Not for publication or presentation

A G E N D A
CIBMTR WORKING COMMITTEE FOR PLASMA CELL DISORDERS
Salt Lake City, UT
Thursday, February 5, 2026, 1:00 – 3:00 PM (MT)

Co-Chair:	**Heather Landau, MD; Memorial Sloan Kettering Cancer Center, New York, NY; E-mail: landauh@mskcc.org**
Co-Chair:	**Yvonne Efebera, MD, MPH; OhioHealth, Columbus, OH; E-mail: yvonne.efebera@ohiohealth.com**
Co-Chair:	**Taiga Nishihori, MBBS; Moffitt Cancer Center, Tampa, FL; E-mail: taiga.nishihori@moffitt.org**
Scientific Director:	**Othman Akhtar, MD, MBBS; CIBMTR® (Center for International Blood and Marrow Transplant Research), Milwaukee, WI; E-mail: oakhtar@mcw.edu**
Statistical Director:	**Tao Wang, PhD; CIBMTR® (Center for International Blood and Marrow Transplant Research), Milwaukee, WI; E-mail: taowang@mcw.edu**
Statistician:	**Temitope Oloyede, MPH, CPH; CIBMTR® (Center for International Blood and Marrow Transplant Research), Milwaukee, WI; E-mail: toloyede@mcw.edu**

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1. **Introduction**
   a. Minutes from last Tandem WC meeting in February 2025 (**Attachment 1**)

2. **Presentations, Publications or Submitted papers**
   a. **MM23-01a** Sidana S, Ahmed N, Akhtar OS, Brazauskas R, Oloyede T, Bye M, Hansen D, Ferreri C, Freeman CL, Afrough A, Anderson LD Jr., Dhakal B, Dhanda D, Gowda L, Hashmi H, Harrison MJ, Kitali A, Landau H, Mirza AS, Patwardhan P, Qazilbash M, Usmani S, Patel K, Nishihori T, Ganguly S, Pasquini MC. Standard-of-care idecabtagene vicleucel for relapsed/refractory multiple myeloma. **Blood. 2025 Jul 10; 146(2):167-177. doi:10.1182/blood.2024026216. Epub 2025 Apr 8.**
   b. **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 Submitted.***
   c. **MM24-01a** Safety and Efficacy of Ciltacabtagene Autoleucel for Relapsed/Refractory Multiple Myeloma: A CIBMTR Registry Study. (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/ T Nishihori/ H Mian/ M Mohan/ M Faisal). ***Manuscript Submitted. Poster Presentation, IMS 2025.***
   d. **MM24-01b** Efficacy and safety of frail adults treated with ciltacabtagene autoleucel in the real-world: A CIBMTR analysis (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/ T Nishihori/ H Mian/ M Mohan/ M Faisal). ***Manuscript Submitted. Oral Presentation, ASH 2025.***

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). ***Poster Presentation, IMS 2025.***

3. Studies in progress (**Attachment 2**)

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 to be updated/combined with 2025 study (to include Monoclonal Gammopathy of Renal Significance** (H Shaikh/ Y Efebera)**).**
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 Submitted.**
d. **MM24-01a** Safety and Efficacy of Ciltacabtagene Autoleucel for Relapsed/Refractory Multiple Myeloma: A CIBMTR Registry Study. (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/ T Nishihori/ H Mian/ M Mohan/ M Faisal). ***Manuscript Submitted.***
e. **MM24-01b** Efficacy and safety of frail adults treated with ciltacabtagene autoleucel in the real-world: A CIBMTR analysis (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/ T Nishihori/ H Mian/ M Mohan/ M Faisal). ***Manuscript Submitted*.**
f. **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.**
g. **MM25-01** 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/ H Hashmi/ S Mailankody/ S Usmani). **Protocol Development.**
h. **MM25-02** 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). **Protocol Development.**

4. Future/proposed studies

a. **PROP 2505-01; 2506-02; 2507-01; 2509-82; 2509-85; 2509-189** Comparative effectiveness of second line or later autologous stem cell transplantation versus CAR T cell therapy for relapsed multiple myeloma. (L Holmberg/ C Khouderchah/ J Kort/ L Shune/ A Afrough/ L Anderson/ L Liu/ M Janakiram) (**Attachment 3**)
b. **PROP 2508-07; 2509-80; 2509-92; 2509-106; 2509-111; 2509-172; 2509-174; 2509-226; 2509-233** Real World Comparative Effectiveness of Early versus Late CAR T-cell Therapy in Multiple Myeloma: A CIBMTR Analysis (S Zanwar/ M Ho/ K Lim/ S Adroja/ S Ganguly/ A Aljundi/ T Bahar/S Farhan/ H Hashmi/ N Abdallah/ A Bidikian/ J Cala Garcia/ A Afrough/ L Anderson/ M Janakiram/ L Liu) (**Attachment 4**)
c. **PROP 2509-01; 2509-03; 2509-42** Impact of Lenalidomide Alone vs. Lenalidomide + anti-CD38 Monoclonal Antibody Maintenance on Outcomes in Post-Autologous Stem Cell Transplant Patients with Multiple Myeloma (M Sanchez/ A Avila/ T Schmidt/ P Abraham/ A Afrough) (**Attachment 5**)

d. **PROP 2509-31; 2509-103; 2509-166; 2509-168; 2509-216** Role of stem cell transplant and maintenance therapy in the management of AL amyloidosis in the era of Daratumumab (H Shaikh/ E Muchtar/ S Maqbool/ F Answer/ Z Gong/ M S Faisal/ Y Efebera/ R Tokarski/ S Devarakonda) (**Attachment 6**)
e. **PROP 2509-74** INSIGHT-BCMA: AI-Enabled Risk & Outcome Modeling Using the CIBMTR Registry (C Freeman/ I El Naqa) (**Attachment 7**)
f. **PROP 2509-127** BCMA directed CAR-T cell therapy in plasma cell leukemia (N Sharma/ S Devarakonda) (**Attachment 8**)

Proposed studies; not accepted for consideration at this time

g. **PROP 2506-01** Outcomes of Myeloma patients who fail manufacturing of Ciltacabtagene autoleucel (Carvykti) (R Kamble). ***Dropped due to overlap with current study/publication.***
h. **PROP 2508-04** Validating IMS/IMWG beta-2 microglobulin thresholds for high-risk multiple myeloma in the modern era (R Banerjee). ***Dropped due to low scientific impact.***
i. **PROP 2508-12** Outcomes of patients with CKD undergoing CART for ALL/B-cell Lymphoma/MM – A CIBMTR analysis on outcomes and recommendations for practice approaches (N Hossain/ P Munshi). ***Dropped due to overlap with current study/publication and non-compliance with proposal submission guidelines.***
j. **PROP 2509-07** Impact of Prior Stem Cell Transplantation on CAR-T Therapy Outcomes in Multiple Myeloma: A CIBMTR Registry-based Analysis. (O Oyebanji/ T O'Brien). ***Dropped due to overlap with current study/publication.***
k. **PROP 2509-10** cyclin D1 - Is it truly standard risk in Myeloma? (M Ramanathan). ***Dropped due to low scientific impact.***
l. **PROP 2509-14** Patient-reported outcomes with CAR-T therapy and ASCT in myeloma (R Banerjee). ***Dropped due to small sample size.***
m. **PROP 2509-27** Clinical Outcomes Based on High-Risk Molecular Cytogenetics Defined by the IMS/IMWG Criteria in Patients with Multiple Myeloma Receiving Novel Agent-Based Induction Therapy and an Upfront Autologous Stem Cell Transplant. (M Mohan/ M Shah). ***Dropped due to low scientific impact.***
n. **PROP 2509-28** Clinical Outcomes by High-Risk Molecular Cytogenetics Defined by the IMS/IMWG Criteria in Patients with Multiple Myeloma Treated with BCMA-Directed Chimeric Antigen Receptor (CAR) T-Cell Therapy. (M Mohan/ C Schinke). ***Dropped due to overlap with current study/publication.***
o. **PROP 2509-34** Predictors of Durable Response to BCMA-Directed CAR-T Therapy in Relapsed/Refractory Multiple Myeloma (D Kaldas/ D Hansen). ***Dropped due to limited follow-up for assessment of durable response.***
p. **PROP 2509-35** Predicators of Treatment Related Mortality Following BCMA Directed CAR-T Therapy in Relapsed/Refractory Multiple Myeloma (D Kaldas/ D Hansen). ***Dropped due to overlap with current study/publication.***
q. **PROP 2509-55** Patient-Reported Outcome (PRO) Assessment of Patients Treated with BCMA targeting Chimeric Antigen Receptor (CAR) T-Cell Therapies in Patients with Multiple Myeloma (MM) (H Hashmi). ***Dropped due to small sample size.***
r. **PROP 2509-77** Assessing the Clinical Utility of the Cellular Therapy Comorbidity Index (CT-CI) Score in Predicting Outcomes for Myeloma Patients Treated with BCMA directed Chimeric Antigen Receptor (CAR) T-Cell Therapy (M Shah/ M Mohan). ***Dropped due to non-compliance with proposal submission guidelines.***
s. **PROP 2509-107** Challenging Depth of Response and Measurable Residual Disease Paradigms in t(11;14) Myeloma (S Zanwar/ S Kumar). ***Dropped due to low scientific impact.***

t. **PROP 2509-121** Safety and efficacy of CAR-T cell therapy in older adults with multiple myeloma (S Devarakonda/ L Shune). ***Dropped due to overlap with current study/publication.***
u. **PROP 2509-125** CAR-T cell therapy in multiple myeloma patients with CNS involvement (N Sharma/ S Devarakonda). ***Dropped due to need of supplemental data.***
v. **PROP 2509- 134** Real-World Safety and Efficacy of Anti-BCMA CAR-T Therapy for Systemic (AL) Amyloidosis (A Ravindra/ C Strouse). ***Dropped due to small sample size.***
w. **PROP 2509-160** Outcomes of HIV+ Patients undergoing Autologous HCT for Multiple Myeloma (H Murthy/ M Aldapt). ***Dropped due to low scientific impact.***
x. **PROP 2509-169** Impact of Anti-CD 38 Antibody Based Induction Therapy on Outcomes in Patients with Primary Plasma cell Leukemia (PCL) Undergoing Upfront Autologous Stem Cell Transplant (Auto-SCT) (Binoy). ***Dropped due to small sample size.***
y. **PROP 2509-184** Impact of Induction Therapy and Maintenance Therapy on Outcomes of Autologous Stem Cell Transplantation in POEMS Syndrome (J Kort/ L Shune). ***Dropped due to small sample size.***
z. **PROP 2509-200** Bispecific Antibodies vs Alkylator Therapy as Bridging Therapies for Patients with Relapsed Refractory Multiple Myeloma Undergoing CAR-T Cell Therapy. (M Sanchez/ A Avila). ***Dropped due to small sample size.***
aa. **PROP 2509-217** Outcomes of BCMA CAR-T after BCMA-directed Therapies (L Lee/ M Janakiram). ***Dropped due to overlap with current study/publication.***
bb. **PROP 2509-229** Real-world safety and efficacy of anti-BCMA CAR-T Therapy in patients with AL Amyloidosis (Z Gahvari/ N Callander). ***Dropped due to small sample size.***

5. Other business

MINUTES
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**
Scientific Director:	**Othman Akhtar, MD, MBBS; CIBMTR® (Center for International Blood and Marrow Transplant Research), Milwaukee, WI; E-mail: oakhtar@mcw.edu**
Statistical Director:	**Tao Wang, PhD; CIBMTR® (Center for International Blood and Marrow Transplant Research), Milwaukee, WI; Telephone: 414-955-4339; E-mail: taowang@mcw.edu**
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)

Dr. Kaur presented.

- *Comments included concerns that this topic may already be addressed in current studies, with limited novel contribution.*
- *There was a question regarding the availability of bridging therapy data, which was addressed by the Scientific Director.*
- ***Study Title:*** *Predictors of Early Relapse and Durable Remissions in Multiple Myeloma Treated with BCMA-Targeted CAR T-Cell Therapy*
- ***Hypothesis:*** *Identify predictors of early relapse (within 6 months) vs. late relapse*
- ***Objectives:*** *Assess patient-, disease-, product-, and treatment-related factors influencing response durability.*

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)

Dr. Liu presented.

- *Several comments highlighted the need to match for response and disease aggression.*
- *Concerns were raised regarding selection bias; it was suggested that the analysis match for time from first auto to CAR-T infusion.*
- ***Study Title:*** *Comparative Effectiveness Between Second Autologous Transplant and CAR T-Cell Therapy in Relapsed/Refractory Multiple Myeloma*
- ***Hypothesis:*** *BCMA-directed CAR T-cell therapy is superior to second autologous transplant.*

- ***Objectives:*** *Compare PFS, OS, and other outcomes in key subgroups.*

c. **PROP 2410-35** Impact of Autologous Stem Cell Transplantation on Outcomes with High-risk Multiple Myeloma (S Zanwar/ S Kumar) (Attachment 6)

Dr. Zanwar presented.
- *This was viewed as a good study, but concerns were raised that it may miss high-risk patients who do not make it to transplant.*
- ***Study Title:*** *Impact of Autologous Stem Cell Transplantation on Outcomes in High-Risk Multiple Myeloma*
- ***Hypothesis:*** *ASCT mitigates the negative prognostic impact of high-risk cytogenetics.*
- ***Objectives:*** *Compare PFS and OS in high-risk and ultra-high-risk patients vs. standard-risk patients.*

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)

Dr. Hashmi presented.
- *Questions were raised about whether to use CAR-HEMATOTOX or develop a new model.*
- *Clarification was sought on how many patients had complete data.*
- ***Study Title:*** *Inflammatory Biomarker Signature Predicts CAR T Treatment Failure in Multiple Myeloma*
- ***Hypothesis:*** *Inflammatory biomarker signature at time of infusion predicts treatment failure and severe toxicities.*
- ***Objectives:*** *Develop and validate a prediction model using accessible lab data.*

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)

Dr. Abraham presented.
- *Comments focused on comparisons between DARA alone, DARA+POM, and other maintenance regimens.*
- *Induction regimen from protocol 1803 was noted.*
- *There was interest in looking at PFS2, specifically among patients who started with LEN-only and later added DARA.*
- ***Study Title:*** *Impact of Lenalidomide vs. Lenalidomide Plus CD38 Monoclonal Antibody Maintenance on Outcomes Post-Autologous Stem Cell Transplant*
- ***Hypothesis:*** *Dual maintenance therapy improves outcomes over LEN alone.*
- ***Objectives:*** *Evaluate safety, efficacy, toxicity, and subgroup benefit.*

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)

Dr. Bidikian presented.
- *Comments noted small sample size.*
- *Observations were made that follow-up was longer than expected.*

- ***Study Title:*** *Real-World Safety, Efficacy, and Outcomes of Cilta-cel and Ide-cel in Earlier Lines of Treatment for Relapsed/Refractory Multiple Myeloma*
- ***Hypothesis:*** *CAR-T in earlier lines yields better efficacy and safety.*
- ***Objectives:*** *Compare response rates, PFS, OS, and adverse events between earlier vs. later lines of therapy.*

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)

Dr. Mohan presented.

- *Questions focused on lines of therapy and stem cell collection timing.*
- ***Study Title:*** *Trends in Utilization of Delayed Autologous Transplant in Newly Diagnosed Multiple Myeloma*
- ***Presented by:*** *Dr. Nishihori on behalf of Drs. Mohan and Shinky*
- ***Hypothesis:*** *Increasing trend toward delayed transplant with novel agents.*
- ***Objectives:*** *Estimate trends, analyze parameters, and compare outcomes with early transplant.*

h. **PROP 2410-91** Treatment Paradigm of Monoclonal Gammopathy of Renal Significance (H Shaikh/ Y Efebera) (Attachment 11)

Dr. Shaikh presented.

