A G E N D A
CIBMTR WORKING COMMITTEE FOR PLASMA CELL DISORDERS
Orlando, FL
Thursday, February 16, 2023, 12:45 p.m. – 2:15 p.m. (EST)

Co-Chair:	**Muzaffar Qazilbash, MD, M.D. Anderson Cancer Center, Houston, TX; Telephone: 713-745-3458; E-mail: mqazilba@mdanderson.org**
Co-Chair:	**Nina Shah, MD, AstraZeneca, San Francisco, CA; Telephone: 646-335-3506; E-mail: nina.shah@astrazeneca.com**
Co-Chair:	**Heather Landau, MD, Memorial Sloan Kettering Cancer Center, New York, NY; E-mail: landauh@mskcc.org**
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1. **Introduction**
   a. **Leadership: Dr. Shah, outgoing chair (*Thank you!*), Dr. Taiga Nishihori (*Welcome on board!*)**
   b. **Minutes and overview plan from April 2022 meeting** (Attachment 1)
   c. **Instructions for sign-in and voting**

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

3. **Presentations, Published or Submitted Papers**
   a. **MM20-01** Kansagra A, Dispenzieri A, Fraser R, Estrada-Merly N, Sidana S, Nishihori T, Hansen DK, Anderson LD, Banerjee R, Bumma N, Dhakal B, Khouri J, Landau H, Lee C, Mian H, Nathan S, Savani B, Kumar S, Qazilbash M, Shah N, D'Souza A. Outcomes after autologous hematopoietic cell transplantation in POEMS syndrome and comparison with multiple myeloma. ***Blood Advances. 2022 Jul 12; 6(13):3991-3995. doi:10.1182/bloodadvances.2022007218. Epub 2022 May 4. PMC9278304.***
   b. **MM20-02A** Ragon BK, D'Souza A, Estrada-Merly N, Fraser R, George G, Gowda G, Shah N, Qazilbash MH, Kumar S, Horowitz MM, Usmani SZ, Shah MV. Impact of Second Primary Malignancy Post-Autologous Hematopoietic Stem Cell Transplantation on Outcomes of Multiple Myeloma: A CIBMTR Analysis. ***Poster presentation, ASCO 2022.***
   c. **MM20-03** Bumma N, Dhakal B, Fraser R, Estrada-Merly N, Kumar S, Shah N, Qazilbash M, D'Souza A, Sidana S. Impact of bortezomib-based vs. lenalidomide maintenance therapy on outcomes of patients with high-risk multiple myeloma. (N Bumma et al.) ***Oral presentation, Tandem Meetings 2022.***

[illegible] **MM21-01** [illegible] International Differences in Baseline Characteristics and Practice Patterns in Patients with Newly Diagnosed Multiple Myeloma Undergoing Upfront Autologous Stem Cell Transplantation. ***Oral presentation, EBMT 2022 and ASH 2022.***

[illegible] **MM21-01** L. Garderet, L. Gras, L. Koster, A. D'Souza, N. Estrada, H. Parameswaran, W. Saber, A. Cowan, M. Iida, O. Shin, H. Takamatsu, S. Mizuno, K. Kawamura, Y. Kodera, N. Hamad, B. Sheng Ko, C. Liam, H. Kim Wah, A. Sim Goh, S. Keat Tan, AM. Elhaddad, A. Bazarbachi, Q. Chaudhry, R. Alfar, A. Bekadja, M. Benakli, C. Frutos, E. Riva, S. Galaneo, F. Bass, H. Mian, A. McCurdy, F.R. Wang, D. Neumann, M. Koh, J. Snowden, S. Schoenland, I. Yakoub-Agka, H. Greinix, M. Aljurf, Y. Atsuta, D. Niederwieser. Worldwide Network for Blood and Marrow Transplantation (WBMT) Global Study on Baseline Characteristics and Clinical Outcomes in NEWLY Diagnosed Multiple Myeloma Patients Undergoing Upfront Autologous STEM Cell Transplantation, a Study Off 61,725 Patients from 629 Centers. ***Oral presentation, ASH 2022.***

4. **Studies in Progress** (Attachment 3)
   a. **MM20-02A** Impact of Second Primary Malignancy Post-Autologous Hematopoietic Stem Cell Transplantation on Outcomes of Multiple Myeloma: A CIBMTR Analysis. (B Ragon/M Shah/S Usmani) **Manuscript Submitted.**
   b. **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) **Deferred until longer follow-up of patients.**
   c. **MM20-03** Impact of bortezomib-based vs. lenalidomide maintenance therapy on outcomes of patients with high-risk multiple myeloma. (N Bumma/ S Sidana/ B Dhakal) **Manuscript Accepted in Cancer.**
   d. **MM21-01** Differences in outcome on Myeloma treatment worldwide. (L Garderet) **Manuscript Preparation.**
   e. **MM22-01** Outcomes of autologous hematopoietic cell transplantation for light chain deposition disease. (H Hashmi/B Dhakal) **Protocol Development.**

5. **Future/Proposed Studies**
   a. **PROP 2208-03/2209-03/2209-04/2210-06/2210-08/2210-42/2210-51/2210-296** Combined proposal: Real world experience of Feasibility, Safety, and Outcomes Following anti-BCMA CAR T-cell Therapy for Patients with Relapsed or Refractory Multiple Myeloma (N Ahmed/ S Ganguly/ B Dhakal/ C Ferreri/ K Patel/ A Afrough/ L Anderson Jr./ H Hashmi/ S Usmani/ **S Sidana**/ D Hansen/L Gowda/ S Mirza) (Attachment 4a-h)
   Submitted proposals:

PROP 2208-03: Real-life experience and utilization of BCMA-directed CAR-T therapy in patients with Multiple Myeloma (Attachment 4a)
PROP 2209-03: Real-world evidence of safety and efficacy of idecabtagene vicleucel in patients with multiple myeloma (Attachment 4b)
PROP 2209-04: Real-world evidence of safety and efficacy of ciltacabtagene autoleucel in patients with multiple myeloma (Attachment 4c)
PROP 2210-06: Assessment of Feasibility, Safety, and Efficacy of anti-BCMA CAR T-cell Therapy in the Real-World Setting for Patients with Relapsed or Refractory Multiple Myeloma (Attachment 4d)
PROP 2210-08: Real World Experience of Abecma, Chimeric Antigen Receptor (CAR) T-Cells Targeting BCMA in Patients with Multiple Myeloma (MM) (Attachment 4e)
PROP 2210-42: Characteristics and management of post-CAR T cell therapy toxicities in the real world for relapsed refractory multiple myeloma (Attachment 4f)
PROP 2210-51: Real world outcomes with BCMA directed CAR-T cell therapy in multiple myeloma (Attachment 4g)
PROP 2210-296: BCMA CAR-T for Multiple Myeloma: Real World Evidence and Identifying Predictors of toxicity and Efficacy (Attachment 4h)

b. **PROP 2209-01:** Utility of urine testing in post-ASCT response assessments in multiple myeloma (**R Banerjee**/N Shah) (Attachment 5)
c. **PROP 2209-09/2210-20/2210-46/2210-66/2210-128** Combined proposal: Safety and efficacy of CAR T-cell therapy for relapsed/refractory multiple myeloma in areas of unmet need (B Dhakal/ D Hansen/ S Sidana/ H Hashmi/ S Usmani/ C Freeman/ **O Akhtar**) (Attachment 6a-e)
Submitted proposals:
PROP *2209-09: Impact of renal impairment on the safety and outcomes CAR T-cell therapy in multiple myeloma patients (Attachment 6a)*
PROP 2210-20: Outcomes of elderly patients receiving B-Cell Maturation Antigen (BCMA)-directed Chimeric Antigen Receptor (CAR) T-cell Therapy in the standard of care setting (Attachment 6b)
PROP 2210-46: Safety and efficacy of CAR T-cell therapy in areas of unmet need for relapsed refractory multiple myeloma (Attachment 6c)
PROP 2210-66: Impact of obesity on outcomes following B-Cell Maturation Antigen (BCMA)-directed Chimeric Antigen Receptor (CAR) T cell therapy in the standard of care setting (Attachment 6d)
PROP 2210-128: Safety and Efficacy of anti-BCMA CAR-T Therapy in Older Adults with Multiple Myeloma: An Analysis of Real-World Outcomes from the Center for International Blood and Marrow Transplant Research (CIBMTR) and Cellular Therapy Registry (Attachment 6e)
d. **PROP 2210-43/2210-44/2210-273** Combined proposal: Predictors of progression after CAR T-cell therapy for relapsed refractory multiple myeloma (**H Hashmi**/ S Usmani/ B Wirk) (Attachment 7a-c)
Submitted proposals:
PROP *2210-43: Predictors of efficacy and safety of CAR T-cell therapy in patients with relapsed refractory multiple myeloma (Attachment 7a)*
PROP 2210-44: Predictors of early progression after CAR-T cell therapy for relapsed refractory multiple myeloma (Attachment 7b)
PROP 2210-273: Determinants of outcomes after chimeric antigen receptor T-cell therapy for multiple myeloma (Attachment 7c)
e. **PROP 2210-71/2210-72** Combined proposal: Outcomes of autologous hematopoietic cell transplantation for Multiple Myeloma with plasmacytoma(s) (**H Hashmi**) (Attachment 8a-b)
Submitted proposals:
PROP *2210-71: Outcomes of autologous hematopoietic cell transplantation for Macrofocal Multiple Myeloma (Attachment 8a)*

