 3. Laboratory values at the time of initiation of maintenance therapy a. WBC b. Hemoglobin c. Platelet d. Plasma cells in bone marrow aspirate and biopsy or unknown source e. Serum creatinine f. Creatinine clearance (collected at CIBMTR since 9/2022) g. Serum monoclonal Ig (M-spike) h. Serum immunofixation i. Urinary monoclonal light chains j. Urine immunofixation k. Serum free light changes (kappa, lambda, ratio) l. Quantitative immunoglobulins (IgG, IgA, IgM) m. MRD status, and method of MRD assessment n. Plasma cells in bone marrow aspiration and biopsy or unknow source 4. Outcome data a. Overall response rate (ORR) b. Duration of response (DOR) c. Event-free survival (EFS) d. Progression-free survival (PFS)

	e. MRD status at 100-day, 6-month, 1-year, 2-year, and yearly for greater than 2 years post-auto-HCT (if data is available) f. Method of MRD assessment g. Incidence of Secondary primary malignancy h. Relapse or disease progression i. Site of progression j. Date of progression k. Date of death l. Cause of death m. Hematologic response at 100-day, 6-month, 1-year, 2-year, and yearly for greater than 2 years post-auto-HCT n. Best response 5. Subgroup analysis a. Triplet vs quadruplet induction therapy b. CD38 exposed vs CD38 naive c. Non-secretory disease d. High risk characteristics (Can characterize as having >/= 2 high risk features) e. PI + IMID vs CD38 + IMID maintenance therapies in doublet regimens f. Those with suboptimal response to induction and transplant (i.e. did not achieve CR post transplant, and those who were MRD positive post transplant) 6. Maintenance treatment post CAR-T treatment (if applicable) a. Type of maintenance treatment b. Dose of medication c. Number of cycles of maintenance d. Date maintenance started e. Date maintenance stopped f. Cause of maintenance discontinuation g. Addition of proteasome inhibitor to maintenance therapy (with or without CD38) h. Discontinuation rates not due to progression
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	N/A

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	N/A
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:	1. Ashraf Z Badros, et al; Daratumumab with lenalidomide as maintenance after transplant in newly diagnosed multiple myeloma: the AURIGA study. Blood 2024;blood.2024025746. doi:https://doi.org/10.1182/blood.2024025746 Philip L. McCarthy et al., Lenalidomide Maintenance After autologous Stem-Cell Transplantation in Newly Diagnosed Multiple Myeloma: A Meta-Analysis. JCO 35, 3279-3289(2017). DOI:10.1200/JCO.2017.72.6679 2. Attal M, Lauwers-Cances V, Marit G, Caillot D, Moreau P, Facon T, et al. Lenalidomide maintenance after stem-cell transplantation for multiple myeloma. N Engl J Med. 2012;366(19):1782-91. 3. Badros AZ, Foster L, Anderson LD, Jr., Chaulagain CP, Pettijohn EM, Cowan AJ, et al. Daratumumab with lenalidomide as maintenance after transplant in newly diagnosed multi ple myeloma: the AURIGA study. Blood. 2024:blood.2024025746. 4. Bumma N, Dhakal B, et al. Impact of bortezomib-based versus lenalidomide maintenance therapy on outcomes of patients with high-risk multiple myeloma. Cancer. 2023 Jul 15;129(14):2179-2191. doi: 10.1002/cncr.34778. 5. Gay F, Musto P, et al. Carfilzomib with cyclophosphamide and dexamethasone or lenalidomide and dexamethasone plus autologous transplantation or carfilzomib plus lenalidomide and dexamethasone, followed by maintenance with carfilzomib plus lenalidomide or lenalidomide alone for patients with newly diagnosed multiple myeloma (FORTE): a randomised, open-label, phase 2 trial. Lancet Oncol. 2021 Dec;22(12):1705-1720. doi: 10.1016/S1470-2045(21)00535-0. Epub 2021 Nov 11. PMID: 34774221. 6. Goldschmidt H, Mai EK, Bertsch U, Fenk R, Nievergall E, Tichy D, et al. Addition of isatuximab to lenalidomide, bortezomib, and dexamethasone as induction therapy for newly diagnosed, transplantation-eligible patients with multiple myeloma (GMMG-HD7): part 1 of an open-label, multicentre, randomised, active-controlled, phase 3 trial. The Lancet Haematology. 2022;9(11):e810-e21. 7. Jackson GH, Davies FE, Pawlyn C, Cairns DA, Striha A, Collett C, et al. Lenalidomide maintenance versus observation for patients with newly diagnosed multiple myeloma

	(Myeloma XI): a multicentre, open-label, randomised, phase 3 trial. The Lancet Oncology. 2019;20(1):57-73. 8. McCarthy PL, Holstein SA, Petrucci MT, Richardson PG, Hulin C, Tosi P, et al. Lenalidomide Maintenance After Autologous Stem-Cell Transplantation in Newly Diagnosed Multiple Myeloma: A Meta-Analysis. J Clin Oncol. 2017;35(29):3279-89. 9. Moreau P, Attal M, Hulin C, Arnulf B, Belhadj K, Benboubker L, et al. Bortezomib, thalidomide, and dexamethasone with or without daratumumab before and after autologous stem-cell transplantation for newly diagnosed multiple myeloma (CASSIOPEIA): a randomised, open-label, phase 3 study. Lancet. 2019;394(10192):29-38. 10. Palumbo A, Cavallo F, Gay F, Di Raimondo F, Ben Yehuda D, Petrucci MT, et al. Autologous transplantation and maintenance therapy in multiple myeloma. N Engl J Med. 2014;371(10):895-905. 11. Sonneveld P, Dimopoulos MA, et al; PERSEUS Trial Investigators. Daratumumab, Bortezomib, Lenalidomide, and Dexamethasone for Multiple Myeloma. N Engl J Med. 2024 Jan 25;390(4):301-313. doi: 10.1056/NEJMoa2312054. Epub 2023 Dec 12. PMID: 38084760. 12. Voorhees PM, Kaufman JL, Laubach JP, Sborov DW, Reeves B, Rodriguez C, et al. Daratumumab, Lenalidomide, Bortezomib, & Dexamethasone for Transplant-eligible Newly Diagnosed Multiple Myeloma: GRIFFIN. Blood. 2020.
CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning?	
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.	

PROP 2410-58; 2410-143; 2410-161; 2410-187: Impact of Lenalidomide vs. Lenalidomide + CD38 Monoclonal Antibody Maintenance on Outcomes in Post-Autologous Stem Cell Transplant Patients with Multiple Myeloma (M Sanchez/ A Avila/ T Schmidt/ P Rajan Abraham/ A Afrough)

Characteristics of adult patients who received Lenalidomide or Lenalidomide+Daratumumab Post-Autologous Stem Cell Transplant for multiple myeloma between 2016 - 2024, and reported to the CIBMTR

Characteristic	Lenalidomide	Lenalidomide + Daratumumab	Total
No. of patients	25544	3013	28557
No. of centers	231	168	231
Patient-related			
Patient age - median (min-max)	62.8 (20.8-86.2)	62.8 (25.2-82.7)	62.8 (20.8-86.2)
Age, by decades - no. (%)			
20-29	36 (0.1)	3 (0.1)	39 (0.1)
30-39	411 (1.6)	56 (1.9)	467 (1.6)
40-49	2143 (8.4)	287 (9.5)	2430 (8.5)
50-59	7121 (27.9)	841 (27.9)	7962 (27.9)
60-69	11634 (45.5)	1301 (43.2)	12935 (45.3)
70+	4199 (16.4)	525 (17.4)	4724 (16.5)
Sex - no. (%)			
Male	14720 (57.6)	1762 (58.5)	16482 (57.7)
Female	10824 (42.4)	1251 (41.5)	12075 (42.3)
Center region - no. (%)			
US	22462 (87.9)	2943 (97.7)	25405 (89.0)
Canada	1996 (7.8)	36 (1.2)	2032 (7.1)
Europe	2 (0.0)	0 (0.0)	2 (0.0)
Asia	348 (1.4)	3 (0.1)	351 (1.2)
Australia/New Zealand	123 (0.5)	0 (0.0)	123 (0.4)
Mideast/Africa	100 (0.4)	11 (0.4)	111 (0.4)
Central/South America	512 (2.0)	20 (0.7)	532 (1.9)
Not reported	1 (0.0)	0 (0.0)	1 (0.0)
Research track - no. (%)			
TED	23946 (93.7)	2991 (99.3)	26937 (94.3)
CRF[a]	1598 (6.3)	22 (0.7)	1620 (5.7)
Race - no. (%)			
White	17018 (66.6)	2177 (72.3)	19195 (67.2)
Black or African American	4459 (17.5)	478 (15.9)	4937 (17.3)