- *Questions were raised about merging with LCDD data.*
- *Multiple attendees suggested merging with the existing LCDD study.*
- *Need for CRF-level data was noted.*
- ***Study Title:*** *Treatment Paradigm of Monoclonal Gammopathy of Renal Significance (MGRS) Using the CIBMTR Database*
- ***Hypothesis:*** *ASCT is safe and effective in MGRS.*
- ***Objectives:*** *Assess safety, efficacy, and survival outcomes.*

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)

Dr. Dima presented.

- *Clarification needed regarding reasons for out-of-spec (OOS) designation and concerns that this data was not readily available.*
- ***Study Title:*** *Outcomes of Out-of-Spec BCMA-Directed CAR T-Cell Therapies in Heavily Pretreated Relapsed/Refractory Multiple Myeloma*
- ***Hypothesis:*** *OOS CAR-T products have inferior outcomes.*
- ***Objectives:*** *Evaluate ORR, PFS, OS, and safety of OOS vs. in-spec products.*

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

CIBMTR®
A RESEARCH COLLABORATION BETWEEN THE MEDICAL COLLEGE OF WISCONSIN AND NMDP

TO: Plasma Cell Disorders Working Committee Members

FROM: Othman Akhtar, MD; Scientific Director for the Plasma Cell Disorders Working Committee

RE: 2025-2026 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 update the dataset and re-assess feasibility by July 2026.

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: Protocol to be updated/combined with 2025 study (to include Monoclonal Gammopathy of Renal Significance (H Shaikh/ Y Efebera)). The goal is to complete data analysis by December 2026.

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: The manuscript has been submitted.

MM24-01a Safety and Efficacy of Ciltacabtagene Autoleucel for Relapsed/Refractory Multiple Myeloma: A CIBMTR Registry Study (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/ 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: The manuscript has been submitted.

MM24-01b Efficacy and safety of frail adults treated with ciltacabtagene autoleucel in the real world: A CIBMTR analysis (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 frail adult patients receiving cilta-cel in the real-world setting and to examine safety and efficacy outcomes of cilta-cel CAR T-cell therapy for relapsed/refractory multiple myeloma.

Status: The manuscript has been submitted.

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 publication by March 2026.

MM25-01 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/ H Hashmi/ S Mailankody/ S Usmani).
The aim of this study is to use an AI-based model to identify the predictors of early relapse.

Status: This study is in Protocol Development phase with the goal of proceeding to data analysis by May 2026.

MM25-02 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).
The primary objective of this study is to describe the demographic and clinical characteristics and evaluate clinical efficacy outcomes of patients receiving OOS cilta-cel products compared with in-specification (conforming) products administered as the intended standard of care for RRMM. The following outcomes will be assessed:

- Response rates based on IMWG response criteria
- Progression-free survival (PFS)

Status: This study is in Protocol Development phase. The goal is to complete analysis by March 2026.

Field	Response
Proposal Number	2507-01-LIU, 2509-85-LIU, 2505-01-HOLMBERG, 2506-02-HOLMBERG, 2509-189-KORT, PROP 2409-30; 2410-69; 2410-172; 2410-213.
Proposal Title	Comparative effectiveness of second line or later autologous stem cell transplantation versus BCMA CAR T cell therapy for relapsed multiple myeloma
Key Words	Salvage Autologous Stem Cell Transplant (ASCT),delayed autologous stem cell transplant, second autologous stem cell transplant, CAR-T, Ide-cel,idecabtagene, ABECMA, Cilta-cel, ciltacabtagene, CARVYKTI, Real-world data, autoHCT, autoSCT.
Principal Investigator #1: - First and last name, degree(s)	Lawrence Liu, MD
Principal Investigator #1: - Email address	lwliu3779@gmail.com
Principal Investigator #1: - Institution name	Cedars Sinai Medical Center
Principal Investigator #1: - Academic rank	Assistant Professor
Junior investigator status (defined as 𠳐、5 years from fellowship)	Yes
Do you identify as an underrepresented/minority?	No
Principal Investigator #2 (If applicable): - First and last name, degree(s):	Murali Janakiram, MD, MS
Principal Investigator #2 (If applicable): - Email address:)	mjanakiram@coh.org
Principal Investigator #2 (If applicable): - Institution name:	City of Hope
Principal Investigator #2 (If applicable): - Academic rank:	Associate Professor
Junior investigator status (defined as 𠳐、5 years from fellowship)	Yes
Do you identify as an underrepresented/minority?	No
We encourage a maximum of two Principal Investigators per study. If more than one author is listed, please indicate who will be identified as the corresponding PI below:	Murali Janakiram

Field	Response
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:	Previously submitted and presented but the main feedback was need for longer follow up time.
AUTHORS:	Lawrence Liu, Eden Biltibo, Christy Khouderchah, Yuliya Shestovska, Aimaz Afrough, Danai Dima, Jeries Kort, Leyla Shune, Leona Holmberg, Larry Anderson, Henry Fung, Asya Nina Varshavsky-Yanovsky, Adetola Kassim, Murali Janakiram.
RESEARCH QUESTION:	Are B-cell maturation antigen (BCMA) Chimeric antigen receptor (CAR) T-cell therapies (idecabtagene vicleucel [ide-cel] or ciltacabtagene autoleucel [cilta-cel]) superior to second-line or later high dose therapy (HDT)/autologous stem cell transplantation (ASCT) in relapsed or refractory multiple myeloma (RRMM) overall and in key subgroups?
RESEARCH HYPOTHESIS:	We hypothesize that second line or later cilta-cel will be associated with longer progression free survival compared to autoHCT and ide-cel for RRMM.

Field	Response
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	Primary Outcome: Progression free survival-1 (PFS1) Secondary Outcomes: ORR at 6 months ORR at 12 months 6-month PFS1 6-month OS 1-year PFS1 1-year OS 1-year NRM PFS2 Complete Response (CR) rate Duration of response (mDOR) Overall Survival (OS) Non-relapse mortality (NRM) 30-day mortality delayed neurotoxicity (parkinsonism, cranial nerve palsies, etc) Secondary primary malignancy Patient-reported outcomes (PRO) at baseline, Day 30, 100, 180, and 1 year

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.	I.Research comparing 2nd-line or later autoHCT versus CAR T (by individual product) using a large database is limited.The closest study to answer this question had only 63 CAR T patients and focused only on 2nd autoHCT versus CAR T (cilta-cel and ide-cel combined). II. Prior studies of salvage (second) autoHCT, compared to standard of care (SOC), demonstrated conflicting efficacy results. It is important to have a large population-based study to report on the efficacy and safety of either therapy with special attention to key subgroups to be able to be able to guide cellular therapy decisions. III.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. IV.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. V.Both autoHCT and CAR T are powerful and intensive therapies so it is important to know whether there is differential efficacy in key subgroups (early relapse, primary refractory disease, extramedullary disease [EMD], response status prior to index therapy, age) to guide clinical decisions. VI. It is important to understand safety and tolerability of these therapies. We will assess PROs in either therapy along with toxicities. Examine PROs collected under CIBMTR protocols (baseline, Day 30, 100, 180, and 1 year) as a secondary endpoint, assessing physical function, quality of life, and symptom burden.

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.	Prior studies of salvage (second) autoHCT compared to standard of care (SOC) demonstrated conflicting efficacy results. With CAR T therapy now occupying the same niche as salvage autoHCT with the same goal of being a salvage/consolidative strategy for relapsing disease, it is important to use a large database to compare their efficacy overall and in key subgroups to guide treatment decisions. This is a critical question that has not been answered with a large cohort of autoHCT and CAR T patients. 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 2nd-line or later autoHCT for a few reasons: 1) the SOC now includes CAR T, 2) there are much better triplet/quadruplet and even bispecific antibody 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 weaker (doublet only) salvage therapy [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 GMMG 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 delayed or salvage autoHCT versus SOC (CAR T) 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. It is also important to understand which key subgroups benefit the most from CAR T or autoHCT. 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

Field	Response
	bridge the gap in the understanding of safety and efficacy of newer therapies like CAR T cell therapy. Many studies have differences in treatment outcomes in MM with t(11;14). For example, prior studies have demonstrated better outcomes with first-line autoHCT. Other important subgroups are MM with high risk features (early relapse, primary refractory disease, EMD, response status prior to index therapy, age). As such, it will be important to understand the efficacy of 2nd-line or later autoHCT versus CAR T overall and in key subgroups to guide clinical decisions and treatment sequencing.

PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	Inclusion Criteria: Patients with MM: -who have history of one prior autoHCT and now have received ide-cel, cilta-cel, or second salvage autoHCT in the 2nd-line or later setting. -who received the cellular therapy of interest in 2016 or or later. -who have at least 1 year of follow-up data from the date of cellular therapy infusion. Exclusion Criteria: Patients who received allogeneic SCT before cellular therapy of interest. -Patients with amyloidosis. -Patients with two autoHCT within 12 months of each other without evidence of progression. -Patients without prior autoHCT. Exposure: -2nd-line or later autoHCT versus cilta-cel versus ide-cel. Stratification: -Overall -Primary Refractory Disease (defined as less than PR after frontline therapy). - ≤70 and >70 years old. -race/ethnicity -t(11;14) -IMS-IMWG high risk group -Functional high risk (relapse or progression ≤ 18 months of initial therapy) or primary refractory disease status. -presence of EMD -VGPR or better prior to index cellular therapy -autoHCT before cilta-cel versus cilta-cel before autoHCT Co-variables: -Prior autoHCT but no prior CAR T. -age -sex -race -ethnicity -t(11;14) -IMS-IMWG high risk group or High risk by [del(17p), t(14;16), t(4;14), t(14;20), amp 1q] -Functional high risk (relapse or progression ≤ 18 months of initial therapy) or primary refractory disease status.

Field	Response
	-presence of EMD -HCT-CI -KPS/ECOG -ISS -RISS -LDH -albumin -creatinine -BMPC % -prior lines of therapy -prior tandem autoHCT, single autoHCT, or no autoHCT -prior melphalan exposure (outside of autoHCT) -type of bridging, salvage, or re-induction therapy prior to index cellular therapy. -melphalan dose 140 vs 200 -response status prior to index cellular therapy Additional co-variables for OS and PFS2 analyses: -presence of autoHCT, CAR T or bispecific antibody therapy (BCMA, GPRC5D, FcRH5) following the index cellular therapy. Statistical Analysis: Inverse probability of treatment weighting, landmark analysis (by infusion date).
Does this study include pediatric patients?	No
If this study does not include pediatric patients, please provide justification:	Myeloma rarely occurs in pediatric population.

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.

Forms:
2400 4000 2402 2016 2450 4100 2116 3500

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					

Field	Response

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

PROs at baseline, Day 30, 100, 180, and 1 year

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

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	n/a
MACHINE LEARNING: Please indicate if the study requires methodology related to machine-learning and clinical predictions.	n/a
SAMPLE REQUIREMENTS: If the study requires biologic samples from the CIBMTR Repository, the proposal should also include: 1) A detailed description of the proposed testing methodology and sample requirements; 2) A summary of the investigator's previous e	n/a
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:	Goldschmidt H, et al. Salvage autologous transplant and lenalidomide maintenance vs. lenalidomide/dexamethasone for relapsed multiple myeloma: the randomized GMMG phase III trial ReLApsE. Leukemia. 2021 Apr;35(4):1134-1144. doi: 10.1038/s41375-020-0948-0. Baertsch MA, et al. Salvage Autologous Transplant and Lenalidomide Maintenance Versus Continuous Lenalidomide/Dexamethasone for Relapsed Multiple Myeloma: Long Term Follow up Results of the Randomized GMMG Phase III Multicenter Trial Relapse. Blood 2023; 142 (Supplement 1): 782. doi: https://doi.org/10.1182/blood-2023-178835 Attal M, et al. A prospective, randomized trial of autologous bone marrow transplantation and chemotherapy in multiple myeloma. Intergroupe Fran ais du My lome. N Engl J Med. 1996;335(2):91-97. Elice F, et al. Prolonged overall survival with second on-demand autologous transplant in multiple myeloma. Am J Hematol. 2006;81(6):426-431. doi:10.1002/ajh.20641 Atanackovic D, et al. Second autologous transplant as salvage therapy in multiple myeloma. Br J Haematol. 2013;163(5):565-572. doi:10.1111/bjh.12579 Shah N, et al. Durable remission with salvage second autotransplants in patients with multiple myeloma. Cancer. 2012;118(14):3549-3555. doi:10.1002/cncr.26662 Gossi U, et al. Prolonged survival after second autologous transplantation and lenalidomide maintenance for salvage treatment of myeloma patients at first relapse after prior autograft. Hematol Oncol. 2018;36(2):436-444. doi:10.1002/hon.2490 Cook G, et al. The effect of salvage autologous stem-cell transplantation on overall survival in patients with relapsed multiple myeloma (final results from BSBMT/UKMF Myeloma X Relapse [Intensive]): a randomised, open-label, phase 3 trial. Lancet Haematol. 2016;3(7):e340-e351. Cook G, et al. High-dose chemotherapy plus autologous stem-cell transplantation as consolidation therapy in patients with relapsed multiple myeloma after previous autologous stem-cell transplantation (NCRI Myeloma X Relapse [Intensive trial]): a randomised, open-label, phase 3 trial, The Lancet Oncology, 2014, https://doi.org/10.1016/S1470-2045 (14)70245-1. Andre A, et al. Impact of second autologous stem-cell transplantation at relapsed multiple myeloma: A French multicentric real-life study. Hemasphere. 2024;8(8):e106. Published 2024

	Jul 29. doi:10.1002/hem3.106 Badar T, et al. African Americans with translocation t(11;14) have superior survival after autologous hematopoietic cell transplantation for multiple myeloma in comparison with Whites in the United States. Cancer. 2020. https://doi.org/10.1002/cncr.33208 Bumma N, et al. Outcomes of Autologous Stem Cell Transplant (ASCT) in Patients with t(11;14) Multiple Myeloma (MM). Biol Blood Marrow Transplant. 2020;26(3). DOI: 10.1016/j.bbmt.2019.12.358. Neeraj Y, et al. Impact of t(11;14) on the Outcome of Autologous Transplantation in Multiple Myeloma: A Matched-Pair Analysis. Blood 2018; 132 (Supplement 1): 4607. doi: https://doi.org/10.1182/blood-2018-99 -116862 Gagelmann N, et al. Salvage Transplant Versus CAR-T Cell Therapy for Relapsed Multiple Myeloma. Blood 2023; 142 (Supplement 1): 3592. doi: https://doi.org/10.1182/blood-2023-184945 Dhakal B, et al. Salvage second transplantation in relapsed multiple myeloma. Leukemia. 2021 Apr;35(4):1214-1217. doi: 10.1038/s41375-020-1005-8. Lemieux C, et al. Outcomes after delayed and second autologous stem cell transplant in patients with relapsed multiple myeloma. Bone Marrow Transplant. 2021 Nov;56(11):2664-2671. doi: 10.1038/s41409-021-01371-1. Green AK, Tabatabai SM, Aghajanian C, et al. Clinical Trial Participation Among Older Adult Medicare Fee-for-Service Beneficiaries With Cancer. JAMA Oncol. 2022;8(12):1786-1792. doi:10.1001/jamaoncol.2022.5020 Allison K, Patel D, Kaur R. Assessing Multiple Factors Affecting Minority Participation in Clinical Trials: Development of the Clinical Trials Participation Barriers Survey. Cureus. 2022;14(4):e24424. Published 2022 Apr 23. doi:10.7759/cureus.24424 Kanapuru B, Fernandes LL, Fashoyin-Aje LA, et al. Analysis of racial and ethnic disparities in multiple myeloma US FDA drug approval trials. Blood Adv. 2022;6(6):1684-1691. doi:10.1182/bloodadvances.2021005482 Kanapuru B, Fernandes LL, Baines A, et al. Eligibility criteria and enrollment of a diverse racial and ethnic population in multiple myeloma clinical trials. Blood. 2023;142(3):235-243. doi:10.1182/blood.2022018657 Waxman AJ, Mink PJ, Devesa SS, et al. Racial disparities in incidence and outcome in multiple myeloma: a population-based study. Blood. Dec 16 2010;116(25):5501-6.