PROP 2210-72: Outcomes of autologous hematopoietic cell transplantation for Multiple Myeloma with plasmacytoma(s) (Attachment 8b)

f. **PROP 2210-170** Machine learning in predicting the factors associated with early relapse after autologous stem cell transplant in Multiple myeloma patients (S Vuyyala/ **S Farhan**) (Attachment 9)

g. **PROP 2210-223** Comparison of survival outcomes for patients with relapsed multiple myeloma with salvage autologous SCT versus novel therapies (**S Devarakonda**/ Y Efebera)(Attachment 10)

Dropped Proposed Studies

a. **PROP 2210-53** Outcomes of BCMA CAR T Therapy Among Patients with Multiple Myeloma who Relapse After Allogeneic Hematopoietic Cell Transplantation. *Dropped for small sample size*.

b. **PROP 2210-73** Upfront versus Delayed Autologous Hematopoietic Cell Transplantation in Newly Diagnosed Multiple Myeloma. *Dropped for low scientific impact among proposals*.

c. **PROP 2210-97** Clinical Outcome of Multiple Myeloma Patients with Renal Failure Treated with CD38-Targeting Monoclonal Antibody-Based Induction Therapy. *Dropped - supplemental data needed*.

d. **PROP 2210-98** Trends in utilization of a delayed autologous transplant approach (ASCT) in Newly Diagnosed Multiple Myeloma (NDMM). *Dropped for low scientific impact among proposals*.

e. **PROP 2210-99** Stacking machine learning algorithms into an ensemble to predict treatment related mortality and overall survival in patients with systemic light chain amyloidosis at time of diagnosis and after autologous hematopoietic cell transplant. *Dropped - supplemental data needed*.

f. **PROP 2210-116** Impact of prior B Cell Maturation Antigen (BCMA) directed therapy on outcomes of myeloma patients receiving BCMA Chimeric Antigen Receptor (CAR) T cell therapy in the standard of care setting. *Dropped for small sample size*.

g. **PROP 2210-130** Stacking machine learning algorithms into an ensemble to predict treatment related mortality and overall survival in patients with systemic light chain amyloidosis at time of diagnosis and after autologous hematopoietic cell transplant. *Duplicate*.

h. **PROP 2210-139** Role of allogenic hematopoietic stem cell transplants for multiple myeloma in the era of novel immunotherapeutics. *Dropped for low scientific impact among studies.*

i. **PROP 2210-156** Impact of Induction Therapy with anti-CD38 antibodies-based Regimen on outcomes in Patient with Multiple Myeloma Undergoing Autologous Stem Cell Transplantation. *Dropped -supplemental data needed*.

j. **PROP 2210-160** The role of autologous HSCT in the era of daratumumab for AL amyloidosis. *Dropped -supplemental data needed*.

k. **PROP 2210-182** Real-world comparison of idecabtagene vicleucel (ide-cel) and ciltacabtagene autoleucel (cilta-cel) Chimeric Antigen Receptor (CAR) T-Cells versus clinical trial outcomes achieved by patients with Relapsed/Refractory Multiple Myeloma. *Dropped for small sample size; supplemental data needed*.

l. **PROP 2210-206** Evaluation of Patient, Disease and Social Factors/Characteristics That Predict Overall Survival Advantage with Early Autologous Transplantation in Multiple Myeloma. *Dropped for low scientific impact among studies*.

m. **PROP 2210-208** Outcomes of BCMA-directed CAR-T after prior BCMA directed therapy. *Dropped - small sample size*.

n. **PROP 2210-213** BCMA-Targeted Chimeric Antigen Receptor (CAR) T-Cell Therapy for Relapsed/Refractory Multiple Myeloma after Allogeneic Hematopoietic Stem Cell Transplantation: Real-World Data from the Center for International Blood and Marrow Transplant Research (CIBMTR). *Dropped for small sample size*.
o. **PROP 2210-224** Impact of Dose-adjusted Melphalan in Obese and Non-obese Adults with Multiple Myeloma After an Autologous Hematopoietic Stem Cell Transplantation. *Dropped for low scientific impact among studies*.
p. **PROP 2210-261** Impact of cytogenetics and daratumumab containing induction on transplant outcomes of patients with light chain amyloidosis. *Dropped - supplemental data needed*.
q. **PROP 2210-262** BCMA-directed Chimeric Antigen Receptor T-cell therapy for Relapsed Refractory Multiple Myeloma: Can we choose better between two products? *Dropped for small sample size; supplemental data needed*.

MINUTES AND OVERVIEW PLAN
CIBMTR WORKING COMMITTEE FOR PLASMA CELL DISORDERS
Salt Lake City, UT
Monday, April 25, 2022, 12:15 pm – 1:45 PM MDT

Co-Chair:	**Muzaffar Qazilbash, MD, MD Anderson Cancer Center, Houston, TX; Telephone: 713-745-3458; E-mail: mqazilba@mdanderson.org**
Co-Chair:	**Shaji Kumar, MD, Mayo Clinic Rochester, Rochester, MN; Telephone: 507-284-2017; E-mail: kumar.shaji@mayo.edu**
Co-Chair:	**Nina Shah, MD, University of California, San Francisco, CA; Telephone: 415-514-6354; E-mail: nina.shah@ucsf.edu**
Scientific Director:	**Anita D'Souza, MD, MS, CIBMTR Statistical Center, Milwaukee, WI; Telephone: 414-805-0637; E-mail: anitadsouza@mcw.edu**
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1. Introduction

The Plasma Cell Disorders Working Committee (PCDWC) met on Monday, April 25, 2022, at 12:15 p.m. The chairs, scientific director and statisticians were all present at the meeting. Attendees were asked to have their name badges scanned at the front gate for attendance purpose and expressed that those members attending the meeting virtually will be part the committee membership roster.
As scientific director of the PCDWC, Dr. Anita D'Souza welcomed the attendees on behalf of the working committee leadership and started the welcome presentation by introducing each member of the working committee leadership, then explained how to gain and maintain membership, the goals, and expectations of the working committee. Dr. D'Souza acknowledged Dr. Shaji Kumar, for all his effort during the past years as Co-Chair and introduced Dr. Heather Landau as the newly appointed Chair for the Working Committee starting May 1, 2022.

Dr. D'Souza introduced the committee goal and expectations to the audience, then emphasized the scoring process and scoring guide. She then discussed the rules of authorship and the publicly available dataset for secondary analysis in the CIBMTR webpage. Resources for additional information in the CIBMTR website was provided. Dr. D'Souza encouraged the attendance to the Collaborative Study Proposal Session, where a proposal submitted to the Working Committee was selected for presentation. Presentations, publications and submitted papers in 2021 were reviewed, and update on the status of ongoing studies and their goals for July 2022 was shared. Dr. D'Souza continued with the productivity and engagement of the committee in the previous year. Then discussed important details about how the committee works, CIBMTR study development cycle and explained the different sources of CIBMTR data collection. The voting process was

reiterated and it was emphasized that each proposal will be given 5 minutes for presentation and 7-10 minutes for discussion.

2. Accrual summary

The accrual summary was referenced for review but not formally presented due to full agenda. The link to the full accrual summary was available online as part of the attachments. The accrual summary provides information about the number of patients available in the registration level and research level for potential studies. As of December 2022, 106,799 plasma cell disorder cases were reported at the TED level only and 16,114 cases at the research level to the CIBMTR for first autologous transplant. For first allogeneic transplants, these numbers are 5,164 cases and 2,119 cases respectively.

3. Presentations, Published or Submitted Papers

The published or submitted papers as well as abstracts that have been presented at various conferences in 2021 are shown below demonstrating that it was a very productive year for our committee. These include:

a. **MM19-01:** Sidana S, Kumar S, Fraser R, Estrada-Merly N, Giralt S, Agrawal V, Anderson LD Jr, Aljurf M, Banerjee R, Bashey A, Battiwalla M, Beitinjaneh A, Chakraborty R, Chhabra S, Dhakal B, Dholaria B, Hashmi S, Janakiram M, Lee C, Lekakis L, Murthy HS, Parrondo R, Wangjam T, Usmani S, Shah N, Qazilbash M, D'Souza A. Impact of induction therapy with VRD versus VCD on outcomes in patients with multiple myeloma in partial response or better undergoing upfront autologous stem cell transplantation. **Transplantation and Cellular Therapy. 2022 Feb 3; 8(2):e1-83.e9. doi:10.1016/j.jtct.2021.10.022. Epub 2021 Nov 12. PMC8900987.** ***Poster presentation, ASH 2020.***

b. **MM19-02:** Pasvolsky O, Yeshurun M, Fraser R, Estrada-Merly N, Rozovski U, Shargian-Alon L, Assal A, Banerjee R, Bumma N, Gale RP, Hagen P, Holmberg L, Hossain NM, Lazarus HM, Lee C, Mian H, Miller KC, Nathan S, Nagler A, Nishihori T, Parrondo RD, Patel S, Schroeder MA, Usmani SZ, Wang T, Wirk B, Kumar S, Shah N, Qazilbash MH, D'Souza A. Maintenance therapy after second autologous hematopoietic cell transplantation for multiple myeloma. A CIBMTR analysis. **Bone Marrow Transplantation. 2022 Jan 1; 57(1):31-37. doi:10.1038/s41409-021-01455-y. Epub 2021 Oct 4. PMC8764606.** ***Poster presentation, ASCO 2021.***