Characteristic	Lenalidomide	Lenalidomide + Daratumumab	Total
Asian	748 (2.9)	93 (3.1)	841 (2.9)
Native Hawaiian or other Pacific Islander	55 (0.2)	2 (0.1)	57 (0.2)
American Indian or Alaska Native	132 (0.5)	22 (0.7)	154 (0.5)
More than one race	112 (0.4)	15 (0.5)	127 (0.4)
Not reported	3020 (11.8)	226 (7.5)	3246 (11.4)
Ethnicity - no. (%)			
Hispanic or Latino	2416 (9.5)	323 (10.7)	2739 (9.6)
Non-Hispanic or Latino	19646 (76.9)	2527 (83.9)	22173 (77.6)
Non-resident of the U.S.	2743 (10.7)	63 (2.1)	2806 (9.8)
Not reported	739 (2.9)	100 (3.3)	839 (2.9)
HCT-CI - no. (%)			
0	6709 (26.3)	805 (26.7)	7514 (26.3)
1	3771 (14.8)	478 (15.9)	4249 (14.9)
2	4258 (16.7)	518 (17.2)	4776 (16.7)
3	4582 (17.9)	515 (17.1)	5097 (17.8)
4	2792 (10.9)	278 (9.2)	3070 (10.8)
5+	3337 (13.1)	404 (13.4)	3741 (13.1)
Not reported	95 (0.4)	15 (0.5)	110 (0.4)
Karnofsky score prior to HCT - no. (%)			
90-100%	13555 (53.1)	1695 (56.3)	15250 (53.4)
< 90%	11484 (45.0)	1272 (42.2)	12756 (44.7)
Not reported	505 (2.0)	46 (1.5)	551 (1.9)
Disease-related			
Sub-disease - no. (%)			
Multiple myeloma, NOS	10939 (42.8)	2182 (72.4)	13121 (45.9)
Multiple myeloma-IgG	7115 (27.9)	208 (6.9)	7323 (25.6)
Multiple myeloma-IgA	2290 (9.0)	54 (1.8)	2344 (8.2)
Multiple myeloma-IgD	51 (0.2)	0 (0.0)	51 (0.2)
Multiple myeloma-IgE	4 (0.0)	0 (0.0)	4 (0.0)
Multiple myeloma-IgM	52 (0.2)	2 (0.1)	54 (0.2)
Mult myeloma-light chain	4789 (18.7)	548 (18.2)	5337 (18.7)
Mult myeloma-non-secretory	304 (1.2)	19 (0.6)	323 (1.1)
Disease status prior to transplant - no. (%)			
sCR/CR	4484 (17.6)	397 (13.2)	4881 (17.1)
VGPR	12373 (48.4)	1564 (51.9)	13937 (48.8)
PR	7549 (29.6)	933 (31.0)	8482 (29.7)
SD	782 (3.1)	82 (2.7)	864 (3.0)

Characteristic	Lenalidomide	Lenalidomide + Daratumumab	Total
PD/Relapse	235 (0.9)	29 (1.0)	264 (0.9)
Not Reported	121 (0.5)	8 (0.3)	129 (0.5)
Transplant-related			
Conditioning regimen - no. (%)			
TBI/Mel	2 (0.0)	0 (0.0)	2 (0.0)
Bu/Cy	1 (0.0)	0 (0.0)	1 (0.0)
Bu/Mel	128 (0.5)	14 (0.5)	142 (0.5)
Flu/Mel	3 (0.0)	0 (0.0)	3 (0.0)
BEAM	12 (0.0)	2 (0.1)	14 (0.0)
BEAM like	37 (0.1)	1 (0.0)	38 (0.1)
Mel alone	24959 (97.7)	2974 (98.7)	27933 (97.8)
Mel/other(s)	244 (1.0)	10 (0.3)	254 (0.9)
Other(s)	17 (0.1)	2 (0.1)	19 (0.1)
None	3 (0.0)	0 (0.0)	3 (0.0)
Not Reported	138 (0.5)	10 (0.3)	148 (0.5)
Product type - no. (%)			
BM	14 (0.1)	2 (0.1)	16 (0.1)
PBSC	25529 (99.9)	3011 (99.9)	28540 (99.9)
Not reported	1 (0.0)	0 (0.0)	1 (0.0)
Year of transplant - no. (%)			
2016	2518 (9.9)	53 (1.8)	2571 (9.0)
2017	3065 (12.0)	62 (2.1)	3127 (11.0)
2018	3293 (12.9)	88 (2.9)	3381 (11.8)
2019	3243 (12.7)	158 (5.2)	3401 (11.9)
2020	3101 (12.1)	313 (10.4)	3414 (12.0)
2021	3339 (13.1)	515 (17.1)	3854 (13.5)
2022	3519 (13.8)	785 (26.1)	4304 (15.1)
2023	3112 (12.2)	911 (30.2)	4023 (14.1)
2024	354 (1.4)	128 (4.2)	482 (1.7)
Follow-up of survivors - median (range)	36.7 (0.7-103.8)	14.0 (1.8-101.9)	36.1 (0.7-103.8)

**Data source: HCT Essentials October 2024*

[a]CRF data not complete in current database

Field	Response
Proposal Numbers	2410-71-HASHMI, 2410-210-BIDIKIAN, 2410-228-ABDALLAH
Proposal Title	Real-World Safety, Efficacy, and Outcomes of Cilta-cel and Ide-cel Treatment in Earlier Lines for Patients with Relapsed or Refractory Multiple Myeloma
Key Words	Multiple myeloma, CAR-T cell, Ide-cel, Cilta-cel, B-cell maturation antigen (BCMA), survival, Early, Late
Principal Investigator #1	Aram Bidikian, MD – **Junior investigator**
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	Yale New Haven Hospital, Yale School of Medicine
Principal Investigator #2	Lohith Gowda, MD, MRCP
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	Yale School of Medicine
Principal Investigator #3	Nadine Abdallah, MD – **Junior Investigator**
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Principal Investigator #4	Supriya Gupta – **Junior Investigator**
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Principal Investigator #5	Hamza Hashmi, M.D. – **Junior investigator**
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	Memorial Sloan Kettering Cancer Center
Principal Investigator #7	Saad Z Usmani, M.D.
	usmanis@mskcc.org
	Memorial Sloan Kettering Cancer Center
PROPOSED WORKING COMMITTEE:	Plasma Cell Disorders
RESEARCH QUESTION:	Are there any differences in the safety and efficacy of BCMA CAR T cell therapies (cilta-cel and ide-cel) when used in earlier (1-2) versus later (≥4) lines of therapy patients with relapsed or refractory multiple myeloma in the real-world setting?
RESEARCH HYPOTHESIS:	Using BCMA CAR T cell therapies (cilta-cel and ide-cel) in earlier lines of treatment (1-2) for relapsed or refractory multiple myeloma is associated with improved efficacy and safety compared to their use in later lines (≥ 4).

Field	Response
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	To compare the following endpoints between patients with relapsed or refractory multiple myeloma who received BCMA CAR T cell therapies (cilta-cel and ide-cel) in earlier (1-3) versus later (≥4) lines of therapy: <u>Efficacy:</u> -Treatment responses: ORR, ≥VGPR, CR, measurable residual disease (MRD) negativity -Progression-free survival -Overall survival <u>Safety:</u> -Incidence and grades of cytokine release syndrome, Immune effector cell associated neurotoxicity syndrome, and other neurological toxicities. -Incidence, severity and duration of cytopenias -Incidence and severity of infections -Incidence of secondary malignancies -Non-relapse mortality - OOS product rates
SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.	<u>This study has the potential to:</u> - Provide valuable insight into the safety and efficacy of cilta-cel and ide-cel as earlier treatment options for relapsed or refractory multiple myeloma in the general population, including patient subgroups underrepesented in clinical trials. -Identify patients with the highest benefit and least toxicity from an early CAR T. -Allow predictive modeling of factors that impact efficacy, safety, and survival outcomes with earlier use of BCMA CAR-T products in patients with realpsed refractory multiple myeloma, which can guide treatment selection, and resource allocation, and clinical trial design for high-risk populations.

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.	Ide-cel and cilta-cel are Bcma CAR-T products which gained FDA approval in 2021 and 2022, respectively, for the treatment of RRMM after four or more prior lines of therapy, including an IMiD, a PI, and an anti-CD38 monoclonal antibody[15, 16]. These approvals were based on results of the KarMMa-2and CARTITUDE-1 trials for ide-cel and cilta-cel, respectively. In phase 3 trials both Ide-cel (KarMMa-3) and cilta-cel (CARTITUDE-4) demonstrated superior response rates and survival outcomes when each was compared to a control arm of standard treatment for RRMM [21, 22]. In KarMMa-3, ide-cel was associated with a median PFS of 13.3 months compared to 4.4 months for the standard treatment arm, demonstrating a significant improvement. The ORR to ide-cel was 71% vs 42 in the control arm, with CR rates of 39% vs 5%[21]. In CARTITUDE-4 patients receiving cilta-cel had a median PFS that was not reached after a median follow up of 15.9 months vs 11.8 months for the control arm. The ORR to cilta-cel was 85% vs 67% in the control arm and CR rates of 73% vs 22%[22]. Notably, patients enrolled in the both KarMMa-3 and CARTITUDE-4 trials were exposed to significantly fewer previous lines of therapy when compared to their corresponding phase 1/2 trials. Patients enrolled in KarMMa-3 had received a median of 3 prior lines of therapy (range 2-4) compared with median of 6 (3-12) in KarMMa-2. Similarly, more than 70% of patients enrolled in CARTITUDE-4 had received only 1-2 prior lines of therapy, compared with a median of 6 (4-8) previous lines of therapy among patients enrolled in CARTITUDE-1[19-22]. The above data highlight the significantly improved response and survival associated with the use of CAR-T cell therapies in earlier rather than later lines of therapy. The use of CAR-T in earlier lines has also been supported by the observation of fewer CAR-T-related side effects and improved sensitivity to CAR-T therapy in patients with a lower disease burden, which minimizes the need for bridging therapies [23, 24]. All of this prompted the FDA approval of both cilta-cel and ide-cel as a treatment for RRMM in earlier lines, starting at the second line for cilta-cel after the failure of an IMiD and PI, and starting at the third line for ide-cel after the failure of IMiD, PI and anti-CD38 monoclonal antibody[17, 18]. Given recent approval, real-world data on the outcomes of patients who received Ide-cel or Cilta-