Field	Response
	doi:10.1182/blood-2010-07-298760 Peres LC, Oswald LB, Dillard C, et al. Racial and Ethnic Differences in Clinical Outcomes Among Multiple Myeloma Patients Treated with CAR T Therapy. Blood (2022) 140(Supplement 1): 623 625. doi.org/10.1182/blood-2022-158478
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.	L Liu: Received honorarium from Medscape, MJH life sciences, CAHON (all < $5000). Stocks in Pfizer and Roche. A Afrough: Reports research funding from Abbvi,Adaptive Biotech, K36-therapeutics, J&J, Regeneronpharmaceuticals Advisory role for Karyopharm, BMS, Sanofi, J&J, Pfizer. E Biltibo: Consultancy: BeiGene USA. J Kort: no COI. C Khouderchah: no COI L Holmberg: Grants from Seattle Genetics, Sanofi, Millennium-Takeda, Bristol-Myers Squibb, Merck, and Iteos outside the submitted work as well as royalties from UpToDate. L Shune: Advisory boards: BMS and Janssen. L Anderson: Consulting/Advisory Board activity with: Janssen, Celgene, BMS, Amgen, GSK, AbbVie, Beigene, Cellectar, Sanofi, Prothena. Research Funding: BMS, Janssen, GSK, Abbvie. A Varshavsky-Yanovsky: Advisory/ consulting: Pfizer, Janssen, BMS H Fung: Honorarium, consultancy/ speaker bureau: Janssen, Bioline RX, Astra Zeneca. M Janakiram: Honoraria: Janssen, BMS, Legend Biotech. Research funding: BMS, Janssen, and Fate Therapeutics.

PROP 2505-01; 2506-02; 2507-01; 2509-82; 2509-85; 2509-189: Comparative effectiveness of second line or later autologous stem cell transplantation versus CAR T cell therapy for relapsed multiple myeloma (L Holmberg/ C Khouderchah/ J Kort/ L Shune/ A Afrough/ L Anderson/ L Liu/ M Janakiram)

Table. Characteristics of patients who underwent second autoHCT or first CAR-T for Multiple Myeloma between 2016-2025, and reported to the CIBMTR

Characteristic	2nd auto TED	2nd auto CRF	Ide-cel	Cilta-cel	Total
No. of patients	2727	368	1422	2023	6540
No. of centers	147	91	84	82	152
Patient-related					
Age, by decades, no. (%)					
Median (range)	64 (29-81)	63 (35-81)	68 (35-90)	65 (33-87)	65 (29-90)
20-29	1 (0)	0 (0)	0 (0)	0 (0)	1 (0)
30-39	14 (1)	6 (2)	9 (1)	18 (1)	47 (1)
40-49	175 (6)	29 (8)	58 (4)	127 (6)	389 (6)
50-59	740 (27)	102 (28)	236 (17)	464 (23)	1542 (24)
60-69	1266 (46)	173 (47)	548 (39)	825 (41)	2812 (43)
70+	531 (19)	58 (16)	571 (40)	589 (29)	1749 (27)
Recipient Sex, no. (%)					
Male	1545 (57)	223 (61)	821 (58)	1149 (57)	3738 (57)
Female	1182 (43)	145 (39)	601 (42)	874 (43)	2802 (43)
Recipient race, no. (%)					
White	2024 (74)	220 (60)	1092 (77)	1534 (76)	4870 (74)
Black or African American	492 (18)	118 (32)	234 (16)	307 (15)	1151 (18)
Asian	79 (3)	8 (2)	31 (2)	63 (3)	181 (3)
Native Hawaiian or other Pacific Islander	4 (0)	0 (0)	3 (0)	3 (0)	10 (0)
American Indian or Alaska Native	19 (1)	6 (2)	6 (0)	7 (0)	38 (1)
Other	0 (0)	0 (0)	3 (0)	12 (1)	15 (0)
More than one race	17 (1)	3 (1)	35 (2)	70 (3)	125 (2)
Not reported	92 (3)	13 (4)	18 (1)	27 (1)	150 (2)
Ethnicity, no. (%)					
Hispanic or Latino	286 (10)	25 (7)	118 (8)	194 (10)	623 (10)
Not Hispanic or Latino	2401 (88)	335 (91)	1267 (89)	1764 (87)	5767 (88)
Non-resident of the U.S.	2 (0)	0 (0)	0 (0)	4 (0)	6 (0)
Not reported	38 (1)	8 (2)	37 (3)	61 (3)	144 (2)
Karnofsky performance score prior to HCT/CT, no. (%)					
90-100	1217 (45)	150 (41)	459 (32)	889 (44)	2715 (42)
80	914 (34)	131 (36)	526 (37)	596 (29)	2167 (33)
< 80	524 (19)	69 (19)	296 (21)	276 (14)	1165 (18)

Characteristic	2nd auto TED	2nd auto CRF	Ide-cel	Cilta-cel	Total
Not reported	72 (3)	18 (5)	141 (10)	262 (13)	493 (8)
HCT comorbidity score, no. (%)					
0	503 (18)	69 (19)	287 (20)	569 (28)	1428 (22)
1	323 (12)	35 (10)	232 (16)	392 (19)	982 (15)
2	479 (18)	67 (18)	210 (15)	291 (14)	1047 (16)
3	533 (20)	73 (20)	269 (19)	300 (15)	1175 (18)
4	392 (14)	49 (13)	168 (12)	206 (10)	815 (12)
5+	488 (18)	74 (20)	250 (18)	256 (13)	1068 (16)
Not reported	9 (0)	1 (0)	6 (0)	9 (0)	25 (0)
Disease-related					
Sub-disease, no. (%)					
Multiple myeloma, NOS	1101 (40)	133 (36)	1061 (75)	1592 (79)	3887 (59)
Smoldering myeloma	1 (0)	0 (0)	1 (0)	0 (0)	2 (0)
Multiple myeloma - IgG	772 (28)	107 (29)	0 (0)	0 (0)	879 (13)
Multiple myeloma - IgA	278 (10)	44 (12)	0 (0)	0 (0)	322 (5)
Multiple myeloma - IgD	13 (0)	1 (0)	0 (0)	0 (0)	14 (0)
Multiple myeloma - IgM	4 (0)	2 (1)	0 (0)	0 (0)	6 (0)
Multiple myeloma - light chain only	515 (19)	80 (22)	336 (24)	410 (20)	1341 (21)
Multiple myeloma - non-secretory	43 (2)	1 (0)	24 (2)	21 (1)	89 (1)
Disease status prior to HCT/CT, no. (%)					
sCR/CR	328 (12)	53 (14)	23 (2)	76 (4)	480 (7)
VGPR	861 (32)	110 (30)	119 (8)	246 (12)	1336 (20)
PR	738 (27)	101 (27)	195 (14)	308 (15)	1342 (21)
SD	258 (9)	44 (12)	222 (16)	391 (19)	915 (14)
PD/Relapse	531 (19)	57 (15)	860 (60)	991 (49)	2439 (37)
Not reported	11 (0)	3 (1)	3 (0)	11 (1)	28 (0)
Treatment-related					
Subsequent CAR-T, no. (%)					
No	2458 (90)	330 (90)	1027 (72)	747 (37)	4562 (70)
Yes	269 (10)	38 (10)	24 (2)	10 (0)	341 (5)
Not reported	0 (0)	0 (0)	371 (26)	1266 (63)	1637 (25)
Number of lines of prior therapies (including HCT and CT), no. (%)[1]					
Median (range)	-	-	6 (1-20)	5 (1-18)	5 (1-20)
1	-	-	6 (0)	19 (1)	25 (1)
2	-	-	35 (2)	108 (5)	143 (4)
3	-	-	38 (3)	210 (10)	248 (7)
4+	-	-	729 (51)	1504 (74)	2233 (65)
Not reported	-	-	614 (43)	182 (9)	796 (23)
Types of prior HCTs, no. (%)					

Characteristic	2nd auto TED	2nd auto CRF	Ide-cel	Cilta-cel	Total
No	0 (0)	0 (0)	347 (24)	459 (23)	806 (12)
Yes	2727 (100)	368 (100)	1075 (76)	1564 (77)	5734 (88)
Prior allo-HCT	0 (0)	0 (0)	9 (1)	7 (0)	16 (0)
Prior auto-HCT	2725 (100)	367 (100)	1048 (74)	1540 (76)	5680 (87)
Prior auto and allo-HCT	2 (0)	1 (0)	18 (1)	17 (1)	38 (1)
Year of HCT/CT, no. (%)					
2016	328 (12)	45 (12)	0 (0)	0 (0)	373 (6)
2017	329 (12)	59 (16)	0 (0)	0 (0)	388 (6)
2018	386 (14)	47 (13)	0 (0)	0 (0)	433 (7)
2019	372 (14)	50 (14)	0 (0)	0 (0)	422 (6)
2020	304 (11)	41 (11)	0 (0)	0 (0)	345 (5)
2021	286 (10)	40 (11)	211 (15)	0 (0)	537 (8)
2022	292 (11)	34 (9)	405 (28)	146 (7)	877 (13)
2023	220 (8)	26 (7)	463 (33)	557 (28)	1266 (19)
2024	149 (5)	13 (4)	302 (21)	1086 (54)	1550 (24)
2025[2]	61 (2)	13 (4)	41 (3)	234 (12)	349 (5)
Follow-up of survivors, months, median (range)	54.6 (0.0-110.1)	50.0 (0.0-108.2)	23.4 (1.4-48.6)	7.2 (1.0-36.8)	24.2 (0.0-110.1)

Data source: CT Extract September 2025, HCT Essentials September 2025

[1] CAR-T population only

[2] Data incomplete for year 2025

Title: Real-World Comparative Effectiveness of Early Versus Late CAR T-cell Therapy in Multiple Myeloma: A CIBMTR Analysis

Proposed Working Committee:

Plasma cell disorders.

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Research Question:

Among patients with relapsed/refractory multiple myeloma (RRMM), who receive BCMA-directed CAR T-cell therapy, does administering CAR T-cell therapy in earlier (defined as 1-3 prior lines) vs later (≥4 prior lines) improve outcomes?

Hypothesis:

BCMA-directed CAR T-cell therapy (Cilta-cel and Ide-cel) in earlier line (1-3) is associated with improved safety and efficacy compared to its use in later lines (≥4) for RRMM.

Scientific Impact:

This study aims at assessing real-world evidence on the optimal timing of CAR T-cell therapy in the rapidly evolving therapeutic landscape of multiple myeloma.
By comparing outcomes of earlier versus later administration, we can:

- Assess safety and efficacy of standard of care CAR T-cell therapy as earlier treatment option for patients with RRMM.

- Allow meaningful comparative analysis of efficacy and safety of CAR T in earlier (1-3) versus later (≥4) line of therapy.

- Assess outcomes and predictors of safety and efficacy in subgroups of interest (elderly, frail, renal insufficiency, presence of EMD, high-risk cytogenetics).

- Inform patient selection, counseling, monitoring and management of toxicities, and clinical trial design for high-risk groups.

Scientific Justification/Background:

Multiple Myeloma comprises 1% of all malignancies and 10% of all hematologic malignancies. Although recent advancements in myeloma-directed therapeutics have led to improved survival and prognosis for patients with relapsed/refractory multiple myeloma (RRMM), relapse is still common in late-line setting with more aggressive and heterogeneous disease biology and decreasing remission duration with each line of therapy (1). Chimeric antigen receptor (CAR) T-cell therapy has emerged as a revolutionary immunotherapeutic strategy for treating RRMM. Two B-cell maturation antigen (BCMA) targeting CAR T-cell products – Idecabtagen vicleucel (Ide-cel, bb2121) and Ciltacabtagen autoleucel (Cilta-cel) have received US Food and Drug Administration (FDA) approval in 2021 and 2022, respectively.

Based on the phase II KarMMa trial, Ide-cel became the first approved therapy for RRMM patients who had received four or more prior lines of therapy (LOT), including a proteasome inhibitor (PI), immunomodulatory drug (IMiD), and an anti-CD38 monoclonal antibody. The overall response rate (ORR) was 73%, with 33% patients achieving complete response (CR). 26% of all treated patients achieved minimal

residual disease (MRD) negativity. The median progression free survival (PFS) was 8.8 months, extending to 20.2 months for patients who achieved CR. The median overall survival (OS) was 19.4 months (2).

Cilta-cel is the second CAR T-cell therapy to be approved after Ide-cel. This product contains two BCMA-targeting high-affinity single-domain antibodies designed to confer avidity. In the phase Ib/II CARTITUDE-1 trial, Cilta-cel demonstrated unprecedented efficacy in heavily pretreated RRMM patients, with a median of 6 prior LOT (3). The ORR was 97%, with 67% patients achieving stringent CR. The median PFS at a median follow-up of 33.4 months was 34.9 months. Median OS was not reached at this point (4).

Given their remarkable efficacy in heavily pretreated patients, these therapies have been studied in earlier treatment lines. The phase 3 KarMMa-3 trial compared Ide-cel to standard of care (SOC) therapies, in patients who received at least 2-4 prior lines of therapies (5). Ide-cel showed superior outcomes compared to SOC, with median PFS of 13.3 vs 4.4 months ($p<0.001$) and higher ORR 71% vs 42% ($p<0.001$). Similarly, in CARTITUDE-4 trial, Cilta-cel was compared to SOC therapies in patients who had received prior 1-3 LOT (6). Cilta-cel demonstrated significantly longer PFS, with 12-month PFS of 76% vs 49% ($p < 0.0001$), median PFS not reached. ORR and CR rates were also higher - 85% vs 67% ($p<0.001$) and 73% vs 22% ($p<0.001$) respectively.

The aim of our proposed study is to assess outcomes when CAR T-cell therapy is administered earlier (defined as within 1-3 LOT) compared to later (defined as ≥4) line of therapy. Administering CAR T-cell therapy earlier in the course of disease allows the use of autologous T cells which have a potentially fitter profile (7) and less exhausted owing to reduced exposure to continuous myeloma-directed therapies. It may also help preserve bone marrow reserve and improve tolerability of therapies, and ultimately reducing cumulative long-term toxicities including hematologic toxicities, marrow suppression, and quality of life compromising adverse events. Moreover, using most effective therapies earlier can help with patient attrition seen with each successive LOT (8). Additionally, in a recent long-term follow-up of CARTITUDE-1 trial, a third of the treated patient population was alive and progression-free ≥ 5 years after Cilta-cel, most of them having achieved stringent CR, teasing perhaps curative potential of the therapy (9).

Taken together, there is a strong rationale for administering CAR T-cell therapy in earlier setting based on the current best available evidence, however real-world evidence is limited in comparing outcomes. CIBMTR is one of the largest real-world registries available for this analysis. Hence, we aim to propose a study to investigate and validate these benefits, which can ultimately help guide clinical decision making and optimizing treatment sequencing.

Participants:

Inclusion Criteria:

- Adult patients treated with Ide-cel and Cilta-cel CAR T-cell therapy for RRMM
- Treated with commercial and/or non-conforming product.
- Patients with at least one follow up post CAR T-cell therapy.

Exclusion Criteria:

- Patients who received CAR T-cell therapy under registration clinical trial.
- Patients with primary amyloidosis.

Objectives:

Primary Objective:

To compare the following outcomes in patients with relapsed/refractory multiple myeloma, receiving BCMA directed CAR T-cell therapy.

1. 6-, 12-, and 24-month overall response rate (ORR) and progression free survival (PFS) in early (1-3) versus late (≥4) administration of ide-cel.
2. 6-, 12-, and 24-month ORR and PFS in early versus late (as defined above) administration of cilta-cel.

Secondary Objective(s):

Compare following efficacy and safety outcomes of ide-cel and cilta-cel in RRMM, early vs late LOT:

- Response rates based on IMWG response criteria, including factors predictive for response (CR, sCR, MRD status).
- Overall survival (OS), including factors predictive for survival.
- Treatment related mortality (TRM) at 12-months.
- Non-relapse mortality (NRM) at 12-months
- Rates and severity of CRS, ICANS, non-ICANS neurotoxicities (NINT) and immune effector cell-associated hemophagocytic lymphohistiocytosis-like syndrome (IEC-HS)
- Infections: Rates and severity (bacterial, viral, fungal and/or a combination thereof), at day +30, day +90, and 1 year.
- Cytopenias: Incidence and severity of prolonged cytopenia at day +30 and day +90 following CAR T-cell therapy.