c. **MM19-03:** Tan CR, Estrada-Merly N, Landau H, Lekakis L, Banerjee R, Mian H, Usmani SZ, Hanbali A, Lazarus HM, Kyle RA, Dholaria B, Bal S, Strouse C, Murthy HS, Wirk B, Nishihori T, Kumar S, Shah N, Qazilbash M, D'Souza A. A second autologous hematopoietic cell transplantation is a safe and effective salvage therapy in select relapsed or refractory AL amyloidosis patients. **Bone Marrow Transplantation. 2022 Feb 1; 57(2):295-298. doi:10.1038/s41409-021-01527-z.** ***Epub 2021 Nov 20. PMC8825695.***

d. **MM20-01:** Kansagra A, Dispenzieri A, Fraser Raphael, Estrada-Merly N, Sidana S, Nishihori T, Hansen D, Anderson LD, Banerjee R, Bumma N, Dhakal B, Khouri J, Landau H, Lee cindyH, Mian H, Nathan S, Savani B, Kumar S, Qazilbash M, Shah N, D'Souza A. Outcomes after Autologous stem cell transplant outcome for patients with POEMS syndrome and comparison with multiple myeloma. **Blood Adv 2022; bloodadvances.2022007218. doi: https://doi.org/10.1182/bloodadvances.2022007218.** ***Oral presentation, ASH 2021.***

e. **MM20-02A:** Impact of Second Primary Malignancy Post-Autologous Hematopoietic Stem Cell Transplantation on Outcomes of Multiple Myeloma: A CIBMTR Analysis. (B Ragon et al.) ***Poster presentation at ASCO 2022.***

f. **MM20-03:** Impact of bortezomib-based vs. lenalidomide maintenance therapy on outcomes of patients with high-risk multiple myeloma. (N Bumma et al.) ***Oral presentation, Tandem Meetings 2022.***

g. **MM21-01:** Differences in treatments and outcomes of Myeloma worldwide. (L Garderet et al.). ***Oral presentation, EBMT 2022.***

4. Studies in Progress

Dr. D'Souza presented the summary of studies in progress.

a. **MM20-01:** Outcomes after Autologous stem cell transplant outcome for patients with POEMS syndrome (Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal protein, Skin changes). (A Kansagra/ A Dispenzieri) ***In Press.***

b. **MM20-02A:** Impact of Second Primary Malignancy Post-Autologous Hematopoietic Stem Cell Transplantation on Outcomes of Multiple Myeloma: A CIBMTR Analysis. (B Ragon/M Shah/S Usmani) ***Manuscript Preparation.***

c. **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) ***Deferred until longer follow-up of patients is available.***

d. **MM20-03:** Impact of bortezomib-based vs. lenalidomide maintenance therapy on outcomes of patients with high-risk multiple myeloma. (N Bumma/S Sidana/B Dhakal) ***Manuscript Submitted.***

e. **MM21-01:** Differences in outcome on Myeloma treatment worldwide. (L Garderet) ***Analysis.***

5. Future/Proposed Studies

Dr. D'Souza thanked the investigators whose proposals were submitted but not selected for presentation. This year, we had record of 50 proposals received, 5 of which were invited to present at the meeting. Dr. D'Souza emphasized that the majority were dropped due to overlaps with current studies and data availability issues. Also reiterated the voting process. Dr. D'Souza introduced the presenter for the first proposal.

a. **PROP 2109-27:** Outcomes of autologous hematopoietic cell transplantation for Light Chain Deposition Disease. (H Hashmi/ B Dhakal)

Dr. Hashmi presented the proposal on behalf of the group. This study hypothesizes that Hematopoietic cell transplantation (HCT) results in long-term disease control for Light Chain Deposition Disease (LCDD). The primary objective of this proposal is to determine overall survival (OS) after autologous HCT for LCDD and secondary objective to determine disease response [hematological, clinical], progression-free survival (PFS), transplant-related mortality (TRM), cumulative incidence of relapse after HCT for LCDD. There are 260 patients who underwent first Auto-HCT for multiple myeloma from 2000-2019. But only 74 have CRF level data. Dr. Hashmi referenced the scoring criteria and emphasized that this proposal fulfils all the requirements for selection.

Then the floor was opened for questions/comments. An audience member asked about the possibility of benchmarking the study cohort with CIBMTR patients transplanted for primary amyloidosis or MM to compare outcomes and see if there is a difference. A question was asked about the availability of data for renal function after transplant to determine how long it will be before patients need dialysis and stem

cell dose and mucositis. a question asking whether the study cohort included only those with renal biopsy showing light chain deposition disease or cases with MGRS. There were suggestions on the possibility of selecting a subset of patients and reaching out to reporting centers to obtain LCD/MGRS information. A question was raised on which response criteria will be used for these patients. Leadership suggested the MM response criteria. Another question asked about patients with MM + LCDD/MIDD and Dr. Hashmi responded that patients with bone lesions will be excluded and Dr. D'Souza mentioned that this data may not be uniformly available in CIBMTR data.

b. **PROP 2110-18:** Utility of urine testing in post-ASCT response assessments in multiple myeloma. (R Banerjee/N Shah)

Dr. Nina Shah introduced Dr. Banerjee presented the proposal on behalf of the group. This study hypothesizes that a modified set of CIBMTR response criteria that omits all urine testing for each grade of pre-ASCT and post-ASCT response assessments (urine-free CIBMTR) will perform similarly to traditional CIBMTR response criteria among patients with multiple myeloma. Specifically, Harrell's concordance indices for urine-free CIBMTR and traditional CIBMTR response criteria regarding progression-free survival (PFS) will fall no greater than 0.1 points of each other. Additionally, this study hypothesizes that fewer than 5% of patients will have divergent response assessments using urine-free CIBMTR versus traditional CIBMTR response criteria. The primary objective of this proposal is to determine Harrell's concordance indices for PFS using current CIBMTR response criteria as well as urine-free CIBMTR response criteria (measured both pre-ASCT and post-ASCT). The secondary objectives are to assess the real-world rates of omission of 24-hour urine testing from CIBMTR response criteria, and concordance between urine-free and traditional CIBMTR response criteria. There are 6935 patients who underwent HCT for multiple myeloma in the US from 2008-2019 with CRF level data. But only 2748 have known urine testing results. Dr. Banerjee discussed the strengths and limitations of the study, then welcomed questions and comments from the audience. A member of the audience asked about the method that will be used to assess and adjust for confounding, as it is one of the potential limitations of this proposal. Suggestions were made by the audience to utilize the CRF data to address some of these confounding factors such as geographic location (urban vs rural). A question was asked about availability of pre-transplant data on urine testing and Dr. D'Souza explained that there is a high number of missing data for pre-transplant urine testing. A question was asked via chat on availability of 24-hour IFE data in CIBMTR forms. Another question was asked on the inclusion of patients who are monitored by Bence-Jones protein. Concerns about the effect of missing data on key analysis were raised by the audience.

c. **PROP 2110-238:** Consolidation or Maintenance therapy in AL Amyloidosis Following Autologous Stem Cell Transplantation. (S Cingam/ S Sidana)

Dr. Nina Shah introduced Dr. Cingam presented the proposal on behalf of the group. This study hypothesizes that patients with AL amyloidosis who receive consolidation/ maintenance therapy after autologous stem cell transplant have longer PFS. The primary objective of the study is to evaluate the outcomes in patients with AL amyloidosis receiving maintenance/consolidation therapy compared to patients which did not receive any therapy after an autologous stem cell transplant (Auto-SCT). A sub-group analysis will be performed, stratifying by day 90 post-transplant response (i) at least VGPR without evidence of organ related disease progression, (ii)less than VGPR (or) with organ related disease progression. There are 516 US adult patients who underwent Auto-HCT for Amyloidosis from 2015-2019 and have CRF level data. From those 160 cases received post-HCT therapy.

The proposal was opened for questions from the audience. A member of the audience suggested using the term 'post-transplant therapy' instead of consolidation/maintenance therapy given that the CIBMTR

data may not provide sufficient data to reliably differentiate these. Another suggestion was made to limit data to 2015-2018 as only few patients were included in 2019. A question was asked about inclusion of patients with concurrent MM and Amyloidosis. Responding to a question about how response is assessed, Dr. D'Souza mentioned that the CIBMTR captures the best response for patient. A suggestion was made that the plasma cell percentage should be taken into consideration in the analysis. A question was asked about data availability on duration of maintenance therapy and time to next therapy. Leadership mentioned that CIBMTR captures data on maintenance therapy but data on time to next therapy may not be available due to inconsistent reporting after relapse.

d. **PROP2109-29/PROP2110-65** Combined proposal: Trends in utilization of a delayed autologous transplant approach (ASCT) in Newly Diagnosed Multiple Myeloma (NDMM). (M Mohan/ H Hashmi/ S Usmani)

Submitted proposals:

PROP 2109-29: Outcomes of early versus delayed autologous hematopoietic cell transplantation for patients with multiple myeloma.

PROP 2110-65: Delayed upfront autologous stem cell transplant (ASCT) in MM is emerging as an acceptable treatment option particularly with the use of highly effective drugs inducing deeper and durable remission.

Dr. Hashmi presented the proposal on behalf of the group. This study hypothesizes that autologous hematopoietic cell transplantation (AHCT) within 12 months of diagnosis of multiple myeloma (early) leads to deeper durable remission. The specific aims of this proposal are to estimate the trends in utilization of a delayed ASCT approach in NDMM. Delayed ASCT will be defined as patients who have upfront stem cell collection but underwent first ASCT in NDMM ≥ 1 years from diagnosis. They will analyze the clinical parameters in this group of patients; compare clinical characteristics and outcomes of the group that received delayed ASCT. There are 6532 patients who underwent first Auto-HCT for multiple myeloma from 2008-2019 who met the selection criteria. Out of these, 5055 had upfront HCT and 1477 had delayed HCT.