Field	Response
	cel in earlier lines of therapy is limited. With the wide range of available therapies in the 2nd and 3rd line settings, with varying toxicity profiles, the choice of optimal therapy in earlier lines is challenging. The CIBMTR registry is the largest data set till date with patients treated with CAR-T cell therapy for RRMM. This real-world data will help allow an indirect comparison (matched adjusted indirect comparison) of the efficacy and safety of CAR T in early versus later lines of therapy. We hypothesize, based on the above, that earlier use of cilta-cel or ide-cel would result in higher response rates, longer PFS, and OS, and less treatment-related side effects compared to later use (4th line and beyond).
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	Inclusion Criteria: -Patients with RRMM patients treated with standard-of-care idecabtagene viculeucel or ciltacabtagene autoleucel. -Patients have at least one follow-up timepoint completed in the database or have experienced mortality before the first follow-up. Exclusion Criteria: Patients treated with Cilta-cel or Ide-cel as part of registration clinical trials.
Does this study include pediatric patients?	No
If this study does not include pediatric patients, please provide justification:	MM is not a disease of the pediatric patient population. Cilta-cel and Ide-cel are only approved for treatment of adult patients.

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.	<u>Patient related</u> •Age at CAR T-cell therapy •Gender: male vs. female •Race: Caucasian vs. African American vs. vs. Hispanic •Ethnicity: Hispanic or Latino vs. Non-Hispanic or non-Latino vs. non-resident of the U.S. •ECOG Performance status <u>Disease-related:</u> •Myeloma subtype: IgG versus IgA versus IgM versus light chain [kappa versus lambda] •High risk disease [del 17, 4;14, 14; 16] •Presence of 1q abnormalities (gain of 1q versus amplification 1q) •R-ISS at CAR-T infusion •Number of prior lines of chemotherapy: 1 vs 2 vs 4 or more •Prior therapy [lenalidomide, pomalidomide, bortezomib, carfilzomib, daratumumab]: Exposed versus refractory •Prior autologous transplant •History of extramedullary disease •Extramedullary disease prior to infusion •Bone marrow plasma cell percentage prior to infusion •Functionally high risk: yes or no •Disease status prior to infusion •Baseline markers (CRP, Ferritin, LDH) prior to infusion •Exposure to BCMA agent (commercial versus trial) •Exposure to GPRC5D agent (commercial versus trial) <u>CAR T-cell therapy related:</u> •CAR T product: ide-cel versus cilta-cel •Time from diagnosis to infusion •Time from leukapheresis to infusion •Use of bridging therapy •Type of bridging therapy: Chemotherapy versus radiotherapy versus both chemo and radiotherapy •Bridging chemotherapy regimen Reponse to bridging therapy •CAR-T cell dose •CRS: grade, onset,duration •ICANS: grade, onset, duration •Delyaed neurotoxicity (CN palsies, MNT) •IEC-HLH •Infections: onset, grade •Secondary malignancies •Use of tocilizumab

Field	Response
	•Use of corticosteroids •Persistent cytopenias at day +30 and day +90 •Use of G-CSF •Use of TPO agonists Use of stem cell boost •Response at 1 month,3-month, 6 months, 9 months, 12 months •Time from infusion to progression •Date of Death •Cause of death •Date of last contact We will work with CIBMTR statistician after receiving the initial set of data to better identify the possibility and feasibility of stratifying the above data by the specific line of therapy (Patients who received CAR-T after only 1 vs 2 vs 3 vs ≥4 lines of therapy). We would also work closely to better define and categorize the above variables in univariate and multivariate analyses
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	No PRO specific hypotheses
MACHINE LEARNING: Please indicate if the study requires methodology related to machine-learning and clinical predictions.	No machine learning
SAMPLE REQUIREMENTS: If the study requires biologic samples from the CIBMTR Repository, the proposal should also include: 1) A detailed description of the proposed testing methodology and sample requirements; 2) A summary of the investigator's previous e	No sample requirements
NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required.	No Non-CIBMTR data source

REFERENCES:	1. Rajkumar, S.V., Multiple myeloma: 2022 update on diagnosis, risk stratification, and management. American Journal of Hematology, 2022. 97(8): p. 1086-1107. 2. Attal, M., et al., Lenalidomide, Bortezomib, and Dexamethasone with Transplantation for Myeloma. New England Journal of Medicine, 2017. 376(14): p. 1311-1320. 3. Moreau, P., et al., Bortezomib, thalidomide, and dexamethasone with or without daratumumab before and after autologous stem-cell transplantation for newly diagnosed multiple myeloma (CASSIOPEIA): a randomised, open-label, phase 3 study. The Lancet, 2019. 394(10192): p. 29-38. 4. Facon, T., et al., Daratumumab plus Lenalidomide and Dexamethasone for Untreated Myeloma. New England Journal of Medicine, 2019. 380(22): p. 2104-2115. 5. Kumar, S.K., et al., Carfilzomib or bortezomib in combination with lenalidomide and dexamethasone for patients with newly diagnosed multiple myeloma without intention for immediate autologous stem-cell transplantation (ENDURANCE): a multicentre, open-label, phase 3, randomised, controlled trial. The Lancet Oncology, 2020. 21(10): p. 1317-1330. 6. Facon, T., et al., Oral ixazomib, lenalidomide, and dexamethasone for transplant-ineligible patients with newly diagnosed multiple myeloma. Blood, 2021. 137(26): p. 3616-3628. 7. Attal, M., et al., Isatuximab plus pomalidomide and low-dose dexamethasone versus pomalidomide and low-dose dexamethasone in patients with relapsed and refractory multiple myeloma (ICARIA-MM): a randomised, multicentre, open-label, phase 3 study. The Lancet, 2019. 394(10214): p. 2096-2107. 8. Shah, J.J., et al., Carfilzomib, pomalidomide, and dexamethasone for relapsed or refractory myeloma. Blood, 2015. 126(20): p. 2284-2290. 9. Siegel, D.S., et al., Improvement in Overall Survival With Carfilzomib, Lenalidomide, and Dexamethasone in Patients With Relapsed or Refractory Multiple Myeloma. Journal of Clinical Oncology, 2018. 36(8): p. 728-734. 10. Dimopoulos, M.A., et al., Daratumumab, Lenalidomide, and Dexamethasone for Multiple Myeloma. New England Journal of Medicine, 2016. 375(14): p. 1319-1331. 11. Dimopoulos, M.A., et al., Daratumumab plus pomalidomide and dexamethasone versus pomalidomide and dexamethasone alone in previously treated multiple myeloma (APOLLO): an open-label, randomised, phase 3 trial. The Lancet Oncology, 2021. 22(6): p. 801-812. 12. Moreau, P., et al., Isatuximab,

	carfilzomib, and dexamethasone in relapsed multiple myeloma (IKEMA): a multicentre, open-label, randomised phase 3 trial. The Lancet, 2021. 397(10292): p. 2361-2371. 13. Palumbo, A., et al., Daratumumab, Bortezomib, and Dexamethasone for Multiple Myeloma. New England Journal of Medicine, 2016. 375(8): p. 754-766. 14. Shah, N., et al., B-cell maturation antigen (BCMA) in multiple myeloma: rationale for targeting and current therapeutic approaches. Leukemia, 2020. 34(4): p. 985-1005. 15. FDA approves idecabtagene vicleucel for multiple myeloma. 2021; Available from: https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-idecabtagene-vicleucel-multiple-myeloma. 16. FDA approves ciltacabtagene autoleucel for relapsed or refractory multiple myeloma 2022; Available from: https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-ciltacabtagene-autoleucel-relapsed-or-refractory-multiple-myeloma. 17. CARVYKTI. 2024; Available from: https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/carvykti. 18. ABECMA (idecabtagene vicleucel). 2024; Available from: https://www.fda.gov/vaccines-blood-biologics/abecma-idecabtagene-vicleucel. 19. Munshi, N.C., et al., Idecabtagene Vicleucel in Relapsed and Refractory Multiple Myeloma. New England Journal of Medicine, 2021. 384(8): p. 705-716. 20. Berdeja, J.G., et al., Ciltacabtagene autoleucel, a B-cell maturation antigen-directed chimeric antigen receptor T-cell therapy in patients with relapsed or refractory multiple myeloma (CARTITUDE-1): a phase 1b/2 open-label study. The Lancet, 2021. 398(10297): p. 314-324. 21. Rodriguez-Otero, P., et al., Ide-cel or Standard Regimens in Relapsed and Refractory Multiple Myeloma. New England Journal of Medicine, 2023. 388(11): p. 1002-1014. 22. San-Miguel, J., et al., Cilta-cel or Standard Care in Lenalidomide-Refractory Multiple Myeloma. New England Journal of Medicine, 2023. 389(4): p. 335-347. 23. Anderson, L.D., Jr., et al., Chimeric Antigen Receptor T Cell Therapy for Myeloma: Where Are We Now and What Is Needed to Move Chimeric Antigen Receptor T Cells Forward to Earlier Lines of Therapy? Expert Panel Opinion from the American Society for Transplantation and Cellular Therapy. Transplant Cell Ther, 2024. 30(1): p. 17-37. 24. Dhakal, B., Chimeric Antigen Receptor T-