- Second primary malignancies (SPM): Defined as any new primary neoplasm developed after CAR T-cell therapy.
- Out of specification product rates.
- Cause of death (descriptive)

Data Requirements:

Patient-Specific Variables:

- Age at CAR T
- Gender (Male/Female)
- Race and ethnicity (combined if necessary: non-Hispanic White, non-Hispanic Black, Hispanic, Other)
- ECOG performance status (0–1 vs ≥2)
- HCT Comorbidity Index (HCT-CI ≥3)
- Clinically significant comorbidities (according to HCT-CI, renal insufficiency, dialysis status, heart failure, and prior malignancy, etc)

Disease-Specific Variables:

- Number and type (if available) of prior lines of therapy
- R-ISS stage (I, II, III) – at the time of infusion
- High-risk cytogenetics
- Bone marrow plasma cell burden > 50% (prior to lymphodepletion)
- Extramedullary disease/plasmacytomas (prior to infusion)
- Plasma cell leukemia
- Functional high-risk status (relapse within 12 months of ASCT or PFS with frontline therapy <18 months), if available
- Disease status prior to infusion (≥VGPR vs PR vs SD/PD)
- Triple-class and penta-drug exposed / refractory status (yes/no)
- Prior exposure to BCMA-targeting therapy (commercial and on trial)
- Prior exposure to GPRC5D-targeting therapy (commercial and on trial)
- Baseline degree of cytopenias (platelets <50 × 10^9/L, ANC <500/mm³)
- Baseline and maximum inflammatory markers (ferritin, CRP, LDH, IL-6, sIL-2r if available) prior to infusion

Infusion-/Treatment-Specific Variables:

- CAR T product (Ide-cel vs Cilta-cel), timing of administration (which number of LOT), dose of cells If available (> 0.7 million cells, Y/N)
- Bridging therapy (Y/N), type of therapy used (chemo/radiation/both), regimen used
- Out-of-specification product (Y/N)
- Lymphodepletion chemotherapy regimen
- Vein-to-vein time (time from apheresis to infusion of CAR T-cells)
- CRS and ICANS: grade, onset, duration
- Non-ICANS Neurotoxicity (including cranial nerve palsies, peripheral neuropathies, and movement and neurocognitive treatment-emergent adverse events): grade, onset, duration
- IEC-HS/Macrophage activation syndrome (MAS) like symptoms
- Cytopenias – at D +30, +90, and beyond
- Infections: onset, type, grade
- Use of tocilizumab, corticosteroids, anakinra
- Use of growth factors (G-CSF), TPO-agonists, or stem cell boosts
- Response at 1, 3, 6, 9, and 12 months
- Time from infusion to progression and next therapy
- Cause of death

We will work with the CIBMTR statistical team after receiving the initial set of data to better identify the possibility and feasibility of stratifying the above data by specific LOT and a univariate and multivariate analysis based on the above variables.

Conflicts of Interest

None.

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PROP 2508-07; 2509-80; 2509-92; 2509-106; 2509-111; 2509-172; 2509-174; 2509-226; 2509-233: Real World Comparative Effectiveness of Early versus Late CAR T-cell Therapy in Multiple Myeloma: A CIBMTR Analysis (S Zanwar/ M Ho/ K Lim/ S Adroja/ S Ganguly/ A Aljundi/ T Bahar/ S Farhan/ H Hashmi/ N Abdallah/ A Bidikian/ J Cala Garcia/ A Afrough/ L Anderson/ M Janakiram/ L Liu)

Table. Characteristics of patients who underwent first CAR-T for Multiple Myeloma between 2021 – 2025, and reported to the CIBMTR

	Early (1-3 prior lines of therapy)			Later (4+ prior lines of therapy)			
Characteristic	**Ide-cel**	**Cilta-cel**	**Total**	**Ide-cel**	**Cilta-cel**	**Total**	**TOTAL**
No. of patients	103	375	478	904	1780	2684	3162
No. of centers	47	69	79	59	74	83	90
Patient-related							
Age, by decades, no. (%)							
Median (range)	67 (35-83)	65 (36-86)	65 (35-86)	66 (29-90)	65 (33-87)	65 (29-90)	65 (29-90)
20-29	0 (0)	0 (0)	0 (0)	1 (0)	0 (0)	1 (0)	1 (0)
30-39	1 (1)	5 (1)	6 (1)	5 (1)	13 (1)	18 (1)	24 (1)
40-49	6 (6)	20 (5)	26 (5)	43 (5)	113 (6)	156 (6)	182 (6)
50-59	21 (20)	92 (25)	113 (24)	179 (20)	415 (23)	594 (22)	707 (22)
60-69	38 (37)	140 (37)	178 (37)	370 (41)	743 (42)	1113 (41)	1291 (41)
70+	37 (36)	118 (31)	155 (32)	306 (34)	496 (28)	802 (30)	957 (30)
Recipient Sex, no. (%)							
Male	59 (57)	211 (56)	270 (56)	515 (57)	1009 (57)	1524 (57)	1794 (57)
Female	44 (43)	164 (44)	208 (44)	389 (43)	769 (43)	1158 (43)	1366 (43)
Not reported	0 (0)	0 (0)	0 (0)	0 (0)	2 (0)	2 (0)	2 (0)
Recipient race, no. (%)							
White	77 (75)	277 (74)	354 (74)	717 (79)	1364 (77)	2081 (78)	2435 (77)
Black or African American	24 (23)	71 (19)	95 (20)	135 (15)	255 (14)	390 (15)	485 (15)
Asian	0 (0)	9 (2)	9 (2)	20 (2)	51 (3)	71 (3)	80 (3)
Native Hawaiian or other Pacific Islander	0 (0)	0 (0)	0 (0)	3 (0)	3 (0)	6 (0)	6 (0)
American Indian or Alaska Native	2 (2)	2 (1)	4 (1)	3 (0)	6 (0)	9 (0)	13 (0)

Characteristic	Early (1-3 prior lines of therapy)			Later (4+ prior lines of therapy)			TOTAL
	Ide-cel	Cilta-cel	Total	Ide-cel	Cilta-cel	Total	
Other	0 (0)	3 (1)	3 (1)	4 (0)	10 (1)	14 (1)	17 (1)
More than one race	0 (0)	8 (2)	8 (2)	13 (1)	65 (4)	78 (3)	86 (3)
Missing	0 (0)	5 (1)	5 (1)	9 (1)	26 (1)	35 (1)	40 (1)
Ethnicity, no. (%)							
Hispanic or Latino	5 (5)	35 (9)	40 (8)	71 (8)	178 (10)	249 (9)	289 (9)
Not Hispanic or Latino	97 (94)	333 (89)	430 (90)	818 (90)	1540 (87)	2358 (88)	2788 (88)
Non-resident of the U.S.	0 (0)	1 (0)	1 (0)	0 (0)	6 (0)	6 (0)	7 (0)
Not reported	1 (1)	6 (2)	7 (1)	15 (2)	56 (3)	71 (3)	78 (2)
Karnofsky performance score prior to CT, no. (%)							
90-100	32 (31)	165 (44)	197 (41)	302 (33)	762 (43)	1064 (40)	1261 (40)
80	41 (40)	107 (29)	148 (31)	362 (40)	538 (30)	900 (34)	1048 (33)
< 80	20 (19)	60 (16)	80 (17)	192 (21)	250 (14)	442 (16)	522 (17)
Not reported	10 (10)	43 (11)	53 (11)	48 (5)	230 (13)	278 (10)	331 (10)
HCT comorbidity score, no. (%)							
0	22 (21)	105 (28)	127 (27)	207 (23)	503 (28)	710 (26)	837 (26)
1	22 (21)	82 (22)	104 (22)	153 (17)	328 (18)	481 (18)	585 (19)
2	15 (15)	56 (15)	71 (15)	128 (14)	248 (14)	376 (14)	447 (14)
3	19 (18)	48 (13)	67 (14)	162 (18)	285 (16)	447 (17)	514 (16)
4	14 (14)	43 (11)	57 (12)	93 (10)	173 (10)	266 (10)	323 (10)
5+	11 (11)	39 (10)	50 (10)	156 (17)	235 (13)	391 (15)	441 (14)
Not reported	0 (0)	2 (1)	2 (0)	5 (1)	8 (0)	13 (0)	15 (0)
Disease-related							
Sub-disease, no. (%)							
Multiple myeloma, NOS	81 (79)	316 (84)	397 (83)	662 (73)	1378 (77)	2040 (76)	2437 (77)
Multiple myeloma - light chain only	21 (20)	55 (15)	76 (16)	222 (25)	374 (21)	596 (22)	672 (21)
Multiple myeloma - non-secretory	1 (1)	4 (1)	5 (1)	20 (2)	28 (2)	48 (2)	53 (2)
Disease status prior to CT for PCD, no. (%)							
Stringent complete remission (sCR)	0 (0)	5 (1)	5 (1)	2 (0)	21 (1)	23 (1)	28 (1)

Characteristic	Early (1-3 prior lines of therapy)			Later (4+ prior lines of therapy)			TOTAL
	Ide-cel	Cilta-cel	Total	Ide-cel	Cilta-cel	Total	
Complete remission (CR)	0 (0)	11 (3)	11 (2)	12 (1)	44 (2)	56 (2)	67 (2)
Very good partial remission (VGPR)	11 (11)	58 (15)	69 (14)	66 (7)	194 (11)	260 (10)	329 (10)
Partial response (PR)/ Not Complete Remission	15 (15)	65 (17)	80 (17)	110 (12)	251 (14)	361 (13)	441 (14)
Stable disease (SD)	23 (22)	82 (22)	105 (22)	127 (14)	341 (19)	468 (17)	573 (18)
Progressive disease (PD)	53 (51)	145 (39)	198 (41)	578 (64)	886 (50)	1464 (55)	1662 (53)
Relapse from CR (Rel) (untreated)	1 (1)	5 (1)	6 (1)	7 (1)	34 (2)	41 (2)	47 (1)
Not reported	0 (0)	4 (1)	4 (1)	2 (0)	9 (1)	11 (0)	15 (0)
Treatment-related							
Number of lines of prior therapies (including HCT and CT), no. (%)							
Median (range)	3 (1-3)	3 (1-3)	3 (1-3)	7 (4-20)	6 (4-20)	6 (4-20)	6 (1-20)
1	7 (7)	19 (5)	26 (5)	0 (0)	0 (0)	0 (0)	26 (1)
2	42 (41)	122 (33)	164 (34)	0 (0)	0 (0)	0 (0)	164 (5)
3	54 (52)	234 (62)	288 (60)	0 (0)	0 (0)	0 (0)	288 (9)
4-6	0 (0)	0 (0)	0 (0)	439 (49)	1173 (66)	1612 (60)	1612 (51)
7+	0 (0)	0 (0)	0 (0)	465 (51)	607 (34)	1072 (40)	1072 (34)
CAR-T product, no. (%)							
Idecabtagene vicleucel	103 (100)	0 (0)	103 (22)	904 (100)	0 (0)	904 (34)	1007 (32)
Ciltacabtagene autoleucel	0 (0)	375 (100)	375 (78)	0 (0)	1780 (100)	1780 (66)	2155 (68)
Year of CT, no. (%)							
2021	21 (20)	0 (0)	21 (4)	235 (26)	0 (0)	235 (9)	256 (8)
2022	38 (37)	9 (2)	47 (10)	405 (45)	162 (9)	567 (21)	614 (19)
2023	35 (34)	43 (11)	78 (16)	258 (29)	579 (33)	837 (31)	915 (29)
2024	5 (5)	236 (63)	241 (50)	5 (1)	883 (50)	888 (33)	1129 (36)
2025[1]	4 (4)	87 (23)	91 (19)	1 (0)	156 (9)	157 (6)	248 (8)
Survival outcome, no. (%)							
Death within 6 months post-infusion	11 (11)	18 (5)	29 (6)	121 (13)	123 (7)	244 (9)	273 (9)
Death 6-12 months post-infusion	14 (14)	8 (2)	22 (5)	98 (11)	75 (4)	173 (6)	195 (6)
Death after 1 year post-infusion	7 (7)	3 (1)	10 (2)	173 (19)	67 (4)	240 (9)	250 (8)

Characteristic	Early (1-3 prior lines of therapy)			Later (4+ prior lines of therapy)			TOTAL
	Ide-cel	Cilta-cel	Total	Ide-cel	Cilta-cel	Total	
N/A – Alive at last follow-up	71 (69)	346 (92)	417 (87)	512 (57)	1515 (85)	2027 (76)	2444 (77)
Follow-up of patients, no. (%)							
< 12 months	37 (36)	310 (83)	347 (73)	238 (26)	925 (52)	1163 (43)	1510 (48)
>= 1 year	66 (64)	65 (17)	131 (27)	666 (74)	855 (48)	1521 (57)	1652 (52)
Follow-up of survivors, months, median (range)	24 (3-37)	6 (3-37)	6 (3-37)	25 (1-49)	12 (1-37)	13 (1-49)	13 (1-49)

Data source: CT Extract September 2025

[1] Incomplete - Data still being reported for year 2025

Field	Response
Proposal Number	PROP 2509-01; 2509-03; 2509-42
Proposal Title	Impact of Lenalidomide Alone vs. Lenalidomide + anti-CD38 Monoclonal Antibody Maintenance on Outcomes in Post-Autologous Stem Cell Transplant Patients with Multiple Myeloma
Key Words	maintenance, lenalidomide, daratumumab, isatuximab, induction, triplet, quadruplet
Junior investigator status (defined as 年、5 years from fellowship)	Yes
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:	Pearl Abraham
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:	Othman Akhthar - want to maintain initial group including Matias Sanchez, Timothy Schmidt, Ana Avila Rodriguez, Aimaz Afrough
RESEARCH QUESTION:	Safety and efficacy data of anti-CD38 monoclonal antibody + 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 anti-CD38 monoclonal antibody + lenalidomide maintenance is superior to lenalidomide alone maintenance in extending the progression free survival in multiple myeloma patients after autologous stem cell transplant

Field	Response
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	Primary endpoint: progression free survival defined as time from ASCT to relapse, progression, or death from any cause Secondary endpoints: Overall survival Sub-group analyses for progression free survival and overall survival • Triplet vs quadruplet induction therapy • Anti-CD38 naive vs anti-CD38 exposed • Non-secretory disease • High risk characteristics • Those with suboptimal response to induction and transplant (i.e. did not achieve CR post transplant, and those who were MRD positive post transplant) Response rates Duration of response • subgroup analysis on total duration of response if patient was initiated on single maintenance therapy then moved to doublet at first relapse Time to progression Time to next treatment Toxicity profiles Hematologic toxicities Non-relapse mortality 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 anti-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. Lenalidomide (R) is well-established as a maintenance agent based on several large phase 3 randomized-controlled trials which show a substantial benefit to lenalidomide maintenance over placebo or observation, and an overall survival benefit seen in the CALGB100104 trial and a meta-analysis that included other similar trials done in the same era. However, despite this benefit of lenalidomide maintenance, a vast majority of patients with multiple myeloma still relapse, leading to additional research to help achieve better outcomes. Over the past five years, it has become apparent that the addition of CD38 antibodies to standard therapy improves outcomes in newly diagnosed multiple myeloma. 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. In both PERSEUS and GRIFFIN, patients were randomized to receive daratumumab throughout the entirety of first-line therapy (induction, consolidation, and maintenance), versus no daratumumab, and as such, it is impossible to determine if the PFS benefit from the addition of daratumumab comes from its use during induction, maintenance, or both. In CASSIOPEIA, patients underwent two randomizations one prior to induction, and the other after transplant and prior to maintenance. The longest PFS benefit was seen in patients who received daratumumab+VTD induction then daratumumab maintenance versus D-VTd with observation (median not reached [74·6–NE] vs 72·1 months [52·8–NE]; 0·76 [0·58–1·00]; p=0·048) and VTd with daratumumab maintenance versus VTd with observation (median not reached [66·9–NE] vs 32·7 months [27·2–38·7]; 0·34 [0·26–0·44]; p<0·0001). While this study underscores the importance of maintenance therapy regardless of induction, it does not tell us the optimal maintenance agent (Daratumumab vs lenalidomide). In the AURIGA trial, patients who were MRD-positive after transplant were randomized to receive either daratumumab + lenalidomide (dara-R) or lenalidomide alone. Patients receiving Dara-R maintenance had an improvement in MRD-negativity after 12 months of therapy, with favorable impact on PFS at follow up of 35.6 months. MRD-negative (10−5) conversion rates by 12 months of maintenance were higher for D-R versus R across cytogenetically high-risk