The proposal was opened for questions from the audience, a member of the audience asked about availability of data to determine reasons for delayed transplant. Dr. Hashmi responded that data on lines of therapy and response assessment prior to transplant, might be used as surrogates. A suggestion was made to include time to second progression in the analysis. A question submitted via chat asked how data collected over the last 2 decades can inform the knowledge gap in the modern era. Dr. Hashmi mentioned the possibility of grouping the data by year of transplant. Another member of the audience emphasized the importance of restricting to recent data as therapy options have evolved over time. A question was asked about availability of data on duration between cell collection and transplant. There were concerns about effect of confounding factors on the analysis.

In response to questions submitted via chat, Dr. D'Souza mentioned that the analysis will compare standard to high-risk cytogenetics patients.

e. **PROP2109-28/PROP2109-30** Combined proposal: Outcomes of autologous hematopoietic cell transplantation for Multiple Myeloma with plasmacytoma(s) (H Hashmi/B Dhakal/ S Usmani)

Submitted proposals:

PROP 2109-28 : Outcomes of autologous hematopoietic cell transplantation for Multiple Myeloma with plasmacytoma(s).

PROP 2109-30: Outcomes of autologous hematopoietic cell transplantation for Macrofocal Multiple Myeloma.

Dr. Hashmi presented the proposal on behalf of the group. This study hypothesizes that autologous hematopoietic cell transplantation (AHCT) results in long-term disease control for patients with multiple myeloma with current or prior plasmacytoma(s). The specific aims of this proposal are to determine overall survival (OS) after AHCT for multiple myeloma with prior or current plasmacytoma(s) and compare this outcome with patients with multiple myeloma without prior or current plasmacytomas; and to determine disease response (hematological, radiological). There are 277 patients who received auto-HCT for multiple myeloma with current or previous plasmacytomas from 2000 - 2019 and have CRF level data.

The proposal was opened for questions from the audience, questions were raised about the availability of data on extramedullary disease, and pretransplant radiation therapy especially as it relates to transformation from plasmacytoma to multiple myeloma. A member of the audience requested clarification on the criteria used to define the diagnosis of plasmacytoma. A question was asked about how differences in diagnostic imaging will be addressed given the advancement of imaging modalities in the modern era. A concern was raised regarding misdiagnosis of patients.

Drs. Hashmi and D'Souza addressed chat questions on availability of cytogenetic data, bone marrow involvement, and evaluation of response. A member of the audience expressed concerns about the use of data backing up to 20 years and suggested limiting the analysis to more recent data.

Forty-two additional proposals were submitted but not presented as listed below:

a. **PROP 2012-02**: Clinical Outcome and Impact of immunoglobulin light chain subtype (k vs λ) in Multiple Myeloma patients who undergo first auto SCT. ***Dropped for low scientific impact among proposals.***

b. **PROP2105-03**: Real world patient characteristics and outcomes in relapsed/refractory multiple myeloma with idecantagene vicleucel ***Dropped for small sample size.***

c. **PROP 2109-13**: Comparing infection risk and L/M (lymphosite/ monosite) ratio in Multiple Myeloma (MM) Patients, who had Bortezomib based induction therapy with non-bortezomib based induction chemotherapy in autologous stem cell transplantation (ASCT). ***Dropped-supplemental data needed.***

d. **PROP 2110-03**: Does autologous stem cell transplant improve hematological and/or organ responses in patients with newly diagnosed AL amyloidosis who achieve less than very good partial remission induction chemotherapy. ***Dropped due to overlap with recent publication.***

e. **PROP 2110-53**: Identifying prognostic factors at first relapse in myeloma after autologous stem cell transplant ***Dropped due to overlap with recent publication.***

f. **PROP 2110-58**: Impact of clinical trial participation on outcomes of patients undergoing autologous peripheral blood stem cell transplantation for multiple myeloma. ***Dropped for sample size concerns.***

g. **PROP 2110-61**: Using an ensemble stack of machine learning algorithms to predict morbidity and mortality following autologous hematopoietic cell transplant (HCT) in patients diagnosed with systemic light chain amyloidosis (AL). ***Dropped for low scientific impact among proposals.***

h. **PROP 2110-71**: Timing of second (tandem) autologous hematopoietic stem cell transplantation for newly diagnosed multiple myeloma patients (MM) – a CIBMTR analysis. ***Dropped for small sample size.***

i. **PROP 2110-75**: "Comparative effectiveness of KRD versus VRD induction therapy in patients with newly diagnosed multiple myeloma undergoing upfront autologous hematopoietic cell Transplantation. ***Dropped for small sample size.***

j. **PROP 2110-86**: Impact of the use of plerixafor in relapse free survival on Multiple Myeloma patients subjected to autologous stem cell transplantation first line therapy. ***Dropped due to overlap with current study.***

k. **PROP 2110-87**: Anti-BCMA directed Chimeric Antigen Receptor (CAR) T-Cell Therapy for Relapsed/Refractory Multiple Myeloma: Real World Experience from the Center for International Blood and Marrow Transplant Research (CIBMTR) and Cellular Therapy (CT) Registry and comparison with clinical trial. ***Dropped-supplemental data needed****.*

l. **PROP 2110-100**: Impact of Induction with Daratumumab-VRD vs. VRD on the Outcome of Patients with Multiple Myeloma After an Autologous Hematopoietic Stem Cell Transplantation. ***Dropped for small sample size.***

m. **PROP 2110-101**: New Cancers after Autologous Hematopoietic Cell Transplantation for Systemic Light-Chain Amyloidosis. ***Dropped for small sample size.***

n. **PROP 2110-102**: Impact of autologous hematopoietic cell transplantation on the outcomes of Waldenstrom Macroglobulinemia and Lymphoplasmacytic Lymphoma. ***Dropped overlap with recent study.***

o. **PROP 2110-106**: Effects of Chromosome 1 Abnormalities (1q21 gain, 1q21 amplification and deletion 1p) on Clinical Outcomes in Patients Undergoing Upfront Autologous Stem Cell Transplantation in Multiple Myeloma. ***Dropped overlap with current study.***

p. **PROP 2110-112**: Determinants of outcomes after chimeric antigen receptor T cells for multiple myeloma. ***Dropped for small sample size.***

q. **PROP 2110-119**: Real-world evidence of safety and efficacy of idecabtagene vicleucel in patients with multiple myeloma. ***Dropped for small sample size.***

r. **PROP 2110-143**: Myeloma tumor burden and outcomes after treatment with anti-B cell maturation antigen (BCMA) chimeric antigen receptor (CAR) T-cell therapy. ***Dropped for small sample size.***
s. **PROP 2110-146**: Real World Experience of Abecma, Chimeric Antigen Receptor (CAR) T-Cells Targeting BCMA in Patients with Multiple Myeloma. ***Dropped for small sample size.***

t. **PROP 2110-03**: Real world outcomes with idecabtagene vicleucel in multiple myeloma. ***Dropped for small sample size.***

u. **PROP 2110-157**: Real world outcomes with idecabtagene vicleucel in multiple myeloma. ***Dropped for small sample size.***

v. **PROP 2110-160**: Survival in Multiple Myeloma Patients Undergoing Autologous SCT over the Years: A Time Trend Analysis. ***Dropped overlap with recent study.***

w. **PROP 2110-162**: Impact of prior B Cell Maturation Antigen (BCMA) directed therapy on outcomes of myeloma patients receiving BCMA Chimeric Antigen Receptor (CAR) T cell therapy in the standard of care setting. ***Dropped for small sample size.***

x. **PROP 2110-184**: Assessing impact of concomitant cytogenetic abnormalities on outcome of multiple myeloma patient with 1q gain who undergo autologous hematopoietic stem cell transplantation. ***Dropped due to overlap with current study.***

y. **PROP 2110-185**: Role of Tandem Autologous Stem Cell Transplantation in High-Risk Multiple Myeloma. ***Dropped for small sample size.***

z. **PROP 2110-200**: Autologous hematopoietic cell transplant (AHCT) for the treatment of patients with Waldenstrom's Macroglobulinemia (WM)/Lymphoplasmacytic Lymphoma (LPL): A Center for International Blood and Marrow Transplant Research Analysis. ***Dropped overlap with recent study.***

aa. **PROP 2110-205**: Assessing outcomes of patients with Monoclonal gammopathy with renal significance after autologous stem cell transplant. ***Dropped for small sample size.***

bb. **PROP 2110-230**: Assessment of Feasibility, Safety, and Efficacy of anti-BCMA CAR T-cell Therapy in the Real-World Setting for Patients with Relapsed or Refractory Multiple Myeloma. ***Dropped for small sample size.***

cc. **PROP 2110-234**: Anti-BCMA Chimeric Antigen Receptor (CAR) T-Cell Therapy for Relapsed/Refractory Multiple Myeloma after Allogeneic Hematopoietic Stem Cell transplantation: Real-World Data from the Center for International Blood and Marrow Transplant Research (CIBMTR). ***Dropped for small sample size.***

dd. **PROP 2110-253**: Patient specific factors associated with incidence of salvage autologous stem cell transplant for relapsed multiple myeloma. ***Dropped due to overlap with recent publication****.*

ee. **PROP 2110-262**: Impact of Daratumumab in the treatment of High-Risk Multiple Myeloma. ***Dropped for small sample size.***

ff. **PROP 2110-267**: Outcomes of patients with Light Chain Amyloidosis treated with Autologous Stem Cell Transplantation, with focus on the impact of depth of response to induction therapy prior to transplant and potential role of post-transplant interventions.