Field	Response
	cell Therapy for First Relapse in Multiple Myeloma: A Promising Strategy Hematologist, 2024.
CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning?	None of the investigators 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.	No COI

PROP 2410-71; 2410-210; 2410-228: Real-World Safety, Efficacy, and Outcomes of Cilta-cel and Ide-cel Treatment in Earlier Lines for Patients with Relapsed or Refractory Multiple Myeloma (H Hashmi/ S Mailankody/ S Usmani/ A Bidikian/ L Gowda/ N Abdallah/ S Gupta)

Table: Characteristics of patients with Relapsed or Refractory Multiple Myeloma treated with Cilta-cel and Ide-cel in earlier vs later lines, and reported to the CIBMTR

Characteristic	Earlier (1-3 prior lines)	Later (4+ prior lines)	Total
No. of patients	170	1923	2093
No. of centers	63	81	85
Patient-related			
Age, by decades - no. (%)			
Median (min-max)	67 (35-84)	65 (29-90)	66 (29-90)
20-29	0 (0)	1 (0)	1 (0)
30-39	2 (1)	15 (1)	17 (1)
40-49	11 (6)	111 (6)	122 (6)
50-59	39 (23)	417 (22)	456 (22)
60-69	63 (37)	808 (42)	871 (42)
70+	55 (32)	571 (30)	626 (30)
Recipient Sex - no. (%)			
Male	93 (55)	1096 (57)	1189 (57)
Female	77 (45)	827 (43)	904 (43)
Recipient race - no. (%)			
White	123 (72)	1515 (79)	1638 (78)
African-American	38 (22)	271 (14)	309 (15)
Asian	2 (1)	50 (3)	52 (2)
Pacific Islander	0 (0)	6 (0)	6 (0)
Native American	2 (1)	4 (0)	6 (0)
More than one race	1 (1)	8 (0)	9 (0)
Not reported	4 (2)	69 (4)	73 (3)
Ethnicity - no. (%)			
Hispanic or Latino	8 (5)	166 (9)	174 (8)
Non-Hispanic or Latino	158 (93)	1707 (89)	1865 (89)
Non-resident of the U.S.	2 (1)	4 (0)	6 (0)
Not reported	2 (1)	46 (2)	48 (2)
Karnofsky performance score prior to CT - no. (%)			
90-100	62 (36)	745 (39)	807 (39)
80	65 (38)	686 (36)	751 (36)
< 80	31 (18)	332 (17)	363 (17)
Not reported	12 (7)	160 (8)	172 (8)
HCT-CI Score - no. (%)			

Characteristic	Earlier (1-3 prior lines)	Later (4+ prior lines)	Total
0	43 (25)	496 (26)	539 (26)
1	40 (24)	343 (18)	383 (18)
2	22 (13)	284 (15)	306 (15)
3	31 (18)	321 (17)	352 (17)
4	20 (12)	193 (10)	213 (10)
5+	13 (8)	274 (14)	287 (14)
Not reported	1 (1)	12 (1)	13 (1)
Disease-related			
Sub-disease - no. (%)			
Multiple myeloma, NOS	139 (82)	1426 (74)	1565 (75)
Multiple myeloma - light chain only	30 (18)	457 (24)	487 (23)
Multiple myeloma - non-secretory	1 (1)	40 (2)	41 (2)
Disease status prior to CT - no. (%)			
Stringent complete remission (sCR)	1 (1)	15 (1)	16 (1)
Complete remission (CR)	1 (1)	37 (2)	38 (2)
Very good partial remission (VGPR)	16 (9)	166 (9)	182 (9)
Partial response (PR) / Not Complete Remission	24 (14)	230 (12)	254 (12)
Stable disease (SD)	42 (25)	307 (16)	349 (17)
Progressive disease (PD)	83 (49)	1130 (59)	1213 (58)
Relapse from CR (Rel) (untreated)	3 (2)	33 (2)	36 (2)
Not reported	0 (0)	5 (0)	5 (0)
Treatment-related			
No. of lines of prior therapies (including HCT and CT) - no. (%)			
Median (min-max)	3 (1-3)	6 (4-20)	6 (1-20)
1	11 (6)	0 (0)	11 (1)
2	55 (32)	0 (0)	55 (3)
3	104 (61)	0 (0)	104 (5)
4	0 (0)	288 (15)	288 (14)
5	0 (0)	360 (19)	360 (17)
6	0 (0)	377 (20)	377 (18)
7	0 (0)	294 (15)	294 (14)
8	0 (0)	202 (11)	202 (10)
9	0 (0)	137 (7)	137 (7)
10	0 (0)	91 (5)	91 (4)
11	0 (0)	79 (4)	79 (4)
12	0 (0)	35 (2)	35 (2)
13	0 (0)	15 (1)	15 (1)
14	0 (0)	18 (1)	18 (1)
15	0 (0)	9 (0)	9 (0)
16	0 (0)	8 (0)	8 (0)

Characteristic	Earlier (1-3 prior lines)	Later (4+ prior lines)	Total
17	0 (0)	3 (0)	3 (0)
18	0 (0)	2 (0)	2 (0)
19	0 (0)	2 (0)	2 (0)
20	0 (0)	3 (0)	3 (0)
CAR-T Product - no. (%)			
Idecabtagene vicleucel	94 (55)	935 (49)	1029 (49)
Ciltacabtagene autoleucel	76 (45)	988 (51)	1064 (51)
Year of CT - no. (%)			
2021	23 (14)	242 (13)	265 (13)
2022	47 (28)	595 (31)	642 (31)
2023	77 (45)	859 (45)	936 (45)
2024	23 (14)	227 (12)	250 (12)
Follow-up of survivors, months - median (range)	12 (3-36)	12 (1-37)	12 (1-37)

**Data source: CT Extract November 2024*

Field	Response
Proposal Number	2410-74-MOHAN
Proposal Title	Trends In Utilization of a Delayed Autologous Transplant Approach (ASCT) In Newly Diagnosed Multiple Myeloma (NDMM)
Key Words	Delayed upfront ASCT, NDMM
Principal Investigator #1: - First and last name, degree(s)	Meera Mohan MD
Principal Investigator #1: - Email address	memohan@mcw.edu
Principal Investigator #1: - Institution name	Medical College of Wisconsin
Principal Investigator #1: - Academic rank	Assistant Professor of Medicine
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):	Carolina Schinke
Principal Investigator #2 (If applicable): - Email address:)	cdschinke@uams.edu
Principal Investigator #2 (If applicable): - Institution name:	University of Arkansas for Medical Sciences
Principal Investigator #2 (If applicable): - Academic rank:	Associate Professor of Medicine
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.	-
Do any of the PI(s) within this proposal have a CIBMTR WC study in manuscript preparation >6 months?	No
PROPOSED WORKING COMMITTEE:	Plasma Cell Disorders
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:	-
RESEARCH QUESTION:	The objective of this study is to understand the trends in the utilization of delayed ASCT, long-term clinical outcome and possibly identify the subset of patients that benefit from this approach.

Field	Response
RESEARCH HYPOTHESIS:	Randomized control trials comparing an early versus delayed ASCT in the era of PIs and IMiDs have consistently showed progression free survival (PFS) benefit with an early ASCT approach while the differences in overall survival (OS) have been inconsistent(1). Availability of newer induction regimens with a favorable side effect profile, that induces a deeper and faster response coupled with the enormity of salvage therapeutic options rationalize such a delayed ASCT approach in at least a subset of patients. The real-world utilization of this approach is largely unknown. We hypothesis that there is an increasing trend towards a delayed ASCT approach in NDMM patients in the current era of novel agents and anti-CD38 monoclonal antibodies. The objective of this study is to understand the trends in the utilization of delayed ASCT, long-term clinical outcome and possibly identify the subset of patients that benefit from this approach.
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	Specific Aims: 1.Estimate the trends in utilization of a delayed ASCT approach in NDMM. Delayed ASCT will be defined as patients who have upfront stem cell collection but underwent first ASCT in NDMM ≥ 1 years from diagnosis. 2.Analyse the clinical parameters in this group of patients including age, gender, race/ethnicity, ISS stage, cytogenetic risk at diagnosis, type of induction therapy and duration of treatment, timing of stem cell collection and dose, myeloma disease response pre-ASCT, duration of pre-ASCT remission, HCT CI, use of post-ASCT therapy, time of next progression and overall survival . 3. Compare clinical characteristics and outcomes of the group that received delayed ASCT and compare with previously published data from an upfront ASCT approach (as in BMT CTN Protocol 0702).
SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.	There is emerging data to support the use of a delayed autologous HCT approach in patients with NDMM. The reasons for this vary from patients/ physician preference, disease status, availability of newer induction regimens that induce a deeper and sustained response, perception that delayed ASCT in the current era has insignificant consequence on OS, which is the ultimate determinant of clinical efficacy of any given treatment. The prospects of a salvage ASCT likely explains the lack of OS, nonetheless, in a subset of these patients a delayed ASCT is not feasible due worsening medical co morbidities, aggressive clinical relapse etc. While several real-world studies have showed the feasibility of delayed ASCT, it is not clear which subgroup of patients can benefit the most from a delayed ASCT(2, 3). This data will inform patients and physicians the trends, clinical characteristics, potential impact of a delayed ASCT approach and potentially identify subset of patients where such an approach is most beneficial.