Field	Response
	subgroups per modified IMS 2024 (41.2% vs 0%) criteria and cytogenetically ultra-high–risk disease (≥2 revised HRCAs; 54.5% vs 0%). 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. The proposal aims to evaluate impact of anti-CD38 antibody + lenalidomide maintenance therapy in anti-CD38 exposed patients. This study will also help identify other subgroups that would potentially benefit from anti-CD38 antibody + lenalidomide maintenance therapy

Field	Response
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, 2015 to December 31, 2025 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 5. Patient with second autologous transplant 6. Lenalidomide not included in maintenance regimen
Does this study include pediatric patients?	No

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.	Baseline patient characteristics Age at diagnosis Age at maintenance therapy initiation Gender Weight 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 Renal function Cytogenetic by karyotype (conventional) Cytogenetic by FISH International Staging System (ISS) Revised ISS Date of HCT Time from diagnosis to HCT Extramedullary plasmacytoma(s) Treatments prior to maintenance therapy Drug class exposure during induction IMiD PI CD38 IMiD + PI (no CD38) CD38 + PI (no IMiD) CD38 + IMiD (no PI) CD38 + IMiD + PI Other (eg VTD-PACE) Melphalan dose (140mg/m2 vs 200mg/m2) Duration of induction treatment Date of autologous transplant Date of maintenance therapy initiation Best response after autologous transplant MRD status after transplant (if known) Laboratory values at the time of initiation of maintenance therapy WBC Hemoglobin Platelet Plasma cells in bone marrow aspirate and biopsy or unknown source Serum creatinine Creatinine clearance (collected at CIBMTR since 9/2022) Serum monoclonal Ig (M-spike) Serum

	immunofixation Urinary monoclonal light chains Urine immunofixation Serum free light changes (kappa, lambda, ratio) Quantitative immunoglobulins (IgG, IgA, IgM) MRD status, and method of MRD assessment Plasma cells in bone marrow aspiration and biopsy or unknow source Outcome data Overall response rate (ORR) Duration of response (DOR) Event-free survival (EFS) Progression-free survival (PFS) 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) Method of MRD assessment Incidence of Secondary primary malignancy Relapse or disease progression Site of progression Date of progression Date of death Cause of death Hematologic response at 100-day, 6-month, 1-year, 2-year, and yearly for greater than 2 years post-auto-HCT Best response If on single agent maintenance therapy, total duration of therapy from maintenance to first relapse Subgroup analysis Triplet vs quadruplet induction therapy matched cohorts CD38 exposed vs CD38 naive Non-secretory disease High risk characteristics PI + IMID vs CD38 + IMID maintenance therapies in doublet regimens Those with suboptimal response to induction and transplant (i.e. did not achieve CR post transplant, and those who were MRD positive post transplant) Maintenance treatment

Field	Response
	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 Addition of proteasome inhibitor to maintenance therapy (with or without CD38) Discontinuation rates not due to progression
Types of cellular therapy data this proposal includes:	Hematopoietic Cell Transplantation (HCT)

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	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. 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. 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. 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. 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.

Field	Response
	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. 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. 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. • Moreau, Philippe et al. Bortezomib, thalidomide, and dexamethasone with or without daratumumab and followed by daratumumab maintenance or observation in transplant-eligible newly diagnosed multiple myeloma: long-term follow-up of the CASSIOPEIA randomised controlled phase 3 trial The Lancet Oncology, Volume 25, Issue 8, 1003 – 1014 • Foster, L., Anderson, L.D., Chung, A. et al. Daratumumab plus lenalidomide maintenance in newly diagnosed multiple myeloma after transplant: AURIGA subgroup analyses. Blood Cancer J. 15, 154 (2025). https://doi.org/10.1038/s41408-025-01355-
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

PROP 2509-01; 2509-03; 2509-42: Impact of Lenalidomide Alone vs. Lenalidomide + anti-CD38 Monoclonal Antibody Maintenance on Outcomes in Post-Autologous Stem Cell Transplant Patients with Multiple Myeloma (M Sanchez/ A Avila/ T Schmidt/ P Abraham/ A Afrough)

Table. Characteristics of patients with Plasma cell Disorders transplanted between 2008-2025 with lenalidomide alone vs lenalidomide + anti-CD38 mAB (daratumumab/isatuximab) maintenance after first autoHCT (CRF-Track), and reported to CIBMTR

Characteristic	Lenalidomide alone	Lenalidomide + anti-CD38 mAB (daratumumab/isatuximab)[1]	Total
No. of patients	2628	136	2764
No. of centers	140	53	140
Patient-related characteristics			
Age, by decades, no. (%)			
Median (range)	61 (20-81)	65 (32-77)	61 (20-81)
20-29	5 (0)	0 (0)	5 (0)
30-39	57 (2)	2 (1)	59 (2)
40-49	272 (10)	16 (12)	288 (10)
50-59	832 (32)	23 (17)	855 (31)
60-69	1149 (44)	67 (49)	1216 (44)
70+	313 (12)	28 (21)	341 (12)
Sex, no. (%)			
Male	1428 (54)	79 (58)	1507 (55)
Female	1200 (46)	57 (42)	1257 (45)
Race, no. (%)			
White	1517 (58)	89 (65)	1606 (58)
Black or African American	910 (35)	36 (26)	946 (34)
Asian	87 (3)	3 (2)	90 (3)
Native Hawaiian or other Pacific Islander	2 (0)	0 (0)	2 (0)
American Indian or Alaska Native	20 (1)	0 (0)	20 (1)

Characteristic	Lenalidomide alone	Lenalidomide + anti-CD38 mAB (daratumumab/isatuximab)[1]	Total
More than one race	19 (1)	1 (1)	20 (1)
Not reported	73 (3)	7 (5)	80 (3)
Ethnicity, no. (%)			
Hispanic or Latino	192 (7)	11 (8)	203 (7)
Non-Hispanic or Latino	2358 (90)	117 (86)	2475 (90)
Non-resident of the U.S.	42 (2)	0 (0)	42 (2)
Not reported	36 (1)	8 (6)	44 (2)
Center region at transplant, no. (%)			
US	2574 (98)	136 (100)	2710 (98)
Canada	16 (1)	0 (0)	16 (1)
Asia	12 (0)	0 (0)	12 (0)
Australia/New Zealand	1 (0)	0 (0)	1 (0)
Mideast/Africa	1 (0)	0 (0)	1 (0)
Central/South America	24 (1)	0 (0)	24 (1)
Karnofsky score prior to HCT, no. (%)			
90-100%	1302 (50)	76 (56)	1378 (50)
< 90%	1271 (48)	58 (43)	1329 (48)
Not reported	55 (2)	2 (1)	57 (2)
HCT-CI, no. (%)			
0	681 (26)	36 (26)	717 (26)
1	379 (14)	15 (11)	394 (14)
2	450 (17)	28 (21)	478 (17)
3	477 (18)	27 (20)	504 (18)
4	295 (11)	15 (11)	310 (11)
5+	332 (13)	15 (11)	347 (13)
Not reported	14 (1)	0 (0)	14 (1)

Characteristic	Lenalidomide alone	Lenalidomide + anti-CD38 mAB (daratumumab/isatuximab)[1]	Total
Disease-related characteristics			
Sub-disease classification, no. (%)			
Plasma cell disorder	1 (0)	0 (0)	1 (0)
Multiple myeloma, NOS:	357 (14)	89 (65)	446 (16)
Solitary plasmacytoma:	4 (0)	0 (0)	4 (0)
Osteosclerotic myeloma/POEMS syndrome:	7 (0)	0 (0)	7 (0)
Light chain deposition disease:	13 (0)	0 (0)	13 (0)
Other plasma cell disorder, specify:	8 (0)	0 (0)	8 (0)
Smoldering myeloma - asymptomatic:	1 (0)	0 (0)	1 (0)
TED Multiple myeloma-IgG:	1282 (49)	15 (11)	1297 (47)
TED Multiple myeloma-IgA:	394 (15)	7 (5)	401 (15)
TED Multiple myeloma-IgD:	13 (0)	0 (0)	13 (0)
TED Multiple myeloma-IgE:	2 (0)	0 (0)	2 (0)
Multiple myeloma-IgM:	5 (0)	0 (0)	5 (0)
TED Mult myeloma-light chain:	506 (19)	25 (18)	531 (19)
TED Mult myeloma-non-secretory:	35 (1)	0 (0)	35 (1)
Interval from diagnosis to HCT, months, median (range)	7 (2-219)	7 (4-98)	7 (2-219)
MM pre-HCT disease stage, no. (%)			
CR1	478 (18)	21 (15)	499 (18)
CR2	2009 (76)	112 (82)	2121 (77)
PR	124 (5)	3 (2)	127 (5)
Not reported	17 (1)	0 (0)	17 (1)
Transplant-related Characteristics			

Characteristic	Lenalidomide alone	Lenalidomide + anti-CD38 mAB (daratumumab/isatuximab)[1]	Total
Conditioning regimen, no. (%)			
TBI/Mel	1 (0)	0 (0)	1 (0)
Bu/Mel	4 (0)	0 (0)	4 (0)
BEAM	4 (0)	0 (0)	4 (0)
BEAM like	11 (0)	0 (0)	11 (0)
Mel alone	2588 (98)	134 (99)	2722 (98)
Mel/other(s)	10 (0)	0 (0)	10 (0)
Other(s)	5 (0)	1 (1)	6 (0)
Missing	5 (0)	1 (1)	6 (0)
Year of current transplant, no. (%)			
2008	53 (2)	0 (0)	53 (2)
2009	39 (1)	0 (0)	39 (1)
2010	56 (2)	0 (0)	56 (2)
2011	83 (3)	0 (0)	83 (3)
2012	101 (4)	0 (0)	101 (4)
2013	212 (8)	0 (0)	212 (8)
2014	163 (6)	0 (0)	163 (6)
2015	213 (8)	0 (0)	213 (8)
2016	260 (10)	5 (4)	265 (10)
2017	271 (10)	3 (2)	274 (10)
2018	499 (19)	17 (13)	516 (19)
2019	233 (9)	6 (4)	239 (9)
2020	42 (2)	1 (1)	43 (2)
2021	46 (2)	3 (2)	49 (2)
2022	120 (5)	15 (11)	135 (5)
2023	112 (4)	23 (17)	135 (5)

Characteristic	Lenalidomide alone	Lenalidomide + anti-CD38 mAB (daratumumab/isatuximab)[1]	Total
2024	116 (4)	53 (39)	169 (6)
2025[2]	9 (0)	10 (7)	19 (1)
Follow-up of survivors, median (range), months	73.4 (0.0-204.1)	13.1 (3.8-108.8)	73.0 (0.0-204.1)

Data source: HCT Essentials December 2025

[1] Lenalidomide + daratumumab n=135; Lenalidomide + isatuximab n=1

[2] Incomplete - Data still being reported for year 2025

CIBMTR proposal: Role of stem cell transplant and maintenance therapy in the management of AL amyloidosis in the era of Daratumumab

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Ohio Health Blood and Marrow Transplant Program[1] University of Oklahoma Stephenson Cancer Center[2], Mayo clinic[3], Cleveland Clinic Lerner College of Medicine/ Taussig Cancer Center[4], CenterPoint Medical Center[5], University of Iowa Healthcare[6], Ohio State University[7]

Research question: Autologous stem cell transplant (AHSCT) remains an effective treatment option in carefully selected patients with AL amyloidosis, but outcomes are strongly influenced by depth of hematologic response, organ involvement and organ response before transplant. Daratumumab (dara), a CD38-targeted monoclonal antibody, has transformed frontline therapy for AL amyloidosis after the landmark ANDROMEDA trial showed superior responses when it is added to the triplet consisting of bortezomib, cyclophosphamide, and dexamethasone (Dara-VCD). There is limited data regarding the safety and efficacy of AHSCT in patients with AL amyloidosis receiving dara-based induction therapy. The use of consolidation in patients who fail to achieve hematological complete remission (hCR) and maintenance post AHSCT in patients who achieve hCR in this disease is also not well defined. Understanding hematological and organ response related outcomes using a large dataset such as CIBMTR is critical to assess the safety, efficacy and the utilization of AHSCT before and after the introduction of dara into induction therapy. Lastly, it will also help guide the role and utilization of dara-based consolidation or maintenance post AHSCT in patients with AL amyloidosis.

Research hypothesis: The treatment for AL amyloidosis is complex, the current standard of care for newly diagnosed patients with AL amyloidosis is Dara-VCD based on the ANDROMEDA study[1]. However, this study excluded patients who planned to undergo AHSCT within the first 6 months of treatment. There is scant data about the utilization, safety and efficacy of AHSCT in the era of dara-based induction therapy for AL amyloidosis. We hypothesize that

1. AHSCT in AL Amyloidosis is equally safe with dara- and non-dara-based induction therapies and will deepen response (hematological and organ responses) and show improvement in survival with AHSCT following dara-based induction therapy.
2. With the deep and prolonged responses achieved by dara-based induction, not all patients may need AHSCT.
3. The use of dara as post AHSCT maintenance in AL amyloidosis has increased and is a safe treatment option in this setting

Outcomes:

Primary:

1. Progression free survival (PFS) and overall survival (OS) of patients with AL amyloidosis who received VCD or Dara-VCD followed by AHSCT without maintenance post AHSCT as 1st line of therapy relative to those who did not receive AHSCT but still had induction with VCD or Dara-VCD.
2. PFS and OS of patients with AL amyloidosis who received post ASCT dara maintenance following Dara-VCD or VCD based induction.

Secondary:

1. Comparison of hematologic response rates (CR, VGPR, PR) and organ response of VCD versus Dara-VCD followed by AHSCT in patients with AL amyloidosis.
2. Comparison of hematologic response rates (CR, VGPR, PR) and organ response of VCD versus Dara-VCD prior to undergoing AHSCT in patients with AL amyloidosis.
3. Trends in ASCT utilization before and after the FDA approval of adding daratumumab to the previous standard of VCD in early 2021.
4. Comparison of safety of AHSCT in patients following induction with VCD versus Dara-VCD in patients with AL amyloidosis.
    a. Day-100 non-relapse morality and relapsed mortality
    b. 1-year non-relapse mortality and relapsed mortality
    c. Duration of initial hospitalization for ASCT
    d. Unplanned rehospitalizations within 100 days
    e. Hematological/transplant-related toxicities, including febrile neutropenia, ICU admission during transplant course, delayed neutrophil/platelet/hemoglobin recovery
    f. End-organ complications, including but not limited to peri-transplant arrhythmias, worsened cardiac function cardiac arrest/sudden cardiac death, worsening kidney function and the need for dialysis initiation, respiratory failure requiringmechanical ventilation
    g. Quality of life (QoL) decline within 3−6 months post-AHSCT
5. Further examine baseline risk factors and hematologic response depth and the impact on AHSCT.
6. Further examine the impact of organ transplants (renal, cardiac) prior to or after AHSCT in patient with AL amyloidosis.