gg. **PROP 2110-273**: Assessing impact of high-risk cytogenetic abnormalities on outcomes of multiple myeloma patients and risk for developing secondary MDS/AML following autologous hematopoietic stem cell transplant. ***Dropped due to overlap with current study****.*

hh. **PROP 2110-289**: Outcomes with KRd vs VRd induction in patients with high-risk multiple myeloma undergoing early autologous stem cell transplant. ***Dropped for small sample size.***

ii. **PROP2110-306**: Impact of daratumumab based therapy on outcome of autologous stem cell transplant for systemic AL amyloidosis. ***Dropped for small sample size.***

jj. **PROP 2110-311**: Outcomes of commercial versus noncommercial CAR T therapy in relapsed multiple myeloma. ***Dropped for small sample size.***

kk. **PROP 2110-313**: Outcomes of dual high risk cytogenetic multiple myeloma after autologous stem cell transplant – A CIBMTR analysis. ***Dropped due to overlap with current study****.*

ll. **PROP2110-325**: Autologous transplant outcomes with high-risk cytogenetics in the systemic light-chain (AL) amyloidosis. ***Dropped for small sample size.***

mm. **PROP 2110-332**: Real world Experience of Induction Therapy with KRd or VRd in Patients with Multiple Myeloma Undergoing Early Autologous Stem Cell Transplant. ***Dropped for small sample size.***

nn. **PROP 2110-337**: Bridging and Maintenance Therapy as a Predictor of Post CAR-T Outcomes for multiple myeloma. ***Dropped-supplemental data needed.***

oo. **PROP2110-341**: Real world outcomes in multiple myeloma after autologous transplant failure: impact of cellular therapies and novel drugs in the modern era. ***Dropped-supplemental data needed****.*

pp. **PROP 2110-342**: Impact of Induction with carfilzomib, lenalidomide and dexamethasone vs. bortezomib, lenalidomide and dexamethasone on the Outcome of Patients with Multiple Myeloma with high-risk multiple myeloma after an Autologous Hematopoietic Stem Cell Transplantation. ***Dropped for small sample size.***

The meeting was adjourned on time at 1:45 p.m. The Chairs and Scientific director stayed behind for extra time to meet and interact one on one with committee members.

6. Other Business

The chairs of the working committee, scientific director and statisticians had a post-WC meeting afterwards to discuss proposals. After the new proposals were presented, each attendee had the opportunity to vote the proposals using the provided voting sheets. Based on the voting results, current scientific merit, and impact of the studies on the field, the following study was decided to move forward as the committee's research portfolio for the upcoming year:

a. **PROP 2109-27:** Outcomes of autologous hematopoietic cell transplantation for Light Chain Deposition Disease. (H Hashmi/ B Dhakal)

Working Committee Overview Plan for 2022-2023		
Study Number and Title	**Current Status**	**Chairs Priority**
MM20-02a: Impact of Second Primary Malignancy Post-Autologous Hematopoietic Stem Cell Transplantation on Outcomes of Multiple Myeloma: A CIBMTR Analysis	Manuscript Preparation	2
MM20-02b: Risk factors for and characteristics of secondary primary malignancies following autologous hematopoietic cell transplant for multiple myeloma	Deferred	2
MM20-03: Impact of bortezomib-based versus lenalidomide maintenance therapy on outcomes of patients with high-risk multiple myeloma	Submitted	3
MM21-01: Differences in outcomes on myeloma treatment worldwide	Analysis	3
MM22-01: Outcomes of autologous hematopoietic cell transplantation for light chain deposition disease	Protocol Pending	2

Working Assignments for Working Committee Leadership (May 2022)

Heather Landau:	**MM20-02B:** Risk factors for and characteristics of secondary primary malignancies following autologous hematopoietic cell transplant for multiple myeloma
	MM22-01: Outcomes of autologous hematopoietic cell transplantation for light chain deposition disease
Nina Shah:	**MM20-02:** Impact of Second Primary Malignancy Post-Autologous Hematopoietic Stem Cell Transplantation on Outcomes of Multiple Myeloma: A CIBMTR Analysis.
Muzaffar Qazilbash:	**MM20-03:** Impact of bortezomib-based vs. lenalidomide maintenance therapy on outcomes of patients with high-risk multiple myeloma

Accrual Summary for the Plasma Cell Disorders Working Committee

Recipients of first autologous transplant for **Plasma Cell Disorders** registered to the CIBMTR, 1990-2022

Characteristic	TED N (%)	Research N (%)
No. of patients	116099	16478
No. of centers	512	325
Age at transplant, median (range), years - median (min-max)	61 (18-86)	59 (20-83)
Disease - no. (%)		
Multiple Myeloma	109529 (94)	14524 (88)
Amyloidosis	3565 (3)	1448 (9)
Plasma cell leukemia	1025 (1)	206 (1)
Solitary plasmacytoma	470 (0)	53 (0)
Waldenstrom macroglobulinemia	363 (0)	47 (0)
POEMS Syndrome	627 (1)	91 (1)
Multiple Plasmacytomas	61 (0)	4 (0)
LCDD	339 (0)	94 (1)
Others	120 (0)	11 (0)
Graft type - no. (%)		
BM	441 (0)	82 (0)
PB	114231 (98)	16248 (99)
CB	7 (0)	2 (0)
Missing	1420 (1)	146 (1)
Year of transplant - no. (%)		
1990-1991	207 (0)	44 (0)
1992-1993	322 (0)	70 (0)
1994-1995	630 (1)	243 (1)
1996-1997	1326 (1)	475 (3)
1998-1999	2335 (2)	697 (4)
2000-2001	3504 (3)	929 (6)
2002-2003	4631 (4)	851 (5)
2004-2005	4934 (4)	1489 (9)
2006-2007	5234 (5)	1380 (8)
2008-2009	6332 (5)	1520 (9)
2010-2011	9975 (9)	672 (4)
2012-2013	10864 (9)	1186 (7)
2014-2015	11714 (10)	1913 (12)
2016-2017	14261 (12)	2058 (12)
2018-2019	15036 (13)	2394 (15)
2020-2021	17072 (15)	266 (2)
2022	7722 (7)	291 (2)

Characteristic	TED N (%)	Research N (%)
Follow-up - median (range)	49 (0-347)	71 (0-292)

Small lymphoplasmacytic lymphoma cases were not included.
Cases continue to be reported. Abbreviations: TED=Transplant essential data, CRF=Comprehensive report form.

Recipients of first allogeneic transplant for **Plasma Cell Disorders** registered to the CIBMTR, 1990-2022

Characteristic	TED N (%)	Research N (%)
No. of patients	5214	2126
No. of centers	345	268
Age at transplant, median (range), years - median (min-max)	51 (1-78)	50 (10-79)
Disease - no. (%)		
Multiple Myeloma	4680 (90)	1889 (89)
Amyloidosis	32 (1)	7 (0)
Plasma cell leukemia	274 (5)	134 (6)
Solitary plasmacytoma	41 (1)	6 (0)
Waldenstrom macroglobulinemia	125 (2)	74 (3)
POEMS Syndrome	1 (0)	0 (0)
Multiple Plasmacytomas	3 (0)	1 (0)
Others	58 (1)	15 (1)
Graft type - no. (%)		
BM	1165 (22)	627 (29)
PB	3913 (75)	1455 (68)
CB	43 (1)	40 (2)
Missing	93 (2)	4 (0)
Donor - no. (%)		
HLA-identical sibling	3297 (63)	1323 (62)
Monozygotic twin	166 (3)	135 (6)
Other relative	373 (7)	102 (5)
Unrelated donor	1288 (25)	546 (26)
Missing	90 (2)	20 (1)
Prior Auto transplant - no. (%)		
No	2334 (45)	1199 (56)
Yes	2880 (55)	927 (44)
Year of transplant - no. (%)		
1990-1991	71 (1)	95 (4)
1992-1993	171 (3)	141 (7)
1994-1995	282 (5)	146 (7)

Characteristic	TED N (%)	Research N (%)
1996-1997	339 (7)	144 (7)
1998-1999	311 (6)	128 (6)
2000-2001	460 (9)	248 (12)
2002-2003	567 (11)	208 (10)
2004-2005	457 (9)	255 (12)
2006-2007	350 (7)	203 (10)
2008-2009	407 (8)	134 (6)
2010-2011	432 (8)	59 (3)
2012-2013	388 (7)	49 (2)
2014-2015	358 (7)	90 (4)
2016-2017	303 (6)	93 (4)
2018-2019	135 (3)	107 (5)
2020-2021	147 (3)	20 (1)
2022	36 (1)	6 (0)
Follow-up - median (range)	72 (0-361)	121 (0-288)

Small lymphoplasmacytic lymphoma cases were not included. Cases continue to be reported.
Abbreviations: TED=Transplant essential data, CRF=Comprehensive report form.