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.	We hypothesis that there is increasing trend towards a delayed ASCT approach in NDMM patients in the current era of novel agents. There is an existing knowledge gap in identifying the subset of patients in whom a planned delayed ASCT approach is most beneficial. The proposed study will provide the much need real-world data on utilization, outcome of this approach in the current era of novel agents and upfront anti-CD38 therapeutics and perhaps identify a subset of patients in whom this approach can be adopted without any adverse clinical outcomes.
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	1.Diagnosis of MM 2.First autologous HCT performed in the United States between 2008 and 2015 and collected stem cell collection upfront but underwent ASCT ≥ 1 years from initial diagnosis. 3.Follow-up including disease progression until death or last follow up documented in 2019
Does this study include pediatric patients?	No
If this study does not include pediatric patients, please provide justification:	-
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.	-
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	-
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.	BMT CTN Protocol 0702 (Specifically patients randomized to lenalidomide maintenance after planned upfront ASCT -arm B of the study)

Field	Response
REFERENCES:	1. Attal M, Lauwers-Cances V, Hulin C, Leleu X, Caillot D, Escoffre M, et al. Lenalidomide, Bortezomib, and Dexamethasone with Transplantation for Myeloma. The New England journal of medicine. 2017;376(14):1311-20. 2. Kumar SK, Lacy MQ, Dispenzieri A, Buadi FK, Hayman SR, Dingli D, et al. Early versus delayed autologous transplantation after immunomodulatory agents-based induction therapy in patients with newly diagnosed multiple myeloma. Cancer. 2012;118(6):1585-92. 3. Dunavin NC, Wei L, Elder P, Phillips GS, Benson DM, Jr., Hofmeister CC, et al. Early versus delayed autologous stem cell transplant in patients receiving novel therapies for multiple myeloma. Leukemia & lymphoma. 2013;54(8):1658-64.
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.	-

PROP 2410-74: Trends In Utilization of a Delayed Autologous Transplant Approach (ASCT) In Newly Diagnosed Multiple Myeloma (NDMM) (M Mohan/ C Schinke)

Table: Characteristics of adult patients who underwent Delayed Autologous Transplant Approach (ASCT) for Newly Diagnosed Multiple Myeloma (NDMM) between 2008 - 2024, and reported to the CIBMTR

Characteristic	N (%)
No. of patients	21337
No. of centers	307
Patient-related	
Patient age - median (min-max)	62.2 (18.7-86.2)
Age, by decades - no. (%)	
10-19	2 (0.0)
20-29	29 (0.1)
30-39	335 (1.6)
40-49	1937 (9.1)
50-59	6362 (29.8)
60-69	9656 (45.3)
70+	3016 (14.1)
Sex - no. (%)	
Male	12152 (57.0)
Female	9185 (43.0)
Center region - no. (%)	
US	18517 (86.8)
Canada	477 (2.2)
Europe	413 (1.9)
Asia	224 (1.0)
Australia/New Zealand	109 (0.5)
Mideast/Africa	173 (0.8)
Central/South America	1423 (6.7)
Not reported	1 (0.0)
Race - no. (%)	
White	14056 (65.9)
Black or African American	4342 (20.3)
Asian	653 (3.1)
Native Hawaiian or other Pacific Islander	41 (0.2)
American Indian or Alaska Native	121 (0.6)
More than one race	193 (0.9)
Not reported	1931 (9.1)
Ethnicity - no. (%)	
Hispanic or Latino	2614 (12.3)

Characteristic	N (%)
Not Hispanic or Latino	16349 (76.6)
Non-resident of the U.S.	1920 (9.0)
Not reported	454 (2.1)
Research Track - no. (%)	
CRF	1831 (8.6)
TED	19506 (91.4)
HCT-CI - no. (%)	
0	6347 (29.7)
1	2882 (13.5)
2	3341 (15.7)
3	3407 (16.0)
4	2105 (9.9)
5+	2845 (13.3)
Not reported	410 (1.9)
Karnofsky score prior to HCT - no. (%)	
90-100%	11501 (53.9)
< 90%	9302 (43.6)
Not reported	534 (2.5)
Disease-related	
Sub-disease classification - no. (%)	
Multiple myeloma, NOS	5194 (24.3)
TED Multiple myeloma-IgG	9331 (43.7)
TED Multiple myeloma-IgA	2666 (12.5)
TED Multiple myeloma-IgD	73 (0.3)
TED Multiple myeloma-IgE	4 (0.0)
Multiple myeloma-IgM	80 (0.4)
TED Mult myeloma-light chain	3651 (17.1)
TED Mult myeloma-non-secretory	338 (1.6)
Disease status prior to transplant - no. (%)	
sCR/CR	2975 (13.9)
VGPR	6922 (32.4)
PR	8287 (38.8)
SD	1636 (7.7)
PD/Relapse	1283 (6.0)
Not reported	234 (1.1)
Transplant-related	
Conditioning regimen - no. (%)	
TBI/Cy	1 (0.0)
TBI/Mel	8 (0.0)
TBI/other(s)	1 (0.0)

Characteristic	N (%)
Bu/Cy	27 (0.1)
Bu/Mel	86 (0.4)
Flu/Bu	1 (0.0)
Flu/Mel	2 (0.0)
Cy alone	6 (0.0)
BEAM	50 (0.2)
BEAM like	13 (0.1)
Mel alone	19947 (93.5)
Mel/other(s)	647 (3.0)
Other(s)	39 (0.2)
None	10 (0.0)
Missing	499 (2.3)
Interval from diagnosis to HCT, months - median (min-max)	19.5 (12.0-899.5)
Interval from diagnosis to HCT, years - no. (%)	
1-<2	13164 (61.7)
2-<3	3359 (15.7)
3-<5	2643 (12.4)
5+	2171 (10.2)
Product type - no. (%)	
BM	31 (0.1)
PBSC	21267 (99.7)
Not reported	39 (0.2)
Year of transplant - no. (%)	
2008	881 (4.1)
2009	1066 (5.0)
2010	1267 (5.9)
2011	1276 (6.0)
2012	1337 (6.3)
2013	1252 (5.9)
2014	1272 (6.0)
2015	1318 (6.2)
2016	1363 (6.4)
2017	1371 (6.4)
2018	1388 (6.5)
2019	1319 (6.2)
2020	1394 (6.5)
2021	1485 (7.0)
2022	1524 (7.1)
2023	1501 (7.0)
2024	323 (1.5)

Characteristic	N (%)
Follow-up of survivors - median (range)	61.4 (0.0-194.4)

**Data source: HCT Essentials October 2024*

Field	Response
Proposal Number	2410-91-SHAIKH
Proposal Title	Treatment Paradigm of Monoclonal Gammopathy of Renal Significance
Key Words	MGRS, Stem cell transplant, outcomes, survival, eGFR, treatment
Principal Investigator #1: - First and last name, degree(s)	Hira Shaikh, MD
Principal Investigator #1: - Email address	hira-shaikh@uiowa.edu
Principal Investigator #1: - Institution name	University of Iowa Healthcare
Principal Investigator #1: - Academic rank	Assistant Professor
Junior investigator status (defined as ≤5 years from fellowship)	Yes
Do you identify as an underrepresented/minority?	Yes
Principal Investigator #2 (If applicable): - First and last name, degree(s):	Yvonne Efebera, MD MPH
Principal Investigator #2 (If applicable): - Email address:)	yvonne.efebera@ohiohealth.com
Principal Investigator #2 (If applicable): - Institution name:	OhioHealth
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?	Yes
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:	Hira Shaikh
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:	Plasma Cell Disorders
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:	Yvone Efebera

Field	Response
RESEARCH QUESTION:	1. Assess the frequency and outcomes of autologous stem cell transplant (ASCT) in the upfront management of monoclonal gammopathy of renal significance (MGRS) 2. Assess ORR and survival outcomes (PFS and OS) in MGRS patients who received induction treatment that includes anti-CD38 monoclonal antibodies versus those who did not 3. Evaluate percentage of MGRS patients who used maintenance post ASCT 4. Estimate the frequency of dialysis at diagnosis 5. Assess the improvement in eGFR with treatment
RESEARCH HYPOTHESIS:	Patients receiving novel treatments such as anti-CD38 monoclonal antibodies have better outcomes compared to those who do not. Stem cell transplant is underutilized in the management of MGRS.
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	Primary - Overall response rate (ORR, hematological and renal), progression free survival (PFS) and overall survival (OS) in those who receive ASCT as upfront management of MGRS Co-primary - ORR to treatment and survival outcomes (PFS and OS) in MGRS patients who received induction including anti-CD38 monoclonal antibodies versus those who did not - Compare outcomes (ORR, PFS, and OS) in MGRS pts with maintenance vs no maintenance therapy after ASCT - Frequency of dialysis at diagnosis - Change in eGFR before and after ASCT Secondary - Effect of patient age at diagnosis, eGFR and proteinuria at diagnosis, MGRS type on hematological and renal response after treatment, and survival outcomes by univariate and multivariate analysis