Scientific impact: Systemic light chain (AL) amyloidosis is a clonal plasma cell neoplasm characterized by deposition of amyloid fibrils in tissues. The ANDROMEDA study showed benefit in overall response rate (ORR) and OS with the addition of dara to

VCD[1]. While the ANDROMEDA trial demonstrated remarkable hematologic and organ responses in AL amyloidosis with dara-based induction, it did not address the role of ASCT in this setting. Consequently, the role of AHSCT after daratumumab-based induction remains undefined. There is a randomized phase 3 trial investigating the role of AHSCT in the daratumumab era (SWOG S2213), but due to decreased utilization of AHSCT in recent times, the trial has struggled with slow accrual and is feared to fail to meet the accrual or take an unexpectedly long time. This will result in the absence of direct comparison, which is where the CIBMTR database can help. This study will clarify the evolving role of AHSCT in AL amyloidosis in the era of daratumumab-based induction by directly assessing the safety and outcomes of AHSCT after Dara-VCD. This analysis will provide the first large, real-world evidence of impact of AHSCT on hematological and organ responses and PFS, OS to see whether ASCT remains a viable consolidative option in transplant-eligible patients with AL amyloidosis in the era of dara. These findings will directly inform clinical practice regarding better selection of transplant candidates, risk factors for high mortality and optimal integration of novel antibodies and maintenance therapy with AHSCT.

Scientific justification: AL amyloidosis is a rare plasma cell disorder with historically poor outcomes. It can affect multiple organs, and achieving organ responses is largely contingent upon attaining a deep hematological response.[2] Autologous stem cell transplantation, introduced in the 1990s, significantly improved outcomes in selected patients, with long-term survival exceeding 10 years in responders[3]. Over the past two decades, practice has been reshaped by advances in treatment options, most recently by anti-CD38 antibodies. The ANDROMEDA study has established Dara-VCD as the gold standard for newly diagnosed AL amyloidosis patients, showing improvement in hematologic and organ response and OS benefit[1]. Importantly, deeper responses prior to AHSCT are associated with superior survival and organ recovery, suggesting that daratumumab-based induction could further optimize transplant outcomes.[1] However, concerns remain regarding its effects on stem cell mobilization, engraftment, and peri-transplant safety, especially given CD38 expression on progenitor and immune cells[4]. Early reports show evolving case-mix with more relapsed/refractory patients, increased mobilization challenges, and stable early treatment-related mortality.[5]

With the introduction of dara-VCD, which lead to higher number of patients achieving complete hematological responses, the use of AHSCT for AL amyloidosis has declined. Amyloid removal from organs with use of monoclonal antibodies is being tested in phase III trials.[9] In one report from the Mayo Clinic, a referral center for AHSCT for AL amyloidosis, AHSCT is now limited to patients with suboptimal response, relapsed/refractory disease, patients with lymphoplasmacytic clones, or patients with high plasma cell burden.[6]

Unfortunately, maintenance following transplant is also understudied and has remained controversial in AL amyloidosis, unlike multiple myeloma where it is a standard of care showing both improved PFS and OS[7]. To date, there is no study that evaluates the usefulness of maintenance post ASCT in patients with AL Amyloidosis, a related plasma cell disorder.

Given the information above, critical questions remain unanswered: 1. Does AHSCT after daratumumab-based induction further improve outcomes in the modern era? With the deep responses induced by Dara-VCD, it is unknown whether ASCT further prolongs survival in patients who achieve hematological remission or should be reserved for selected genetically high-risk patients. 2.How do the outcomes of AHSCT after daratumumab-based induction compared with those of AHSCT in the pre-daratumumab era? 3. What is additional benefit of ASHCT in patients who fail to achieve complete hematological remission. 4.What is the role of dara maintenance post-SCT in AL amyloidosis?

The CIBMTR registry, with its broad multicenter capture of transplant data, represents a unique opportunity to address this knowledge gap.[8] This analysis will determine the role of stem cell transplant in the era of daratumumab. This will provide much-needed guidance to clinicians as the integration of novel agents with transplant evolves. Ultimately, Findings will directly inform evidence-based treatment algorithms, optimize patient selection for AHSCT, and improve long-term outcomes in this vulnerable population.

Participant selection criteria:

Inclusion criteria:

1. Patients aged ≥18 years old with new diagnosis of AL amyloidosis who received upfront treatment with at least 2 cycles of Dara-VCD or VCD followed by AHSCT within a year of therapy initiation reported to the CIBMTR
2. Peripheral blood stem cell as the graft source
3. Adequate baseline data available on hematologic and organ responses, mobilization, and post-transplant outcomes

Exclusion criteria:

1. Patients with concurrent Multiple Myeloma
2. Patients with non-AL amyloidosis (e.g. ATTR, AA, or hereditary forms)
3. Prior autologous or allogeneic HCT
4. Tandem or planned tandem AHSCT
5. Prior exposure to investigational therapies outside standard regimens that confound analysis (this does NOT exclude patients enrolled in the Andromeda study).

Data points:

A. Patient related
   - Age, gender, race, performance status (KPS and ECOG), medical comorbidities
   - Hematopoietic cell transplantation co-morbidity index (HCT-CI)

B. Disease related factors at diagnosis and at pretransplant assessment if available.
   - Organ involvement and depth of involvement (Renal only, Cardiac only or muti-organ
   - Mayo 2012 stage at diagnosis and renal stage in cases of renal only disease[10]
   - Pre-AHSCT induction therapy disease status at AHSCT
   -
   - Concurrent MUGS or smoldering myeloma or lymphoplasmacytic lymphoma
   - NYHA class, 6-minute walk distance
   - Involved LVEF %, diastolic dysfunction grade, IV septal thickness, LV strain BNP/NT-proBNP, troponin I/T, GLS strain
   - Presence or history of Afib, tachyarrhythmia or VTach or hypotension at diagnosis and at pre-transplant assessment.
   - Bone marrow plasma cell percentage at diagnosis and at pretransplant assessment
   - Serum free light chains, and serum and urineM-protein
   - Proteinuria
   - Serum creatinine
   - Quantification of Nephrotic or sub-nephrotic range proteinuria
   - Dialysis dependence and timing of need for dialysis
   - Cytogenetic abnormality at diagnosis

C. Treatment related
   - Relapse-free interval after ASCT
   - Induction therapy used at initial diagnosis
   - Response pre-ASCT- sCR, CR, VGPR, PR, progression
   - Response 100 day post-ASCT- sCR, CR, VGPR, PR, progression
   - PFS and OS from ASCT
   - Type of progression (hematological, organ)
   - Duration of initial hospitalization for ASCT.
   - Unplanned rehospitalizations within 100 days
   - Hematological/transplant-related toxicities, including febrile neutropenia, ICU admission during

transplant course, delayed neutrophil/platelet/hemoglobin recovery
- End-organ complications, including but not limited to peri-transplant arrhythmias, heart failure decompensation, cardiac arrest/sudden cardiac death, need for dialysis initiation, worsening chronic kidney disease stage, respiratory failure requiring mechanical ventilation
- Quality of life (QoL) decline within 3−6 months
- Date of death, if applicable
    - Day-100 mortality
    - Cause of death, if applicable
- Non-relapse mortality
    - 1-year non-relapse mortality (NRM)

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PROP 2509-31; 2509-103; 2509-166; 2509-168; 2509-216: Role of stem cell transplant and maintenance therapy in the management of AL amyloidosis in the era of Daratumumab (H Shaikh/ E Muchtar/ S Maqbool/ F Answer/ Z Gong/ M S Faisal/ Y Efebera/ R Tokarski/ S Devarakonda)

Table. Characteristics of patients with Amyloidosis who received first autoHCT between 2008-2025, and reported to the CIBMTR (stratified by pre-HCT induction therapy)

		CRF-level data					
Characteristic	**TED-level data[1]**	**Dara-based induction**	**Non-Dara induction**	**Non-systemic induction**	**No induction**	**Unknown**	**Total**
No. of patients	2898	47	689	2	176	137	3949
No. of centers	222	25	92	2	43	42	229
Patient-related characteristics							
Age, by decades, no. (%)							
Median (range)	61 (28-83)	64 (42-75)	61 (28-78)	60 (54-66)	62 (24-77)	58 (26-74)	61 (24-83)
20-29	4 (0)	0 (0)	1 (0)	0 (0)	1 (1)	1 (1)	7 (0)
30-39	54 (2)	0 (0)	16 (2)	0 (0)	2 (1)	5 (4)	77 (2)
40-49	344 (12)	8 (17)	76 (11)	0 (0)	11 (6)	18 (13)	457 (12)
50-59	897 (31)	7 (15)	227 (33)	1 (50)	62 (35)	52 (38)	1246 (32)
60-69	1300 (45)	25 (53)	296 (43)	1 (50)	84 (48)	52 (38)	1758 (45)
70+	299 (10)	7 (15)	73 (11)	0 (0)	16 (9)	9 (7)	404 (10)
Sex, no. (%)							
Male	1720 (59)	31 (66)	390 (57)	0 (0)	99 (56)	81 (59)	2321 (59)
Female	1178 (41)	16 (34)	299 (43)	2 (100)	77 (44)	56 (41)	1628 (41)
Race, no. (%)							
White	2123 (73)	41 (87)	540 (78)	2 (100)	151 (86)	105 (77)	2962 (75)
Black or African American	356 (12)	4 (9)	101 (15)	0 (0)	18 (10)	11 (8)	490 (12)
Asian	116 (4)	0 (0)	15 (2)	0 (0)	4 (2)	4 (3)	139 (4)
Native Hawaiian or other Pacific Islander	7 (0)	0 (0)	1 (0)	0 (0)	0 (0)	0 (0)	8 (0)

Characteristic	TED-level data[1]	CRF-level data					Total
		Dara-based induction	Non-Dara induction	Non-systemic induction	No induction	Unknown	
American Indian or Alaska Native	7 (0)	1 (2)	4 (1)	0 (0)	0 (0)	0 (0)	12 (0)
More than one race	18 (1)	0 (0)	5 (1)	0 (0)	1 (1)	1 (1)	25 (1)
Not reported	271 (9)	1 (2)	23 (3)	0 (0)	2 (1)	16 (12)	313 (8)
Ethnicity, no. (%)							
Hispanic or Latino	211 (7)	6 (13)	43 (6)	1 (50)	10 (6)	8 (6)	279 (7)
Non-Hispanic or Latino	2325 (80)	40 (85)	612 (89)	1 (50)	161 (91)	118 (86)	3257 (82)
Non-resident of the U.S.	296 (10)	0 (0)	17 (2)	0 (0)	0 (0)	11 (8)	324 (8)
Not reported	66 (2)	1 (2)	17 (2)	0 (0)	5 (3)	0 (0)	89 (2)
Center region at transplant, no. (%)							
US	2536 (88)	47 (100)	670 (97)	1 (50)	173 (98)	118 (86)	3545 (90)
Canada	133 (5)	0 (0)	8 (1)	0 (0)	0 (0)	7 (5)	148 (4)
Europe	59 (2)	0 (0)	2 (0)	0 (0)	0 (0)	1 (1)	62 (2)
Asia	66 (2)	0 (0)	3 (0)	0 (0)	1 (1)	2 (1)	72 (2)
Australia/New Zealand	7 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	7 (0)
Mideast/Africa	13 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (2)	16 (0)
Central/South America	84 (3)	0 (0)	6 (1)	1 (50)	2 (1)	6 (4)	99 (3)
Karnofsky score prior to HCT, no. (%)							
90-100%	1470 (51)	17 (36)	305 (44)	1 (50)	87 (49)	60 (44)	1940 (49)
< 90%	1357 (47)	28 (60)	370 (54)	1 (50)	84 (48)	73 (53)	1913 (48)
Not reported	71 (2)	2 (4)	14 (2)	0 (0)	5 (3)	4 (3)	96 (2)
HCT-CI, no. (%)							
0	649 (22)	5 (11)	134 (19)	1 (50)	46 (26)	47 (34)	882 (22)
1	336 (12)	7 (15)	61 (9)	0 (0)	23 (13)	19 (14)	446 (11)

Characteristic	TED-level data[1]	CRF-level data					Total
		Dara-based induction	Non-Dara induction	Non-systemic induction	No induction	Unknown	
2	481 (17)	10 (21)	111 (16)	1 (50)	23 (13)	20 (15)	646 (16)
3	478 (16)	4 (9)	117 (17)	0 (0)	32 (18)	14 (10)	645 (16)
4	327 (11)	10 (21)	96 (14)	0 (0)	24 (14)	15 (11)	472 (12)
5+	559 (19)	11 (23)	161 (23)	0 (0)	28 (16)	19 (14)	778 (20)
Not reported	68 (2)	0 (0)	9 (1)	0 (0)	0 (0)	3 (2)	80 (2)
Disease-related characteristics							
Interval from diagnosis to HCT, months, median (range)	8 (1-760)	9 (4-52)	8 (0-340)	5 (2-8)	3 (1-71)	5 (1-1205)	7 (0-1205)
MM pre-HCT disease stage, no. (%)							
CR1	122 (4)	3 (6)	64 (9)	0 (0)	1 (1)	3 (2)	193 (5)
CR2	555 (19)	10 (21)	231 (34)	0 (0)	6 (3)	20 (15)	822 (21)
PR	309 (11)	1 (2)	135 (20)	2 (100)	61 (35)	17 (12)	525 (13)
Not reported	1912 (66)	33 (70)	259 (38)	0 (0)	108 (61)	97 (71)	2409 (61)
Transplant-related Characteristics							
Conditioning regimen, no. (%)							
Bu/Mel	1 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0)
Cy alone	1 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0)
BEAM	17 (1)	0 (0)	9 (1)	0 (0)	1 (1)	0 (0)	27 (1)
Mel alone	2800 (97)	47 (100)	676 (98)	2 (100)	174 (99)	137 (100)	3836 (97)
Mel/other(s)	10 (0)	0 (0)	4 (1)	0 (0)	1 (1)	0 (0)	15 (0)
Other(s)	1 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0)
Missing	68 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	68 (2)
Year of current transplant, no. (%)							

Characteristic	TED-level data[1]	CRF-level data					Total
		Dara-based induction	Non-Dara induction	Non-systemic induction	No induction	Unknown	
2008	36 (1)	0 (0)	29 (4)	0 (0)	0 (0)	49 (36)	114 (3)
2009	98 (3)	0 (0)	30 (4)	0 (0)	1 (1)	31 (23)	160 (4)
2010	156 (5)	0 (0)	3 (0)	0 (0)	0 (0)	1 (1)	160 (4)
2011	187 (6)	0 (0)	3 (0)	0 (0)	1 (1)	0 (0)	191 (5)
2012	188 (6)	0 (0)	3 (0)	0 (0)	0 (0)	0 (0)	191 (5)
2013	191 (7)	0 (0)	17 (2)	0 (0)	1 (1)	6 (4)	215 (5)
2014	89 (3)	0 (0)	103 (15)	0 (0)	40 (23)	15 (11)	247 (6)
2015	100 (3)	0 (0)	97 (14)	2 (100)	32 (18)	11 (8)	242 (6)
2016	106 (4)	0 (0)	130 (19)	0 (0)	34 (19)	9 (7)	279 (7)
2017	98 (3)	3 (6)	114 (17)	0 (0)	31 (18)	5 (4)	251 (6)
2018	162 (6)	10 (21)	77 (11)	0 (0)	27 (15)	1 (1)	277 (7)
2019	200 (7)	9 (19)	70 (10)	0 (0)	8 (5)	4 (3)	291 (7)
2020	247 (9)	3 (6)	7 (1)	0 (0)	1 (1)	2 (1)	260 (7)
2021	251 (9)	2 (4)	1 (0)	0 (0)	0 (0)	0 (0)	254 (6)
2022	235 (8)	4 (9)	1 (0)	0 (0)	0 (0)	0 (0)	240 (6)
2023	222 (8)	5 (11)	0 (0)	0 (0)	0 (0)	1 (1)	228 (6)
2024	198 (7)	7 (15)	2 (0)	0 (0)	0 (0)	1 (1)	208 (5)
2025[2]	134 (5)	4 (9)	2 (0)	0 (0)	0 (0)	1 (1)	141 (4)
Post-HCT maintenance therapy (CRF only), no. (%)							
No	0 (0)	28 (60)	414 (60)	1 (50)	129 (73)	82 (60)	654 (62)
Yes	0 (0)	18 (38)	267 (39)	1 (50)	47 (27)	29 (21)	362 (34)
Systemic therapy	0 (0)	18 (38)	253 (37)	1 (50)	47 (27)	24 (18)	343 (33)