Recipients of first CAR T-cell infusion for **Plasma Cell Disorders** registered to the CIBMTR, 2016-2022

Characteristic	**N (%)**
No. of patients	1308
No. of centers	79
Age at infusion, yrs - median (min-max)	65 (29-86)
Age at infusion, by category #1 - no. (%)	
20 - 29 years	2 (0)
30 - 39 years	18 (1)
40 - 49 years	93 (7)
50 - 59 years	319 (24)
60 - 69 years	531 (41)
70+ years	345 (26)
Age at infusion, by category #2 - no. (%)	
18 - 39	20 (2)
40 - 65	643 (49)
65+	645 (49)
Gender - no. (%)	
Male	774 (59)
Female	526 (40)
Not reported	8 (1)
Recipient race - no. (%)	
White	1033 (79)
Black or African American	185 (14)
Asian	29 (2)
Native Hawaiian or other Pacific Islander	2 (0)
American Indian or Alaska Native	3 (0)
Other	7 (1)
More than one race	20 (2)
Not reported	29 (2)
Recipient ethnicity - no. (%)	
Hispanic or Latino	82 (6)
Not Hispanic or Latino	1178 (90)
Non-resident of the U.S.	17 (1)
Unknown	31 (2)
Country - no. (%)	
US	1282 (98)
Other	26 (2)
Karnofsky performance score prior to CT - no. (%)	
90-100	481 (37)
80-90	445 (34)

Characteristic	N (%)
< 80	251 (19)
Not reported	131 (10)
ECOG performance status prior to CT - no. (%)	
0 - Asymptomatic	481 (37)
1 - Symptomatic but completely ambulatory	641 (49)
2 - Symptomatic, < 50% in bed during the day	50 (4)
3 - Symptomatic, > 50% in bed, but not bedbound	4 (0)
4 - Bedbound	1 (0)
Not reported	131 (10)
Body mass index (BMI) category at infusion - no. (%)	
< 18.5 - Underweight	21 (2)
>= 18.5 to < 25 - Normal	364 (28)
>= 25 to < 30 - Overweight	482 (37)
>= 30 - Obese	408 (31)
Not reported	33 (3)
Renal disease (moderate/severe), at the time of infusion or prior renal transplant - no. (%)	
No	826 (63)
Yes	71 (5)
Not reported	411 (31)
Sub-disease for CT - no. (%)	
Multiple myeloma	1271 (97)
Plasma cell leukemia	15 (1)
Amyloidosis	2 (0)
Solitary plasmacytoma (no evidence of myeloma)	1 (0)
Light chain deposition disease	1 (0)
Smoldering myeloma	2 (0)
Other plasma cell disorder	2 (0)
Not reported	14 (1)
Age at initial diagnosis - median (min-max)	58 (25-85)
ISS stage at diagnosis - no. (%)	
1 (beta2-mic < 3.5, albumin >= 3.5)	330 (25)
2 (Not fitting stage 1 or 3)	290 (22)
3 (beta2-mic >= 5.5, regardless of albumin)	265 (20)
Not reported	423 (32)
R-ISS stage at diagnosis - no. (%)	
1 (ISS stage I and standard-risk abnormalities by iFISH and normal LDH)	133 (10)
2 (Not R-ISS stage I or III)	307 (23)
3 (ISS stage III and either high-risk chromosomal abnormalities by iFISH or high LDH)	126 (10)
Not reported	742 (57)

Characteristic	N (%)
Time from initial diagnosis to CT - no. (%)	
Median (min-max)	70 (0-324)
>= 0 to < 12 months	51 (4)
>= 12 to < 36 months	197 (15)
>= 36 to < 60 months	295 (23)
>= 60 months	751 (57)
Not reported	14 (1)
Commercial vs. noncommercial CAR-T product - no. (%)	
Commercial	948 (72)
Noncommercial	360 (28)
Clinical trial - no. (%)	
No	927 (71)
Yes	381 (29)
Product - no. (%)	
Abecma	761 (58)
Carvykti	187 (14)
Other	360 (28)
Types of prior HCTs - no. (%)	
No	171 (13)
Yes	1134 (87)
Prior allo-HCT	10 (1)
Prior auto-HCT	1078 (82)
Prior auto and allo-HCT	30 (2)
Not reported	16 (1)
Unknown	1 (0)
Not reported	2 (0)
Total number of prior HCTs - no. (%)	
0	171 (13)
1	836 (64)
2	207 (16)
3	25 (2)
4	2 (0)
5	1 (0)
Not reported	66 (5)
Prior CT - no. (%)	
No	1273 (97)
Yes	35 (3)
CT infusion counting number - no. (%)	
1	1293 (99)
2	14 (1)
3	1 (0)

Characteristic	**N (%)**
Time from prior HCT to CT, months - median (min-max)	
No prior HCT	NE
Prior allo-HCT	36 (9-176)
Prior auto-HCT	47 (0-250)
Prior auto and allo-HCT	53 (5-189)
Time from the latest prior HCT to current CT, days - median (min-max)	1434 (14-7601)
Disease/indication - no. (%)	
Immune reconstitution	2 (0)
Prevent disease relapse	1 (0)
Malignant hematologic disorder	1305 (100)
Disease status prior to infusion - no. (%)	
Stringent complete remission (sCR)	5 (0)
Complete remission (CR)	14 (1)
Partial response (PR)	101 (8)
No response (NR)/Stable disease (SD)	144 (11)
Progressive disease (PD)	201 (15)
Relapse from CR (Rel) (untreated)	796 (61)
Unknown	19 (1)
Not reported	28 (2)
Year of CT - no. (%)	
2016	7 (1)
2017	8 (1)
2018	68 (5)
2019	82 (6)
2020	100 (8)
2021	362 (28)
2022	681 (52)
Follow-up - median (range)	12 (1-53)

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

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Number of patients	940	292	206
Source of data			
CRF	501 (53)	134 (46)	88 (43)
TED	439 (47)	158 (54)	118 (57)
Number of centers	125	79	85
Disease at transplant			
Plasma cell disorder/Multiple Myeloma	940 (100)	292 (100)	206 (100)
Recipient age at transplant			
10-17 years	3 (<1)	0	0
18-29 years	7 (1)	3 (1)	3 (1)
30-39 years	84 (9)	31 (11)	22 (11)
40-49 years	275 (29)	73 (25)	49 (24)
50-59 years	392 (42)	127 (43)	93 (45)
60-69 years	174 (19)	57 (20)	38 (18)
70+ years	5 (1)	1 (<1)	1 (<1)
Median (Range)	53 (10-77)	53 (22-72)	53 (18-74)
Recipient race/ethnicity			
White, Non-Hispanic	791 (84)	252 (86)	158 (77)
Black or African American, Non-Hispanic	59 (6)	19 (7)	5 (2)
Asian, Non-Hispanic	16 (2)	6 (2)	2 (1)
Native Hawaiian or Pacific Islander, Non-Hispanic	1 (<1)	1 (<1)	0
American Indian or Alaska Native, Non-Hispanic	2 (<1)	1 (<1)	0
Hispanic	45 (5)	10 (3)	10 (5)
Missing	26 (3)	3 (1)	31 (15)
Recipient sex			
Male	590 (63)	193 (66)	137 (67)
Female	350 (37)	99 (34)	69 (33)
Karnofsky score			
10-80	385 (41)	136 (47)	80 (39)
90-100	516 (55)	149 (51)	119 (58)
Missing	39 (4)	7 (2)	7 (3)
HLA-A B DRB1 groups - low resolution			
4/6	4 (<1)	0	0
5/6	113 (12)	29 (11)	22 (11)
6/6	801 (87)	229 (89)	173 (89)
Unknown	22 (N/A)	34 (N/A)	11 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	11 (1)	0	1 (1)
6/8	33 (4)	1 (<1)	3 (2)
7/8	142 (17)	29 (14)	29 (20)
8/8	662 (78)	172 (85)	109 (77)
Unknown	92 (N/A)	90 (N/A)	64 (N/A)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
HLA-DPB1 Match			
Double allele mismatch	140 (30)	18 (21)	11 (26)
Single allele mismatch	260 (56)	43 (51)	23 (53)
Full allele matched	68 (15)	23 (27)	9 (21)
Unknown	472 (N/A)	208 (N/A)	163 (N/A)
High resolution release score			
No	560 (60)	292 (100)	203 (99)
Yes	380 (40)	0	3 (1)
KIR typing available			
No	872 (93)	292 (100)	205 (>99)
Yes	68 (7)	0	1 (<1)
Graft type			
Marrow	160 (17)	37 (13)	32 (16)
PBSC	777 (83)	255 (87)	174 (84)
BM+PBSC	2 (<1)	0	0
PBSC+UCB	1 (<1)	0	0
Conditioning regimen			
Myeloablative	325 (35)	107 (37)	82 (40)
RIC/Nonmyeloablative	602 (64)	181 (62)	115 (56)
TBD	13 (1)	4 (1)	9 (4)
Donor age at donation			
To Be Determined/NA	16 (2)	34 (12)	6 (3)
18-29 years	414 (44)	133 (46)	83 (40)
30-39 years	255 (27)	71 (24)	58 (28)
40-49 years	179 (19)	37 (13)	47 (23)
50+ years	76 (8)	17 (6)	12 (6)
Median (Range)	32 (18-61)	30 (18-58)	33 (19-58)
Donor/Recipient CMV serostatus			
+/+	196 (21)	68 (23)	40 (19)
+/-	91 (10)	36 (12)	20 (10)
-/+	271 (29)	78 (27)	54 (26)
-/-	314 (33)	77 (26)	71 (34)
CB - recipient +	1 (<1)	0	0
Missing	67 (7)	33 (11)	21 (10)
GvHD Prophylaxis			
No GVHD prophylaxis	9 (1)	2 (1)	6 (3)
Ex vivo T-cell depletion	18 (2)	9 (3)	7 (3)
CD34 selection	55 (6)	18 (6)	10 (5)
Post-CY + other(s)	45 (5)	19 (7)	7 (3)
Post-CY alone	3 (<1)	1 (<1)	2 (1)
Tacrolimus + MMF +- others	156 (17)	33 (11)	26 (13)
Tacrolimus + MTX +- others (except MMF)	310 (33)	120 (41)	40 (19)
Tacrolimus + others (except MTX, MMF)	46 (5)	13 (4)	10 (5)
Tacrolimus alone	22 (2)	5 (2)	4 (2)
CSA + MMF +- others (except Tacrolimus)	164 (17)	30 (10)	45 (22)
CSA + MTX +- others (except Tacrolimus, MMF)	51 (5)	21 (7)	25 (12)
CSA + others (except Tacrolimus, MTX, MMF)	13 (1)	6 (2)	9 (4)
CSA alone	12 (1)	4 (1)	4 (2)
Other GVHD prophylaxis	31 (3)	11 (4)	7 (3)
Missing	5 (1)	0	4 (2)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Donor/Recipient sex match			
Male-Male	406 (43)	114 (39)	87 (42)
Male-Female	207 (22)	54 (18)	42 (20)
Female-Male	174 (19)	69 (24)	46 (22)
Female-Female	139 (15)	43 (15)	25 (12)
CB - recipient M	1 (<1)	0	0
Missing	13 (1)	12 (4)	6 (3)
Year of transplant			
1986-1990	1 (<1)	0	0
1991-1995	18 (2)	4 (1)	7 (3)
1996-2000	59 (6)	19 (7)	11 (5)
2001-2005	144 (15)	23 (8)	39 (19)
2006-2010	271 (29)	46 (16)	48 (23)
2011-2015	285 (30)	82 (28)	62 (30)
2016-2020	134 (14)	104 (36)	36 (17)
2021-2022	28 (3)	14 (5)	3 (1)
Follow-up among survivors, Months			
N Eval	218	101	53
Median (Range)	60 (0-288)	37 (0-194)	37 (0-216)