Field	Response
SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.	The Term MGRS was not introduced until 2012 by International Kidney and Monoclonal Gammopathy Research Group (IKMG). 1 By definition, patients with MGRS have B-cell clones that do not meet the definition of other malignancy such as multiple myeloma or lymphoma. 1,2 The diagnosis of MGRS is established by kidney biopsy and immunofluorescence studies to identify the monotypic immunoglobulin deposits, in addition to light and electron microscopy. It is a heterogeneous disease, and can manifest as glomerular diseases, tubulopathies, and vascular involvement with varying clinical presentations. Diagnosis is often challenging and frequently delayed because of the wide spectrum of MGRS. It is difficult to establish a link between the presence of the M-protein or serum free light chains and kidney diseases, high incidence of MGUS and other etiologies of renal disease in the elderly. 2 Management of MGRS is indicated to preserve kidney function and prevent recurrence. Clone-directed therapy, which may include autologous stem cell transplantation (ASCT) in eligible patients, often results in improved outcomes. Achievement of ≥VGPR was generally predictive of a renal response (p < 0.0001). 3,4 Autologous stem cell transplantation led to better response than other treatments but is underutilized. 4,5 Mortality and morbidity with ASCT increases with the severity of renal impairment. 6
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.	MGRS is a rare disease and is frequently underdiagnosed, which makes it harder to do multi-institutional clinical trials in patients with this disease. It is excluded from majority of trials studying monoclonal plasma or B-cell disorders. There is no large database studying the management of MGRS. MGRS is associated with high morbidity due to the severity of renal damage (frequently permanent) and sometimes systemic lesions induced by the monoclonal immunoglobulin (MIg). Suppression of MIg secretion by chemotherapy can improve outcomes, hence early recognition and treatment is crucial. 7 There is no consensus on the management of MGRS, particularly the role of ASCT, choice of upfront therapy, maintenance after induction (or ASCT) and treatment for R/R disease. 8 Treatment recommendations are based on the clinical data obtained from treatment of this disorder or disorders closely resembling the type of MGRS.

Field	Response
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	Inclusion - Patients with age ≥18 years old with MGRS (with monoclonal plasma or B-cell clones that do not meet the definition of another malignancy, had hematopathological confirmation via a renal biopsy) diagnosed between January 2004 and December 2023, who received treatment. - At least 3 months follow up Exclusion - Patients with Multiple myeloma or Lymphoplasmacytic lymphoma - MGRS patients who did not receive treatment - MGRS patients without survival outcomes available
Does this study include pediatric patients?	No
If this study does not include pediatric patients, please provide justification:	-
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 data: 1. Age at diagnosis of MGRS 2. Gender 3. Race 4. Ethnicity 5. Any cytogenetic abnormality 6. KPS performance score at diagnosis and transplant 7. Comorbidity score 8. Co-existing diabetes 9. Co-existing hypertension Disease related data: 1. Type of MGRS 2. Clonal diagnosis (MGUS, Smoldering myeloma, etc) a. Heavy chain type (IgG, IgM, IgA, IgD, IgE) b. Light chain type (kappa or lambda) 3. Detectable serum/urine monoclonal protein and/or clonal light chain elevation at baseline and prior to transplant 4. eGFR and Cr at diagnosis, prior to transplant, and after transplant 5. Nephrotic or sub-nephrotic range proteinuria at diagnosis 6. Fanconi syndrome at diagnosis 7. Dialysis dependence 8. Treatment received Post-treatment data: 1. Best hematological response (CR, VGPR) at the end of induction therapy 2. Best renal response at the end of induction therapy 3. Best hematological response (CR, VGPR) day 100 post-transplant 4. Renal response day 100 post-transplant 5. Maintenance therapy after transplant 6. Best response after transplant (CR, PR, VGPR, SD) 7. Date of relapse or progression a. Type of progression (hematological, renal) 8. Date of death 9. Cause of death 10. Non-relapse mortality 11. Date of last follow up
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	None
MACHINE LEARNING: Please indicate if the study requires methodology related to machine-learning and clinical predictions.	None
SAMPLE REQUIREMENTS: If the study requires biologic samples from the CIBMTR Repository, the proposal should also include: 1) A detailed description of the proposed testing methodology and sample requirements; 2) A summary of the investigator's previous e	None
NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required.	None
REFERENCES:	renal significance: a consensus report of the International Kidney and Monoclonal Gammopathy Research Group. Nat Rev Nephrol. 2019;15(1):45-59. 2. Amaador K, Peeters H, Minnema MC, et al. Monoclonal gammopathy of renal significance (MGRS) histopathologic classification, diagnostic workup, and therapeutic options. Neth J Med. 2019;77(7):243-254. 3. Joly F, Cohen C, Javaugue V, et al. Randall-type monoclonal immunoglobulin deposition disease: novel insights from a nationwide cohort study. Blood. 2019;133(6):576-587. 4. Gozzetti A, Guarnieri A, Zamagni E, et al. Monoclonal gammopathy of renal significance (MGRS): Real-world data on outcomes and prognostic factors. Am J Hematol. 2022;97(7):877-884. 5. Stokes MB, Valeri AM, Herlitz L, et al. Light Chain Proximal Tubulopathy: Clinical and Pathologic Characteristics in the Modern Treatment Era. J Am Soc Nephrol. 2016;27(5):1555-1565. 6. Irazabal MV, Eirin A, Gertz MA, et al. Acute kidney injury during leukocyte engraftment after autologous stem cell transplantation in patients with light-chain amyloidosis. Am J Hematol. 2012;87(1):51-54. 7. Bridoux F, Leung N, Hutchison CA, et al. Diagnosis of monoclonal gammopathy of renal significance. Kidney Int. 2015;87(4):698-711. 8. Fermand J-P, Bridoux F, Kyle RA, et al. How I treat monoclonal gammopathy of renal significance (MGRS). Blood. 2013;122(22):3583-3590.

Field	Response
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.	-

PROP 2410-91: Treatment Paradigm of Monoclonal Gammopathy of Renal Significance (H Shaikh/ Y Efebera)

Table: Characteristics of adult patients who underwent autologous HCT for Monoclonal Gammopathy of Renal Significance (MGRS) between 2013 - 2024, and reported to the CIBMTR

Characteristic	N (%)
No. of patients	53
No. of centers	28
Patient-related	
Patient age - median (min-max)	59.6 (23.5-74.5)
Age, by decades - no. (%)	
20-29	2 (3.8)
30-39	1 (1.9)
40-49	9 (17.0)
50-59	17 (32.1)
60-69	18 (34.0)
70+	6 (11.3)
Sex - no. (%)	
Male	36 (67.9)
Female	17 (32.1)
Center region - no. (%)	
US	48 (90.6)
Canada	3 (5.7)
Asia	2 (3.8)
Race - no. (%)	
White	41 (77.4)
Black or African American	4 (7.5)
Asian	3 (5.7)
Not reported	5 (9.4)
Ethnicity - no. (%)	
Hispanic or Latino	3 (5.7)
Not Hispanic or Latino	43 (81.1)
Non-resident of the U.S.	5 (9.4)
Not reported	2 (3.8)
Research Track - no. (%)	
CRF	6 (11.3)
TED	47 (88.7)
HCT-CI - no. (%)	
0	8 (15.1)
1	7 (13.2)
2	8 (15.1)

Characteristic	N (%)
3	10 (18.9)
4	5 (9.4)
5+	15 (28.3)
Karnofsky score prior to HCT - no. (%)	
90-100%	37 (69.8)
< 90%	16 (30.2)
Disease-related	
Sub-disease - no. (%)	
Light chain fanconi syndrome	3 (5.7)
Proximal tubulopathy without crystals	6 (11.3)
Immunotactoid glomerulopathy (ITGN) / (GOMMID)	1 (1.9)
Type 1 cryoglobulinemic glomerulonephritis	9 (17.0)
Proliferative glomerulonephritis with monoclonal immunoglobulin G deposits (PGNMID)	11 (20.8)
C3 glomerulopathy with monoclonal gammopathy	2 (3.8)
Not reported	21 (39.6)
Disease status prior to HCT - no. (%)	
sCR/CR	1 (1.9)
VGPR	3 (5.7)
PR	10 (18.9)
SD	8 (15.1)
Not reported	31 (58.5)
Transplant-related	
Conditioning regimen - no. (%)	
Melphalan alone	52 (98.1)
Not reported	1 (1.9)
Product type - no. (%)	
PBSC	53 (100)
Year of current transplant - no. (%)	
2013	1 (1.9)
2014	3 (5.7)
2015	3 (5.7)
2016	4 (7.5)
2017	3 (5.7)
2018	5 (9.4)
2019	7 (13.2)
2020	2 (3.8)
2021	7 (13.2)
2022	6 (11.3)
2023	11 (20.8)
2024	1 (1.9)

Characteristic	N (%)
Follow-up of survivors - median (range)	26.8 (3.7-120.2)