Characteristic	TED-level data[1]	CRF-level data					Total
		Dara-based induction	Non-Dara induction	Non-systemic induction	No induction	Unknown	
DVD (Daratumumab, Bortezomib, dexamethasone)	0 (0)	0 (0)	5 (1)	0 (0)	0 (0)	3 (2)	8 (1)
KRD (Carfilzomib, Lenalidomide, dexamethasone)	0 (0)	0 (0)	1 (0)	0 (0)	0 (0)	0 (0)	1 (0)
RD (Lenalidomide, dexamethasone)	0 (0)	0 (0)	5 (1)	0 (0)	1 (1)	3 (2)	9 (1)
RVD/VRD (Bortezomib, Lenalidomide, dexamethasone)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1)	0 (0)	1 (0)
VCD/CVD/CyBorD (Bortezomib, Cyclophosphamide, dexamethasone)	0 (0)	0 (0)	7 (1)	0 (0)	2 (1)	2 (1)	11 (1)
Cytarabine (Ara-C)	0 (0)	0 (0)	1 (0)	0 (0)	0 (0)	0 (0)	1 (0)
Systemic drugs - Carfilzomib	0 (0)	0 (0)	8 (1)	0 (0)	3 (2)	1 (1)	12 (1)
Cisplatin (Platinol, CDDP)	0 (0)	0 (0)	1 (0)	0 (0)	0 (0)	0 (0)	1 (0)
Corticosteroids	0 (0)	3 (6)	71 (10)	0 (0)	24 (14)	5 (4)	103 (10)
Cyclophosphamide (Cytoxan)	0 (0)	0 (0)	19 (3)	0 (0)	15 (9)	2 (1)	36 (3)
Systemic drugs - Daratumumab	0 (0)	12 (26)	60 (9)	0 (0)	10 (6)	8 (6)	90 (9)
Systemic drugs - Elotuzumab	0 (0)	0 (0)	2 (0)	0 (0)	0 (0)	0 (0)	2 (0)
Systemic drugs - Ixazomib	0 (0)	2 (4)	16 (2)	0 (0)	2 (1)	1 (1)	21 (2)
Melphalan (L-PAM, Alkeran)	0 (0)	0 (0)	3 (0)	0 (0)	1 (1)	0 (0)	4 (0)
Systemic drugs - Pomalidomide	0 (0)	0 (0)	9 (1)	0 (0)	1 (1)	0 (0)	10 (1)
Lenalidomide (Revlimid)	0 (0)	7 (15)	113 (16)	0 (0)	16 (9)	5 (4)	141 (13)
Systemic drugs - Rituximab	0 (0)	0 (0)	1 (0)	0 (0)	0 (0)	1 (1)	2 (0)
Systemic drugs - Selinexor	0 (0)	0 (0)	1 (0)	0 (0)	0 (0)	0 (0)	1 (0)
Systemic drugs - Thalidomide	0 (0)	0 (0)	3 (0)	0 (0)	0 (0)	0 (0)	3 (0)

Characteristic	TED-level data[1]	CRF-level data					Total
		Dara-based induction	Non-Dara induction	Non-systemic induction	No induction	Unknown	
Systemic drugs - Venetoclax	0 (0)	3 (6)	10 (1)	0 (0)	1 (1)	1 (1)	15 (1)
Bortezomib (Velcade)	0 (0)	1 (2)	110 (16)	1 (50)	34 (19)	7 (5)	153 (15)
Other systemic therapy	0 (0)	2 (4)	89 (13)	0 (0)	18 (10)	6 (4)	115 (11)
Radiation therapy	0 (0)	0 (0)	2 (0)	0 (0)	0 (0)	0 (0)	2 (0)
Not reported	0 (0)	1 (2)	8 (1)	0 (0)	0 (0)	26 (19)	35 (3)
Follow-up of survivors, median (range), months	50.4 (0.0-194.8)	50.0 (0.0-73.8)	95.4 (0.0-208.3)	121.4 (121.4-121.4)	95.8 (18.8-168.7)	169.4 (0.0-199.0)	71.1 (0.0-208.3)

Data source: HCT Essentials December 2025

[1] Induction data not collected on TED forms

[2] Incomplete - Data still being reported for year 2025

Field	Response
Proposal Number	2509-74-FREEMAN
Proposal Title	INSIGHT-BCMA: AI-Enabled Risk & Outcome Modeling Using the CIBMTR Registry
Principal Investigator #1: - First and last name, degree(s)	Ciara Freeman MD PhD MSc
Principal Investigator #1: - Email address	ciara.freeman@moffitt.org
Principal Investigator #1: - Institution name	Moffitt Cancer Center
Principal Investigator #1: - Academic rank	Associate
Junior investigator status (defined as 𝛼、5 years from fellowship)	No
Do you identify as an underrepresented/minority?	No
Principal Investigator #2 (If applicable): - First and last name, degree(s):	Issam M. El Naqa
Principal Investigator #2 (If applicable): - Email address:)	issam.elnaqa@moffitt.org
Principal Investigator #2 (If applicable): - Institution name:	Moffitt Cancer Center
Principal Investigator #2 (If applicable): - Academic rank:	Chair, Machine Learning
Junior investigator status (defined as 𝛼、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:	Ciara Freeman
Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.	Involved in the weighted comparison between ide-cel and cilta-cel, I was senior author on the poster presentation just presented at IMS and provided input into the analysis and presented findings.
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:	Dr Taiga Nishihori

Field	Response
RESEARCH QUESTION:	Validate an AI-enabled model that predicts early treatment failure (disease-specific survival) following BCMA CAR-T therapy
RESEARCH HYPOTHESIS:	In real-world rrMM patients receiving ide-cel or cilta-cel, an AI model using CIBMTR data will more accurately predict 12-month Early Treatment Failure (ETF) than SCOPE, CAR-HEMATOTOX and GPS score, and will provide actionable, therapy-normalized percentile risk that improves clinical decision utility.
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	Primary Aim Validate an AI-enabled model that predicts 12-month Early Treatment Failure (ETF) after BCMA CAR-T. ETF will be operationalized as disease-specific treatment failure by day 365 from infusion (death related to myeloma, IMWG-defined progression/relapse, or initiation of non-maintenance next therapy). Performance targets: ΔAUC/C-index 0.05 vs. best comparator, calibration slope 0.9 1.1, Brier ↓ 0.01, and superior net benefit on decision-curve analysis. Secondary Aims Validate companion AI models for 12-month toxicity risks: non-relapse mortality (NRM), prolonged grade 3 cytopenias, delayed neurotoxicity (beyond acute ICANS), and severe grade 3 infections. Conduct product-level comparisons (ide-cel vs. cilta-cel) across efficacy (ETF, PFS), safety (CRS/ICANS, cytopenias, infections, NRM), and logistics (LOS, ICU use, time-to-infusion) using the completed dataset. Benchmark AI models against CAR-HEMATOTOX, EASIX-MM, GPS, and SCOPE for discrimination, calibration, reclassification (category-free NRI 0.10), and clinical utility. Demonstrate transportability with temporal, center, and product hold-outs (<10% relative AUC drop) and equity guardrails (calibration-in-the-large gap <0.05 across key subgroups). Provide interpretable outputs, including absolute 12-month ETF probability and therapy-normalized percentile within product-specific reference distributions to support patient counseling and treatment selection.

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.	Multiple myeloma (MM) is the second most common hematological malignancy and remains incurable, affecting a predominantly older patient population with a median age of diagnosis of 69 with most patients aged between 65-74[1]. In a real-world setting, >50% of myeloma patients are burdened with co-morbidities [2] and >70% of real-world myeloma patients are ineligible for registration trials that lead to therapy approval[3]. In these populations, relapse and toxicity rates remain unacceptably high, and clinical decision-making is often uncertain. The comparative analysis of ide-cel and cilta-cel outcomes has already been performed[4] through both consortium and CIBMTR datasets, providing the most comprehensive product-level benchmarking available. This unique foundation allows the current proposal to go beyond descriptive outcomes and focus on AI-enabled risk modeling, which represents the next logical and high-impact step. Unique aspects and impact include: Transparent, not black-box models: The analytic approach prioritizes interpretable outputs risk tiers, calibrated probabilities, and variable importance rankings that clinicians can trust and apply, rather than opaque predictions. Fills a gap left by existing tools: Current prognostic models (CAR-HEMATOTOX, EASIX-MM, GPS, SCOPE) were developed in restricted populations or limited institution cohorts. As a result, they have not been broadly adopted in practice. CIBMTR AI models will be built on the largest real-world dataset available, ensuring generalizability across centers and patient populations. Actionable clinical relevance: Models will predict early relapse and key toxicities (NRM, cytopenias, delayed neurotoxicity, severe infections), enabling tailored counseling, optimized supportive care, and informed patient selection. In short, the comparative dataset is mature and complete; what is urgently needed and uniquely feasible now is to translate these data into transparent, clinically interpretable predictive tools that can be trusted to guide care in real-world practice.

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.	The comparative outcomes of idecabtagene vicleucel (ide-cel) and ciltacabtagene autoleucel (cilta-cel) in relapsed/refractory multiple myeloma have now been characterized at scale in two complementary datasets: CIBMTR analysis: In the largest registry-based comparison to date, cilta-cel demonstrated deeper responses and superior PFS/OS relative to ide-cel, but at the cost of higher treatment-related mortality and delayed neurotoxicity, underscoring the importance of refined patient selection and risk mitigation (Afrough et al, IMS 2025). Consortium study[4] (Hansen et al., JCO 2025): Across 19 academic centers (n=586 infused), cilta-cel was associated with higher odds of grade 3 CRS, infections, and delayed neurotoxicity, but also with significantly longer survival and higher rates of CR. Importantly, the majority of real-world patients (73% ide-cel, 56% cilta-cel) would not have met pivotal trial eligibility, highlighting the heterogeneity of treated populations. Together, these analyses provide definitive product-level comparisons and confirm both the promise and challenges of BCMA CAR-T in the real world. However, they also expose a critical evidence gap: Results remain population-level averages; clinicians still lack patient-specific tools to estimate risk of early relapse or severe toxicity. Existing models (CAR-HEMATOTOX, EASIX-MM, GPS, SCOPE) were derived from select-institution datasets and have not been broadly implemented in practice. Neither the CIBMTR nor consortium analyses to date provide transparent, individualized predictions that can inform clinical decisions. The next logical step is to harness the depth of the CIBMTR dataset including demographics, disease biology, laboratory markers, and already-curated product comparisons to develop AI-enabled but non black-box predictive models. Such models will: Translate robust comparative findings into clinically usable, explainable risk tools , Identify which patients are most likely to relapse early or suffer high-grade or unique toxicities, Enable tailored supportive care and eligibility decisions Thus, this proposal is justified not to repeat comparative analyses, but to operationalize them into predictive models that address the urgent, unmet need for individualized, real-world risk assessment in BCMA CAR-T therapy.

Field	Response
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	Patient Eligibility Population Inclusion: Adult patients (18 years) with relapsed/refractory multiple myeloma who received idecabtagene vicleucel (ide-cel) or ciltacabtagene autoleucel (cilta-cel) as their first commercial CAR-T therapy following the date of first global approval (March 26, 2021). Exclusion: Patients treated with investigational CAR-T constructs, or with prior CAR-T exposure.
Does this study include pediatric patients?	No
If this study does not include pediatric patients, please provide justification:	Myeloma does not affect children.
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-level (demographics & baseline status) Age at infusion, sex, race/ethnicity; BMI; performance status; baseline organ function (renal, hepatic), cardiac/pulmonary disease; diabetes; prior infections; HCT-CI/comorbidity indicators where captured; prior HCT (auto/allo), time since HCT; payer/insurance (proxy for access). Disease-level (myeloma history & burden) Diagnosis date, ISS/R-ISS* where available, cytogenetic risk* (e.g., del17p/1q gain if present on forms), prior lines, refractory status, bridging therapy use, disease status at infusion (CR/VGPR/PR/SD/PD), baseline LDH, albumin, creatinine, ferritin, CRP, hemoglobin/platelets, marrow plasma cell %, extramedullary disease. Infusion/product-level (treatment details) Product: ide-cel vs cilta-cel; commercial vs protocol; planned number of infusions; cell dose; manufacturing/vein-to-vein dates if present; lymphodepletion regimen/doses; inpatient vs outpatient Follow-up & outcomes (to build 12-mo ETF + safety) Vital status; relapse/progression (IMWG where recorded); initiation of next therapy (date, agent class) to compose ETF; hospitalization/ICU use; CRS and ICANS grades per CIBMTR/ASTCT capture windows (100-day/6-mo/1-yr); NRM; prolonged G3 cytopenias; serious infections (grade 3), non-icans neurotoxicity, readmissions. Center-level (for hierarchical adjustment) Center identifier/volume, country/region, calendar year (practice era)
Types of cellular therapy data this proposal includes:	Chimeric Antigen Receptor (CAR) T-Cell Therapy (CAR-T)

Field	Response
MACHINE LEARNING: Please indicate if the study requires methodology related to machine-learning and clinical predictions.	This study requires machine-learning for clinical prediction using CIBMTR data. Our team has full end-to-end capability (data harmonization → model training → validation → reporting). Issam's group will execute modeling, and results can be verified with the CIBMTR statistical/AI team for methodological concordance and reproducibility.

REFERENCES:	1. SEER: Surveillance, epidemiology, and end results program; cancerstat facts: myeloma. [cited 2021 22 September]; Available from: https://seer.cancer.gov/explorer/application.html?site=89&data_type=1&graph_type=3&compareBy=sex&chk_sex_1=1&rate_type=2&race=1&advopt_precision=1&advopt_show_ci=on. 2. Sverrisdttir, I.S., et al., Comorbidities in multiple myeloma and implications on survival: A population-based study. European Journal of Haematology, 2021. 106(6): p. 774-782. 3. Chari, A., et al., Randomized Clinical Trial Representativeness and Outcomes in Real-World Patients: Comparison of 6 Hallmark Randomized Clinical Trials of Relapsed/Refractory Multiple Myeloma. Clinical Lymphoma Myeloma and Leukemia, 2020. 20(1): p. 8-17.e16. 4. Hansen, D.K., et al., Comparison of Standard-of-Care Idecabtagene Vicleucel and Ciltacabtagene Autoleucel in Relapsed/Refractory Multiple Myeloma. J Clin Oncol, 2025: p. Jco2401730. 5. Cui, S., R.K. Ten Haken, and I. El Naqa, Integrating Multiomics Information in Deep Learning Architectures for Joint Actuarial Outcome Prediction in Non-Small Cell Lung Cancer Patients After Radiation Therapy. Int J Radiat Oncol Biol Phys, 2021. 110(3): p. 893-904. 6. Wei, L., et al., Artificial intelligence (AI) and machine learning (ML) in precision oncology: a review on enhancing discoverability through multiomics integration. Br J Radiol, 2023. 96(1150): p. 20230211. 7. Dudas, D., T.J. Dilling, and I.E. Naqa, A deep learning-informed interpretation of why and when dose metrics outside the PTV can affect the risk of distant metastasis in SBRT NSCLC patients. Radiat Oncol, 2024. 19(1): p. 127. 8. Mayfield, J.D., et al., Presurgical Upgrade Prediction of DCIS to Invasive Ductal Carcinoma Using Time-dependent Deep Learning Models with DCE MRI. Radiol Artif Intell, 2024. 6(5): p. e230348. 9. Mayfield, J.D., et al., Time-Dependent Deep Learning Prediction of Multiple Sclerosis Disability. J Imaging Inform Med, 2024. 37(6): p. 3231-3249. 10. Dudas, D., et al., Deep Learning-Guided Dosimetry for Mitigating Local Failure of Patients With Non-Small Cell Lung Cancer Receiving Stereotactic Body Radiation Therapy. Int J Radiat Oncol Biol Phys, 2024. 119(3): p. 990-1000. 11. Wei, L., et