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

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Number of patients	38	12	13
Source of data			
CRF	30 (79)	6 (50)	6 (46)
TED	8 (21)	6 (50)	7 (54)
Number of centers	19	8	7
Disease at transplant			
Plasma cell disorder/Multiple Myeloma	38 (100)	12 (100)	13 (100)
Recipient age at transplant			
18-29 years	1 (3)	0	1 (8)
30-39 years	2 (5)	0	0
40-49 years	9 (24)	1 (8)	4 (31)
50-59 years	24 (63)	7 (58)	4 (31)
60-69 years	2 (5)	4 (33)	4 (31)
Median (Range)	52 (22-64)	58 (48-67)	52 (19-70)
Recipient race/ethnicity			
White, Non-Hispanic	20 (53)	7 (58)	4 (31)
Black or African American, Non-Hispanic	9 (24)	3 (25)	2 (15)
Asian, Non-Hispanic	1 (3)	0	1 (8)
Hispanic	4 (11)	1 (8)	0
Missing	4 (11)	1 (8)	6 (46)
Recipient sex			
Male	20 (53)	7 (58)	8 (62)
Female	18 (47)	5 (42)	5 (38)
Karnofsky score			
10-80	13 (34)	3 (25)	5 (38)
90-100	25 (66)	7 (58)	8 (62)
Missing	0	2 (17)	0
HLA-A B DRB1 groups - low resolution			
4/6	24 (65)	4 (50)	10 (77)
5/6	12 (32)	3 (38)	2 (15)
6/6	1 (3)	1 (13)	1 (8)
Unknown	1 (N/A)	4 (N/A)	0 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	21 (72)	5 (83)	7 (70)
6/8	5 (17)	1 (17)	3 (30)
7/8	3 (10)	0	0
Unknown	9 (N/A)	6 (N/A)	3 (N/A)
HLA-DPB1 Match			
Double allele mismatch	1 (11)	0	2 (100)
Single allele mismatch	8 (89)	0	0

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Unknown	29 (N/A)	12 (N/A)	11 (N/A)
High resolution release score			
No	34 (89)	12 (100)	13 (100)
Yes	4 (11)	0	0
KIR typing available			
No	35 (92)	12 (100)	13 (100)
Yes	3 (8)	0	0
Graft type			
UCB	36 (95)	12 (100)	11 (85)
PBSC+UCB	2 (5)	0	2 (15)
Number of cord units			
1	29 (76)	0	8 (62)
2	9 (24)	0	5 (38)
Unknown	0 (N/A)	12 (N/A)	0 (N/A)
Conditioning regimen			
Myeloablative	12 (32)	4 (33)	4 (31)
RIC/Nonmyeloablative	24 (63)	7 (58)	9 (69)
TBD	2 (5)	1 (8)	0
Donor age at donation			
To Be Determined/NA	29 (76)	7 (58)	11 (85)
0-9 years	9 (24)	5 (42)	1 (8)
50+ years	0	0	1 (8)
Median (Range)	2 (1-7)	4 (2-7)	33 (2-63)
Donor/Recipient CMV serostatus			
CB - recipient +	25 (66)	5 (42)	8 (62)
CB - recipient -	13 (34)	5 (42)	5 (38)
CB - recipient CMV unknown	0	2 (17)	0
GvHD Prophylaxis			
CD34 selection	1 (3)	0	0
Tacrolimus + MMF +- others	11 (29)	3 (25)	4 (31)
Tacrolimus + MTX +- others (except MMF)	1 (3)	0	2 (15)
Tacrolimus + others (except MTX, MMF)	1 (3)	0	0
Tacrolimus alone	0	2 (17)	0
CSA + MMF +- others (except Tacrolimus)	17 (45)	6 (50)	4 (31)
CSA + MTX +- others (except Tacrolimus, MMF)	0	1 (8)	0
CSA + others (except Tacrolimus, MTX, MMF)	0	0	1 (8)
CSA alone	0	0	2 (15)
Other GVHD prophylaxis	6 (16)	0	0
Missing	1 (3)	0	0
Donor/Recipient sex match			
CB - recipient M	20 (53)	7 (58)	8 (62)
CB - recipient F	18 (47)	5 (42)	5 (38)
Year of transplant			
2006-2010	8 (21)	4 (33)	4 (31)
2011-2015	25 (66)	4 (33)	5 (38)
2016-2020	4 (11)	3 (25)	3 (23)
2021-2022	1 (3)	1 (8)	1 (8)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Follow-up among survivors, Months			
N Eval	5	2	5
Median (Range)	58 (3-72)	68 (64-72)	37 (12-50)