**Data source: HCT Essentials October 2024*

Field	Response
Proposal Number	2410-93-DIMA
Proposal Title	Outcomes of Out-of-specification BCMA-directed Chimeric antigen receptor (CAR) T-cell therapies in patients with Heavily Pretreated Relapsed/Refractory Multiple Myeloma
Key Words	BCMA-targeted CAR-T therapy; idecabtagene vicleucel; ciltacabtagene autoleucel, Out-of-specification products, multiple myeloma, Real-world data
Principal Investigator #1: - First and last name, degree(s)	Danai Dima
Principal Investigator #1: - Email address	danaid@uw.edu
Principal Investigator #1: - Institution name	University of Washington
Principal Investigator #1: - Academic rank	Assistant Professor
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):	Doris Hansen
Principal Investigator #2 (If applicable): - Email address:)	doris.hansen@moffitt.org
Principal Investigator #2 (If applicable): - Institution name:	Moffitt Cancer Center
Principal Investigator #2 (If applicable): - Academic rank:	Assistant Member
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:	Danai Dima
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.	Doris Hansen 2023: - CIBMTR Study MM24-01: Safety and efficacy of ciltacabtagene autoleucel in patients with relapsed or refractory multiple myeloma - CIBMTR Study MM24-02: Real-world comparison of anti-BCMA CAR T-cell therapies in relapsed or refractory multiple myeloma Danai Dima - CIBMTR Study MM24-01: Safety and efficacy of ciltacabtagene in patients with relapsed or refractory multiple myeloma
Do any of the PI(s) within this proposal have a CIBMTR WC study in manuscript preparation >6 months?	Yes

Field	Response
PROPOSED WORKING COMMITTEE:	Plasma Cell Disorders
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:	-
RESEARCH QUESTION:	Outcomes of Out-of-specification anti-BCMA CAR T products in a real-world setting
RESEARCH HYPOTHESIS:	Hypothesis 1: Out-of-specification BCMA-directed CAR T cell products will demonstrate non-inferior clinical outcomes, including overall response rates (ORR), progression-free survival, and overall survival, compared to standard of care CAR T cell products in patients with relapsed or refractory multiple myeloma. Hypothesis 2: Out-of-specification standard of care idecabtagene vicleucel and ciltacabtagene autoleucel will maintain an acceptable safety profile, similar to in-specification products without any new red flags or unexpected toxicities These hypotheses propose that despite not meeting standard manufacturing specifications, the out-of-specification CAR T products may still provide non-inferior treatment for multiple myeloma, without compromising patient safety or efficacy.

Field	Response
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	PRIMARY 1. Response Rate (ORR): Compare the ORR between patients treated with out-of-specification (OOS) and in-specification CAR T cell products. ORR includes complete response (CR), very good partial response (VGPR), and partial response (PR). 2. Progression-Free Survival (PFS): Assess and compare the median PFS between the OOS and the in-specification groups. Determine if the two groups have a significant difference in time to progression or relapse. 3. Explore predictors of OOS manufacture. In detail, evaluate if specific patient, disease, and treatment-related factors are independently associated with OOS manufacture. SECONDARY 1. Manufacturing and product characteristics (if available): Investigate the specific manufacturing deviations (e.g., cell viability, dose, expansion kinetics) and correlate them with clinical outcomes in patients treated with OOS products. 2. Duration of Response (DoR) and Overall Survival (OS): Compare DoR and OS between patients receiving OOS versus in-specification CAR T cell therapies 3. Minimal Residual Disease (MRD) Negativity Rate: Evaluate the proportion of patients who achieve MRD negativity in both groups. 4. Evaluate Safety: Compare the incidence and severity of adverse events, including cytokine release syndrome (CRS), and immune effector cell-associated neurotoxicity syndrome (ICANS), and hematologic toxicities between the OOS and in-specification product groups. Analyze treatment-related and non-relapse mortality between the two groups.

Field	Response
SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.	The evaluation of OOS CAR T cell products (idecabtagene vicleucel or ciltacabtagene autoleucel) in a real-world setting has the potential to significantly impact the field by addressing a critical gap in the current understanding of product variability and its effects on clinical outcomes. Specifically, our study could enhance CAR T cell manufacturing practices. By systematically studying the clinical outcomes of patients receiving OOS CAR T, our proposed study could provide valuable data on the acceptable range of manufacturing deviations, leading to more flexible manufacturing guidelines without compromising patient safety or efficacy, and without needing time-consuming FDA approval process each time an OOS product is planned to be administered to patients. Identifying that OOS products perform comparably to in-specification products could reduce product wastage, expand access to therapy, and optimize resource utilization. In addition, if OOS products are shown to maintain non-inferiority with regard to efficacy with an acceptable safety profile, this study could lead to faster deployment of CAR T therapy in clinical practice, reducing delays for patients awaiting re-manufacture of a new product due to minor deviations. Lastly, the findings from this study could help inform regulatory bodies such as the FDA or EMA about acceptable ranges of product specifications. Overall, our study has the potential to enhance our understanding on efficacy and safety of OOS product, thus improve patient outcomes and reduce treatment costs and unnecessary re-manufactures.

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.	Despite recent advances, patients with relapsed/refractory multiple myeloma (RRMM) face limited treatment options, particularly after failing standard therapies. BCMA-directed CAR T has emerged as a highly effective option for this population, showing remarkable response rates and survival outcomes. Idecabtagene vicleucel was the first product to be approved by the FDA in 2021, followed by ciltacabtagene autoleucel in 2022. However, the production of CAR T cells is complex, and achieving perfect manufacturing conditions can be challenging, leading to the generation of OOS products that do not meet standard release criteria. Given the urgency of treating patients, re-manufacturing is often not feasible due to the rapid progression of the disease. Evaluation of OOS CAR T cell products is justified by the need to optimize the availability and use of CAR T therapies, particularly in the context of manufacturing challenges and disease urgency. CAR T cell manufacturing processes involve multiple steps, including T cell collection, transduction, expansion, and quality control, each of which can be subject to variability. OOS products may exhibit deviations in key parameters like cell viability, dose, or expansion kinetics, which currently lead to product rejection. However, there is limited evidence to date to suggest that these OOS products are inherently ineffective. Small deviations may not significantly impact clinical efficacy or safety, yet they lead to product wastage and delays in treatment. Rejecting OOS CAR T products contributes to substantial manufacturing costs, treatment delays, and product shortages, which may deny patients timely access to life-saving therapies. By evaluating the clinical utility of OOS products, this study could inform clinical practice about potentially more flexible release criteria, thereby optimizing the manufacturing process and reducing waste. A systematic evaluation of these products, thus, is necessary to determine if certain deviations can still result in non-inferiority. Current clinical and regulatory guidelines mandate that the OOS products that do not meet FDA release criteria need an expanded protocol access, a process that can be time-consuming and complicated for the care teams. To date, there is scarce data regarding OOS CAR T products. Notably, the OOS rate of ciltacabtagene autoleucel in the CARTITUDE-1 clinical trial, that led to its approval, was 17% per the drug package insert. Notably, the FDA specification for ciltacabtagene autoleucel is narrower than the product release criteria used in CARTITUDE-1. A recent study by Sidana et al (Blood 2024) assessing

Field	Response
	real-world outcomes of standard-of-care ciltacabtagene autoleucel reported that 19% of all included patients received OOS products. Patients who received an OOS/non-conforming product were more likely to have a history of autologous transplant, receipt of prior bispecific antibody, higher baseline ferritin, and higher baseline CRP (3.4 vs. 1.9 mg/L, p=0.008) compared to patients who received an in-specification/ conforming CART product. However, efficacy and survival outcomes between the OOS and in-specification groups were not included. Taken together all the above, our proposal is important in addressing this knowledge gap and provide rigorous data on the safety and efficacy of OOS CAR T products.
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	Inclusion criteria: 1. Patients with relapsed/refractory myeloma who have received idecabtagene vicleucel or ciltacabtagene autoleucel in a real-world setting 2. Patient age greater than or equal to 18 years Exclusion criteria: 1. Patients who received idecabtagene vicleucel, or ciltacabtagene autoleucel in the setting of a clinical trial.
Does this study include pediatric patients?	No
If this study does not include pediatric patients, please provide justification:	not applicable

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.	1. Baseline patient characteristics Age at diagnosis Age at infusion Gender Race/Ethnicity Date of multiple myeloma diagnosis Disease type (IgG, IgA, IgM, IgD, IgE, light chain only, non-secretory) Light chain type (kappa, lambda, ...) Disease status at the time of infusion Comorbidities/comorbidity Index score Cytogenetic by karyotype (conventional) Cytogenetic by FISH International Staging System (ISS) Revised ISS History of autologous or allogeneic hematopoietic stem cell transplantation (HCT) Date of HCT 2. Treatments prior to CAR-T infusion Types of Treatments Refractoriness status Number of Prior Lines of Therapy Date therapy started Date therapy stopped Best response to prior lines of therapy Relapse/progress following line of therapy Date to relapse/progression Disease status at the last evaluation prior to CAR T infusion 3. Laboratory value At the time of infusion (and prior to chemodepletion) White cell blood count Hemoglobin Platelet count Plasma cells in bone marrow aspirate and biopsy or unknown source Serum albumin Serum beta 2 microglobulin Serum calcium Serum creatinine Creatinine clearance (collected at CIBMTR since 9/2022) Serum monoclonal protein (M-spike) Serum immunofixation Urinary monoclonal light chains Urine immunofixation Serum free light changes (kappa, lambda, ratio) LDH and upper limit of normal for LDH Quantitative immunoglobulins (IgG, IgA, IgM) MRD status, and method of MRD assessment CAR T product specific characteristics (if available, cell viability, dose, expansion kinetics) 4. Outcome data Incidence and severity of cytokine release syndrome (CRS) Incidence and severity of immune effector cell–associated neurotoxicity syndrome (ICANS) Hematologic parameters post infusion (hemoglobin, neutrophils and platelets), at day 30, 60, 90 and 180, date ANC ≥500/mm3, date platelets ≥ 20 x 109/L Response at 100 days, 6 months, 1 year, 2 years, and >2 years (if available) Best response to CAR-T therapy Overall response rate (ORR) Duration of response (DOR) Event-free survival (EFS)