Field	Response
	al., Deep learning prediction of post-SBRT liver function changes and NTCP modeling in hepatocellular carcinoma based on DGAE-MRI. Med Phys, 2023. 50(9): p. 5597-5608. 12. Wei, L., et al., A deep survival interpretable radiomics model of hepatocellular carcinoma patients. Phys Med, 2021. 82: p. 295-305.
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

PROP 2509-74: INSIGHT-BCMA: AI-Enabled Risk & Outcome Modeling Using the CIBMTR Registry (C Freeman/ I El Naqa)

Table. Characteristics of patients who underwent first CAR-T for Multiple Myeloma between 2021-2025, and reported to the CIBMTR

Characteristic	Ide-cel	Cilta-cel	Total
No. of patients	1742	2367	4109
No. of centers	90	83	109
Patient-related			
Age, by decades, no. (%)			
Median (range)	67 (29-90)	65 (33-87)	66 (29-90)
20-29	1 (0)	0 (0)	1 (0)
30-39	9 (1)	19 (1)	28 (1)
40-49	75 (4)	150 (6)	225 (5)
50-59	317 (18)	553 (23)	870 (21)
60-69	674 (39)	970 (41)	1644 (40)
70+	666 (38)	675 (29)	1341 (33)
Recipient Sex, no. (%)			
Male	1017 (58)	1340 (57)	2357 (57)
Female	725 (42)	1025 (43)	1750 (43)
Not reported	0 (0)	2 (0)	2 (0)
Recipient race, no. (%)			
White	1335 (77)	1792 (76)	3127 (76)
Black or African American	292 (17)	361 (15)	653 (16)
Asian	37 (2)	72 (3)	109 (3)
Native Hawaiian or other Pacific Islander	5 (0)	3 (0)	8 (0)
American Indian or Alaska Native	9 (1)	8 (0)	17 (0)
Other	6 (0)	15 (1)	21 (1)
More than one race	38 (2)	83 (4)	121 (3)
Missing	20 (1)	33 (1)	53 (1)
Ethnicity, no. (%)			
Hispanic or Latino	142 (8)	226 (10)	368 (9)
Not Hispanic or Latino	1560 (90)	2066 (87)	3626 (88)
Non-resident of the U.S.	0 (0)	7 (0)	7 (0)
Not reported	40 (2)	68 (3)	108 (3)
Karnofsky performance score prior to CT, no. (%)			
90-100	568 (33)	1016 (43)	1584 (39)
80	640 (37)	710 (30)	1350 (33)
< 80	367 (21)	346 (15)	713 (17)
Not reported	167 (10)	295 (12)	462 (11)
HCT comorbidity score, no. (%)			

Characteristic	Ide-cel	Cilta-cel	Total
0	360 (21)	670 (28)	1030 (25)
1	288 (17)	452 (19)	740 (18)
2	259 (15)	336 (14)	595 (14)
3	324 (19)	363 (15)	687 (17)
4	207 (12)	240 (10)	447 (11)
5+	298 (17)	296 (13)	594 (14)
Not reported	6 (0)	10 (0)	16 (0)
Disease-related			
Sub-disease, no. (%)			
Multiple myeloma, NOS	1299 (75)	1849 (78)	3148 (77)
Smoldering myeloma	1 (0)	0 (0)	1 (0)
Multiple myeloma - light chain only	408 (23)	486 (21)	894 (22)
Multiple myeloma - non-secretory	34 (2)	32 (1)	66 (2)
Disease status prior to CT for PCD, no. (%)			
Stringent complete remission (sCR)	7 (0)	28 (1)	35 (1)
Complete remission (CR)	21 (1)	61 (3)	82 (2)
Very good partial remission (VGPR)	144 (8)	279 (12)	423 (10)
Partial response (PR)/ Not Complete Remission	230 (13)	349 (15)	579 (14)
Stable disease (SD)	272 (16)	464 (20)	736 (18)
Progressive disease (PD)	1047 (60)	1130 (48)	2177 (53)
Relapse from CR (Rel) (untreated)	17 (1)	43 (2)	60 (1)
Not reported	4 (0)	13 (1)	17 (0)
C-Reactive protein prior to infusion, no. (%)			
Data available	438 (25)	1576 (67)	2014 (49)
Data not reported	1304 (75)	791 (33)	2095 (51)
Serum ferritin prior to infusion, no. (%)			
Data available	425 (24)	1493 (63)	1918 (47)
Data not reported	1317 (76)	874 (37)	2191 (53)
Treatment-related			
Number of lines of prior therapies (including HCT and CT), no. (%)			
Median (range)	6 (1-20)	5 (1-20)	6 (1-20)
1	7 (0)	19 (1)	26 (1)
2	42 (2)	122 (5)	164 (4)
3	54 (3)	234 (10)	288 (7)
4+	904 (52)	1780 (75)	2684 (65)
Not reported	735 (42)	212 (9)	947 (23)
Year of CT, no. (%)			
2021	278 (16)	0 (0)	278 (7)
2022	512 (29)	192 (8)	704 (17)
2023	561 (32)	681 (29)	1242 (30)

Characteristic	Ide-cel	Cilta-cel	Total
2024	341 (20)	1230 (52)	1571 (38)
2025[1]	50 (3)	264 (11)	314 (8)
Follow-up of survivors, months, median (range)	24 (1-49)	12 (1-37)	13 (1-49)

Data source: CT Extract September 2025

[1] Data incomplete for year 2025

Field	Response
Proposal Number	2509-127-SHARMA
Proposal Title	BCMA directed CAR-T cell therapy in plasma cell leukemia
Key Words	BCMA, CAR-T, Plasma cell leukemia
Principal Investigator #1: - First and last name, degree(s)	Nidhi Sharma, PhD
Principal Investigator #1: - Email address	nidhi.sharma@osumc.edu
Principal Investigator #1: - Institution name	The Ohio State University
Junior investigator status (defined as 㑊、5 years from fellowship)	No
Do you identify as an underrepresented/minority?	No
Principal Investigator #2 (If applicable): - First and last name, degree(s):	Srinivas, Devarakonda, MD
Principal Investigator #2 (If applicable): - Email address:)	srinivas.devarakonda@osumc.edu
Principal Investigator #2 (If applicable): - Institution name:	The Ohio State University
Principal Investigator #2 (If applicable): - Academic rank:	Associate Professor
Junior investigator status (defined as 㑊、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:	Nidhi Sharma
Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.	Infections in Patients with Relapsed Refractory Multiple Myeloma Receiving Idecabtagene Vicleucel Therapy: Real-World Analysis from CIBMTR 2nd PI (Srinivas Devarakonda) is a Co-I on the above-mentioned project and co-author on the manuscript
Do any of the PI(s) within this proposal have a CIBMTR WC study in manuscript preparation >6 months?	Yes
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

Field	Response
RESEARCH QUESTION:	What is the response rate, survival outcomes and incidence of cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) post chimeric antigen receptor T (CAR-T) therapy in Plasma cell Leukemia patients.
RESEARCH HYPOTHESIS:	Relapsed/refractory plasma cell leukemia patients may benefit from CAR T Cell treatment.
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	Primary: Incidence of adverse events (AE;s), CRS and ICANS) in PCL patients receiving CAR-T cell products. Secondary: Overall response rates and survival rates after CAR T-cell therapy.
SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.	Plasma cell leukemia (PCL) is a rare and highly aggressive form of multiple myeloma (MM) and is often occurring in patients with relapsed/refractory multiple myeloma (RRMM) (1,2). PCL patients have an unfavorable prognosis, and the management of PCL remains challenging (3). PCL patients are mostly underrepresented in clinical trials and hence is an unmet need. The successes seen in MM have prompted further study of CAR T-cells in patients with newly diagnosed MM (4,5). This raises the question of whether these existing plasma-cell-directed CAR T therapies could benefit other challenging plasma cell disorders, particularly those without a clear standard of care or with inferior outcomes. Chimeric antigen receptor T-cell (CAR-T) therapy has emerged as a promising approach for relapsed/refractory plasma cell disorders (6-8). Studies have shown high response rates in PCL, even among patients with high-risk features. However, short progression-free survival and notable toxicity highlight the need for refined patient selection and future trials to optimize outcomes. Despite promising results, short progression-free survival and notable toxicity highlight the need for refined patient selection, treatment protocols, and long-term management to improve outcomes.

Field	Response
SCIENTIFIC JUSTIFICATION: Provide a background summary of previous related research and their strengths and weaknesses, justification of your research and why your research is still necessary.	CAR-T cell therapy is shown to be effective in treating RRMM patients (6-8). However, plasma cell leukemia patients have historically had a poor prognosis, with limited therapeutic options. These patients can now receive commercially available BCMA-directed CAR T-cell therapies; however, the clinical experience has remained limited with the concern that such therapy may potentially increase toxicity. Short progression free survival and notable toxicity highlight the need for refined patient selection and future trials to optimize outcomes. Hence, there is a need for therapy for plasma cell leukemia. Given the low percentage of patients, CIBMTR provides the largest data information to answer this question. This study aims to gain more information on the overall Outcomes, and incidence of CRS and ICANS. This knowledge would perhaps help to optimize therapy to improve the outcomes in this patient population.
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	Inclusion criteria: 1. Patients aged 18 years old with plasma cell leukemia who received CAR-T cell therapy.
Does this study include pediatric patients?	No
If this study does not include pediatric patients, please provide justification:	MM is predominantly a disease of older 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.	Data points: A. Patient related Age, gender, ethnicity, race, performance status, comorbidity index B. Disease related Myeloma protein type, ISS and R-ISS Stage, FISH, cytogenetics, presence/absence of extramedullary disease, prior transplant, CART product, CART- dose, post CART-therapy, disease response pre and post CAR-T therapy C. Treatment related Number of prior lines of therapy Prior treatment with Immune modulators, proteasome inhibitors, anti CD38 monoclonal antibody, bispecific antibodies, selinexor Bridging therapy used Response to bridging therapy Toxicities Refractory disease CRS grade, ICANS grade Neutropenia Anemia Throbocytopenia Non-hematological events Infections Y/N Type of infection bacterial, viral, fungal, atypical Death related to infections Y/N Response to therapy MRD status pre and post CAR-T

Field	Response
Types of cellular therapy data this proposal includes:	Chimeric Antigen Receptor (CAR) T-Cell Therapy (CAR-T)
REFERENCES:	1 Gowin K, Skerget S, Keats JJ, Mikhael J, Cowan AJ. Plasma cell leukemia: A review of the molecular classification, diagnosis, and evidenced-based treatment. Leuk Res. (2021) 111:106687. doi: 10.1016/j.leukres.2021.106687. 2. Gong Z, Khosla M, Vasudevan S, Mohan M. Current status on management of primary plasma cell leukemia. Curr Oncol Rep. (2024) 26(9):1104 12. doi: 10.1007/s11912-024-01563-0. 3 Fernandez de Larrea C, Kyle RA, Durie BG, et al. Plasma cell leukemia: consensus statement on diagnostic requirements, response criteria and treatment recommendations by the International Myeloma Working Group. Leukemia. 2013;27(4):780 791. 4. Castaneda Puglianini O, Chavez JC. CARs moving forward: the development of CAR T-cell therapy in the earlier treatment course of hematologic Malignancies. Semin Hematol. (2024) 61(5):290 6. doi: 10.1053/j.seminhematol.2024.08.005 5. Anderson LD Jr., Dhakal B, Jain T, Oluwole OO, Shah GL, Sidana S, 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) 30:17 37. doi: 10.1016/j.jtct.2023.10.022. 6. Raje N, Berdeja J, Lin Y, et al. Anti-BCMA CAR T cell therapy in relapsed or refractory multiple myeloma. N Engl J Med. 2019;380(18):1726 1737.12. 7. Brudno JN, Maric I, Hartman SD, et al. T cells genetically modified to express an anti-B cell maturation antigen chimeric antigen receptor cause remissions of poor-prognosis relapsed multiple myeloma. J Clin Oncol. 2018;36(22):2267 2280. 8. Rodriguez-Otero P, Ailawadhi S, Arnulf B, Patel K, Cavo M, Nooka AK, et al. Ide-cel or standard regimens in relapsed and refractory multiple myeloma. N Engl J Med. (2023) 388:1002 14. doi: 10.1056/NEJMoa2213614.
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

PROP 2509-127: BCMA directed CAR-T cell therapy in plasma cell leukemia
(N Sharma/ S Devarakonda)

Table. Characteristics of patients who underwent first CAR-T for Plasma Cell Leukemia between 2021-2025, and reported to the CIBMTR

Characteristic	Ide-cel	Cilta-cel	Total
No. of patients	40	47	87
No. of centers	29	27	43
Patient Related			
Age, by decades, no. (%)			
Median (range)	65 (34-80)	61 (36-82)	62 (34-82)
30-39	1 (3)	3 (6)	4 (5)
40-49	3 (8)	6 (13)	9 (10)
50-59	10 (25)	12 (26)	22 (25)
60-69	15 (38)	22 (47)	37 (43)
70+	11 (28)	4 (9)	15 (17)
Recipient Sex, no. (%)			
Male	24 (60)	25 (53)	49 (56)
Female	16 (40)	22 (47)	38 (44)
Recipient race, no. (%)			
White	34 (85)	36 (77)	70 (80)
Black or African American	4 (10)	7 (15)	11 (13)
Asian	1 (3)	3 (6)	4 (5)
More than one race	1 (3)	1 (2)	2 (2)
Ethnicity, no. (%)			
Hispanic or Latino	2 (5)	3 (6)	5 (6)
Not Hispanic or Latino	38 (95)	43 (91)	81 (93)
Not reported	0 (0)	1 (2)	1 (1)
Karnofsky performance score prior to CT, no. (%)			
90-100	9 (23)	21 (45)	30 (34)
80	12 (30)	12 (26)	24 (28)
< 80	16 (40)	7 (15)	23 (26)
Not reported	3 (8)	7 (15)	10 (11)
HCT comorbidity score, no. (%)			
0	9 (23)	19 (40)	28 (32)
1	5 (13)	8 (17)	13 (15)
2	2 (5)	7 (15)	9 (10)
3	14 (35)	6 (13)	20 (23)
4	2 (5)	2 (4)	4 (5)
5+	8 (20)	5 (11)	13 (15)
Disease related			

Characteristic	Ide-cel	Cilta-cel	Total
Disease type, no. (%)			
Plasma cell leukemia	30 (75)	35 (74)	65 (75)
Concomitant PCD[1]	10 (25)	12 (26)	22 (25)
Disease status prior to CT for PCD, no. (%)			
Stringent complete remission (sCR)	0 (0)	2 (4)	2 (2)
Complete remission (CR)	0 (0)	2 (4)	2 (2)
Very good partial remission (VGPR)	6 (15)	6 (13)	12 (14)
Partial response (PR)/ Not Complete Remission	5 (13)	10 (21)	15 (17)
Stable disease (SD)	4 (10)	11 (23)	15 (17)
Progressive disease (PD)	24 (60)	16 (34)	40 (46)
Not reported	1 (3)	0 (0)	1 (1)
Treatment related			
Number of lines of prior therapies (including HCT and CT), no. (%)			
Median (range)	5 (2-10)	5 (2-9)	5 (2-10)
2	3 (8)	3 (6)	6 (7)
3	3 (8)	6 (13)	9 (10)
4+	18 (45)	29 (62)	47 (54)
Not reported	16 (40)	9 (19)	25 (29)
Year of CT, no. (%)			
2021	9 (23)	0 (0)	9 (10)
2022	8 (20)	5 (11)	13 (15)
2023	13 (33)	12 (26)	25 (29)
2024	8 (20)	25 (53)	33 (38)
2025[2]	2 (5)	5 (11)	7 (8)
Follow-up of survivors, months, median (range)	24 (2-36)	12 (3-36)	12 (2-36)

Data source: CT Extract September 2025

[1] Multiple myeloma - not specified n = 15, Multiple myeloma - light chain only n = 5, Multiple myeloma - non-secretory n = 2

[2] Data incomplete for year 2025