Field	Response
	Progression-free survival (PFS) Overall survival (OS) MRD status when available Incidence of Secondary primary malignancy Relapse or disease progression Site of progression Date of progression Date of death Cause of death 5. Maintenance treatment post CAR-T treatment (if applicable) Type of maintenance treatment Dose of medication Number of cycles of maintenance Date maintenance started Date maintenance stopped Cause of maintenance discontinuation Type of toxicity Best response to maintenance treatment with date of evaluation
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	not applicable
MACHINE LEARNING: Please indicate if the study requires methodology related to machine-learning and clinical predictions.	not applicable
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	not applicable
NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required.	not applicable

Field	Response
REFERENCES:	1. Berdeja JG, Madduri D, Usmani SZ, et al. Ciltacabtagene autoleucel, a B-cell maturation antigen-directed chimeric antigen receptor T-cell therapy in patients with relapsed or refractory multiple myeloma (CARTITUDE-1): a phase 1b/2 open-label study [published correction appears in Lancet. 2021 Oct 2;398(10307):1216. doi: 10.1016/S0140-6736(21)02132-2]. Lancet. 2021;398(10297):314-324. doi:10.1016/S0140-6736(21)00933-8 2. Munshi NC, Anderson LD Jr, Shah N, et al. Idecabtagene Vicleucel in Relapsed and Refractory Multiple Myeloma. N Engl J Med. 2021;384(8):705-716. doi:10.1056/NEJMoa2024850 3. Chong EA, Levine BL, Grupp SA, et al. CAR T cell viability release testing and clinical outcomes: is there a lower limit?. Blood. 2019;134(21):1873-1875. doi:10.1182/blood.2019002258 4. Rossoff J, Baggott C, Prabhu S, et al. Out-of-specification tisagenlecleucel does not compromise safety or efficacy in pediatric acute lymphoblastic leukemia. Blood. 2021;138(21):2138-2142. doi:10.1182/blood.2021012392 5. Mikhael J, Fowler J, Shah N. Chimeric Antigen Receptor T-Cell Therapies: Barriers and Solutions to Access. JCO Oncol Pract. 2022;18(12):800-807. doi:10.1200/OP.22.00315 6. Sidana S, Patel KK, Peres LC, et al. Safety and Efficacy of Standard of Care Ciltacabtagene Autoleucel for Relapsed/Refractory Multiple Myeloma. Blood. Published online October 4, 2024. doi:10.1182/blood.2024025945 7. FDA Package Insert JB, Inc: CARVYKTI (ciltacabtagene autoleucel). 2022 8. van der Walle CF, Godbert S, Saito G, Azhari Z. Formulation Considerations for Autologous T Cell Drug Products. Pharmaceutics. 2021;13(8):1317. Published 2021 Aug 23. doi:10.3390/pharmaceutics13081317
CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning?	Yes, I have 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.	Danai Dima: No conflicts of Interest Doris Hansen reports research funding from Bristol-Myers Squibb, Karyopharm, and Adaptive Biotech; Consulting or advisory role for Bristol Myers Squibb, Janssen, Legend Biotech, Pfizer, and Karyopharm.

PROP 2410-93: Outcomes of Out-of-specification BCMA-directed Chimeric antigen receptor (CAR) T-cell therapies in patients with Heavily Pretreated Relapsed/Refractory Multiple Myeloma (D Dima/ D Hansen)

Table: Characteristics of patients who received Out-of-specification BCMA-directed Chimeric antigen receptor (CAR) T-cell therapies for Relapsed/Refractory Multiple Myeloma and reported to the CIBMTR

Characteristic	In spec	Out of spec	Total
No. of patients	2751	237	2988
No. of centers	98	58	99
Patient-related			
Age, by decades - no. (%)			
Median (min-max)	66 (29-90)	66 (34-82)	66 (29-90)
20-29	1 (0)	0 (0)	1 (0)
30-39	22 (1)	4 (2)	26 (1)
40-49	156 (6)	16 (7)	172 (6)
50-59	581 (21)	45 (19)	626 (21)
60-69	1127 (41)	89 (38)	1216 (41)
70+	864 (31)	83 (35)	947 (32)
Recipient Sex - no. (%)			
Male	1588 (58)	135 (57)	1723 (58)
Female	1163 (42)	101 (43)	1264 (42)
Not reported	0 (0)	1 (0)	1 (0)
Recipient race - no. (%)			
White	2108 (77)	179 (76)	2287 (77)
African-American	427 (16)	40 (17)	467 (16)
Asian	74 (3)	6 (3)	80 (3)
Pacific Islander	6 (0)	0 (0)	6 (0)
Native American	8 (0)	1 (0)	9 (0)
More than one race	9 (0)	1 (0)	10 (0)
Not reported	119 (4)	10 (4)	129 (4)
Ethnicity - no. (%)			
Hispanic or Latino	212 (8)	13 (5)	225 (8)
Not Hispanic or Latino	2449 (89)	213 (90)	2662 (89)
Non-resident of the U.S.	24 (1)	2 (1)	26 (1)
Not reported	66 (2)	9 (4)	75 (3)
Karnofsky performance score prior to CT - no. (%)			
90-100	1032 (38)	75 (32)	1107 (37)

Characteristic	In spec	Out of spec	Total
80	968 (35)	94 (40)	1062 (36)
< 80	487 (18)	43 (18)	530 (18)
Not reported	264 (10)	25 (11)	289 (10)
HCT-CI Score - no. (%)			
0	714 (26)	66 (28)	780 (26)
1	489 (18)	49 (21)	538 (18)
2	417 (15)	30 (13)	447 (15)
3	448 (16)	35 (15)	483 (16)
4	296 (11)	25 (11)	321 (11)
5+	373 (14)	32 (14)	405 (14)
Not reported	14 (1)	0 (0)	14 (0)
Disease-related			
Sub-disease - no. (%)			
Multiple myeloma, NOS	2059 (75)	185 (78)	2244 (75)
Multiple myeloma - light chain only	642 (23)	51 (22)	693 (23)
Multiple myeloma - non-secretory	50 (2)	1 (0)	51 (2)
Disease status prior to CT for PCD - no. (%)			
Stringent complete remission (sCR)	22 (1)	1 (0)	23 (1)
Complete remission (CR)	46 (2)	4 (2)	50 (2)
Very good partial remission (VGPR)	256 (9)	32 (14)	288 (10)
Partial response (PR)/ Not Complete Remission	356 (13)	23 (10)	379 (13)
Stable disease (SD)	468 (17)	34 (14)	502 (17)
Progressive disease (PD)	1548 (56)	138 (58)	1686 (56)
Relapse from CR (Rel) (untreated)	49 (2)	5 (2)	54 (2)
Not reported	6 (0)	0 (0)	6 (0)
Treatment-related			
No. of lines of prior therapies (including HCT and CT) - no. (%)			
1	14 (1)	2 (1)	16 (1)
2	85 (3)	6 (3)	91 (3)
3	111 (4)	6 (3)	117 (4)
4	300 (11)	27 (11)	327 (11)
5	374 (14)	37 (16)	411 (14)
6	386 (14)	38 (16)	424 (14)
7	300 (11)	26 (11)	326 (11)
8	205 (7)	35 (15)	240 (8)
9	139 (5)	16 (7)	155 (5)
10	92 (3)	9 (4)	101 (3)

Characteristic	In spec	Out of spec	Total
11	79 (3)	11 (5)	90 (3)
12	36 (1)	1 (0)	37 (1)
13	15 (1)	3 (1)	18 (1)
14	18 (1)	5 (2)	23 (1)
15	9 (0)	1 (0)	10 (0)
16	8 (0)	0 (0)	8 (0)
17	3 (0)	1 (0)	4 (0)
18	2 (0)	0 (0)	2 (0)
19	2 (0)	0 (0)	2 (0)
20	3 (0)	1 (0)	4 (0)
Not reported	570 (21)	12 (5)	582 (19)
Lymphodepleting chemotherapy regimen - no. (%)			
Fludarabine + Cyclophosphamide	2084 (76)	214 (90)	2298 (77)
Bendamustine only	241 (9)	11 (5)	252 (8)
Others	425 (15)	12 (5)	437 (15)
None	1 (0)	0 (0)	1 (0)
CAR-T product - no. (%)			
Idecabtagene vicleucel	1554 (56)	73 (31)	1627 (54)
Ciltacabtagene autoleucel	1197 (44)	164 (69)	1361 (46)
Year of CT - no. (%)			
2018	2 (0)	0 (0)	2 (0)
2019	10 (0)	0 (0)	10 (0)
2020	45 (2)	0 (0)	45 (2)
2021	303 (11)	8 (3)	311 (10)
2022	748 (27)	86 (36)	834 (28)
2023	1270 (46)	104 (44)	1374 (46)
2024	373 (14)	39 (16)	412 (14)
Commercial vs. non-commercial CAR-T product - no. (%)			
Commercial	2658 (97)	194 (82)	2852 (95)
Non-commercial	93 (3)	43 (18)	136 (5)
Recipient participating in a cellular therapy clinical trial - no. (%)			
No	2629 (96)	27 (11)	2656 (89)
Yes	122 (4)	210 (89)	332 (11)
Follow-up of survivors, months - median (range)	12 (1-61)	12 (1-25)	12 (1-61)

**Data source: CT Extract November 2024*