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

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Number of patients	257	39	23
Source of data			
CRF	90 (35)	7 (18)	11 (48)
TED	167 (65)	32 (82)	12 (52)
Number of centers	31	13	7
Disease at transplant			
Plasma cell disorder/Multiple Myeloma	257 (100)	39 (100)	23 (100)
Recipient age at transplant			
18-29 years	4 (2)	0	0
30-39 years	13 (5)	2 (5)	0
40-49 years	64 (25)	9 (23)	5 (22)
50-59 years	107 (42)	19 (49)	10 (43)
60-69 years	63 (25)	9 (23)	7 (30)
70+ years	6 (2)	0	1 (4)
Median (Range)	56 (26-75)	55 (35-69)	56 (40-72)
Recipient race/ethnicity			
White, Non-Hispanic	172 (67)	25 (64)	14 (61)
Black or African American, Non-Hispanic	23 (9)	6 (15)	3 (13)
Asian, Non-Hispanic	13 (5)	1 (3)	1 (4)
Native Hawaiian or Pacific Islander, Non-Hispanic	1 (<1)	0	0
American Indian or Alaska Native, Non-Hispanic	1 (<1)	0	0
Hispanic	43 (17)	7 (18)	3 (13)
Missing	4 (2)	0	2 (9)
Recipient sex			
Male	149 (58)	29 (74)	15 (65)
Female	108 (42)	10 (26)	8 (35)
Karnofsky score			
10-80	103 (40)	13 (33)	7 (30)
90-100	151 (59)	26 (67)	14 (61)
Missing	3 (1)	0	2 (9)
HLA-A B DRB1 groups - low resolution			
<=3/6	35 (18)	2 (8)	2 (13)
4/6	6 (3)	0	1 (7)
5/6	5 (3)	0	0
6/6	154 (77)	24 (92)	12 (80)
Unknown	57 (N/A)	13 (N/A)	8 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	39 (23)	1 (5)	2 (22)
6/8	1 (1)	0	0
7/8	4 (2)	0	0
8/8	129 (75)	21 (95)	7 (78)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Unknown	84 (N/A)	17 (N/A)	14 (N/A)
HLA-DPB1 Match			
Single allele mismatch	10 (23)	0	0
Full allele matched	33 (77)	0	1 (100)
Unknown	214 (N/A)	39 (N/A)	22 (N/A)
High resolution release score			
No	188 (73)	39 (100)	22 (96)
Yes	69 (27)	0	1 (4)
Graft type			
Marrow	22 (9)	1 (3)	2 (9)
PBSC	235 (91)	38 (97)	19 (83)
PBSC+UCB	0	0	2 (9)
Conditioning regimen			
Myeloablative	91 (35)	18 (46)	12 (52)
RIC/Nonmyeloablative	166 (65)	21 (54)	11 (48)
Donor age at donation			
To Be Determined/NA	0	0	1 (4)
0-9 years	1 (<1)	0	0
10-17 years	3 (1)	0	0
18-29 years	27 (11)	2 (5)	1 (4)
30-39 years	25 (10)	4 (10)	4 (17)
40-49 years	62 (24)	9 (23)	1 (4)
50+ years	139 (54)	24 (62)	16 (70)
Median (Range)	51 (0-76)	54 (27-69)	57 (29-74)
Donor/Recipient CMV serostatus			
+/+	101 (39)	16 (41)	6 (26)
+/-	27 (11)	5 (13)	3 (13)
-/+	54 (21)	8 (21)	4 (17)
-/-	72 (28)	10 (26)	7 (30)
CB - recipient +	0	0	2 (9)
Missing	3 (1)	0	1 (4)
GvHD Prophylaxis			
No GVHD prophylaxis	8 (3)	1 (3)	4 (17)
Ex vivo T-cell depletion	2 (1)	0	0
CD34 selection	0	1 (3)	0
Post-CY + other(s)	54 (21)	4 (10)	4 (17)
Post-CY alone	2 (1)	0	0
Tacrolimus + MMF +- others	26 (10)	2 (5)	0
Tacrolimus + MTX +- others (except MMF)	106 (41)	22 (56)	12 (52)
Tacrolimus + others (except MTX, MMF)	10 (4)	4 (10)	1 (4)
Tacrolimus alone	2 (1)	1 (3)	0
CSA + MMF +- others (except Tacrolimus)	6 (2)	0	0
CSA + MTX +- others (except Tacrolimus, MMF)	5 (2)	0	0
CSA + others (except Tacrolimus, MTX, MMF)	1 (<1)	1 (3)	0
CSA alone	1 (<1)	0	0
Other GVHD prophylaxis	15 (6)	0	1 (4)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Missing	19 (7)	3 (8)	1 (4)
Donor/Recipient sex match			
Male-Male	91 (35)	19 (49)	11 (48)
Male-Female	46 (18)	4 (10)	3 (13)
Female-Male	57 (22)	10 (26)	3 (13)
Female-Female	62 (24)	6 (15)	3 (13)
CB - recipient M	0	0	1 (4)
CB - recipient F	0	0	1 (4)
Missing	1 (<1)	0	1 (4)
Year of transplant			
2006-2010	26 (10)	7 (18)	7 (30)
2011-2015	116 (45)	19 (49)	8 (35)
2016-2020	104 (40)	11 (28)	5 (22)
2021-2022	11 (4)	2 (5)	3 (13)
Follow-up among survivors, Months			
N Eval	118	16	11
Median (Range)	49 (0-146)	43 (12-122)	37 (12-122)

CIBMTR®
CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH

TO: Plasma Cell Disorders Working Committee Members

FROM: Marcelo Pasquini, MD; Scientific Director for the Plasma Cell Disorders Working Committee

RE: 2021-2022 Studies in Progress Summary

MM20-02A Impact of Second Primary Malignancy Post-Autologous Hematopoietic Stem Cell Transplantation on Outcomes of Multiple Myeloma: A CIBMTR Analysis (B Ragon/M Shah/S Usmani). This study looks to determine the cumulative incidence of SPM and SHM post auto-HCT in patients with MM and determine the impact of SPM and SHM on overall survival and progression-free survival.
Status: Manuscript submitted to Blood. Goal to have manuscript accepted by July 2023.

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: Deferred until longer follow-up of patients.

MM20-03 Impact of bortezomib-based vs. lenalidomide maintenance therapy on outcomes of patients with high-risk multiple myeloma (N Bumma/ S Sidana/ B Dhakal). This study looks to evaluate PFS and OS in patients with high-risk multiple myeloma receiving lenalidomide only maintenance vs. bortezomib-based (alone or in combination) maintenance (with/without consolidation) after ASCT.
Status: Manuscript accepted in Cancer. Goal to have manuscript published by July 2023.

MM21-01 Differences in treatments and outcomes of Myeloma worldwide. (L Garderet).
This study looks to describe myeloma management and treatment outcome in the different parts of the world. The study a collaborative study with the WBMT. A modified MM1803 dataset was provided to the WBMT to conduct the study.
Status: Manuscript Preparation.

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 Development.

Response Summary:

This form is intended to be completed by a physician/researcher for the purpose of proposing a study. Content should not include Personal Identifiable Information (PII) or Protected Health Information (PHI). If you are a patient, do not complete this form. Patients: Contact your healthcare provider immediately for reports of problems with your treatment or problems with products received for your treatment. The CIBMTR uses de-identified data and is unable to associate reported treatment problems, adverse events, or corrections of information with a center, clinical trial, or healthcare provider.

Q1. Study Title

Real-life experience and utilization of BCMA-directed CAR-T therapy in patients with Multiple Myeloma

Q2. Key Words

chimeric antigen receptor T cell (CART), BCMA CART, multiple myeloma

Q3. PRINCIPAL INVESTIGATOR

Provide the following information for each investigator:

Principal Investigator #1:

First and last name, degree(s):	Nausheen Ahmed, MD
Email address:	nahmed5@kumc.edu
Institution name:	University of Kansas Medical Center
Academic rank:	Assistant Professor

Q4. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- Yes

Q5. Do you identify as an underrepresented/minority?

- Yes

Q6. Principal Investigator #2 (If applicable):

First and last name, degree(s):	Siddhartha Ganguly, MD FACP
Email address:	sganguly@houstonmethodist.org
Institution name:	Houston Methodist Hospital and Cancer Center
Academic rank:	Professor; Chief, Division of Hematology

Q7. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- No

Q8. Do you identify as an underrepresented/minority?

- Yes

Q9. 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:

Nausheen Ahmed, MD

Q10. If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:

- Yes, I am a junior investigator and would like assistance identifying a senior mentor for my project

LETTER OF COMMITMENT:

Please note: *A letter of commitment will be signed by Lead and Last authors as it describes the expectations for filling that role. By signing the letter of commitment, the authors accept their responsibilities and will be held accountable for timely completion of all steps in the project. More details regarding author responsibilities can be found here:* *https://www.cibmtr.org/Studies/Observational/StudyManagement/p*

Q12. CURRENT ONGOING WORK WITH CIBMTR: Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.

I have reviewed and suggested edits to several proposals and manuscripts in process. I am an active participant in several CIBMTR working committees.

Q13. PROPOSED WORKING COMMITTEE:

- Plasma Cell Disorders

Q14. Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.

- No

Q15. RESEARCH QUESTION:

The commercial approval for both idecabtagene vicleucel (ide-cel) and ciltacabtagene autoleucel (cilta-cel) for myeloma patients who are relapsed or refractory to four lines of therapy. These approvals were based on the pivotal KarMMa-2 and CARTITUDE-1 results respectively. There were stringent prerequisites for enrollment in KarMMA and CARTITUDE-1 trials in terms of organ function and fitness, as well as the requirement for at least three therapy at the time of enrollment, which differs from the approved lines of therapy in the commercial setting. The research question is to determine real-world utilization of ide-cel and cilta-cel , especially with regards to patient selection, difficulty in utilization due to delay in getting apheresis slots, financial hurdles and getting
insurance approvals and to determine if there is a difference in 1-year outcomes in the "real world" setting compared to trial data.

Q16. RESEARCH HYPOTHESIS:

Real world experience with commercially available CAR T therapy produces similar response and PFS results compared to published trial results.

Q17. SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.)

Suggested word limit of 200 words:

Primary:
1. 30 day and 100 day Overall Response with commercially available BCMA CAR T therapy

Secondary:
1. 6 month and 12 month PFS after Commercially available CAR T therapy
2. CRS rate with commercially available CAR T therapy
3. ICANS rate with commercially available CAR T therapy

Q18. SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.

Clinical trials are studying BCMA CAR-T after varying lines of therapy. The FDA approval for both ide-cel and cilta-cel are after ≥ 4 lines of therapy. There are patients who have received commercial and clinical trial CAR-T therapy as an earlier line of therapy.

Q19. SCIENTIFIC JUSTIFICATION: Provide a background summary of previous related research and their strengths and weaknesses, justification of your research and why your research is still necessary.

Relapsed refractory multiple myeloma (RRMM) has a poor prognosis, with overall survival of around 6 months for penta-refractory patients, refractory to conventional therapy including immunomodulatory drugs (Imids), proteasome inhibitors (Pis), and CD38-directed therapy [1]. B cell maturation antigen (BCMA) is a novel treatment target for multiple myeloma due to its highly selective expression on plasma cells [2]. CAR T cells have emerged as a potent therapeutic strategy against many B-cell malignancies with unprecedented responses and manageable toxicity [3, 4]. Since 2021, two BCMA-directed chimeric antigen receptor T (CAR-T) cell therapy products have been approved in patients with RRMM who have failed four lines of therapy. Idecabtagene vicleucel (ide-cel) was the first in class BCMA directed CAR-T cell therapy approved on March 26th, 2021, for RRMM patients who progressed after ≥ 4 lines of therapy based on the pivotal phase I/II KarMMa trial data. The overall response rate (ORR) was 73%, with 26% stringent complete responses (sCR) and a median duration of response (DOR) of 11 months in responders, and 20 mo
in patients who had a sCR [5, 6]. While there are guidelines on determining the number of lines of therapy, in the real-world setting, given the complexity of myeloma therapy, and the promise of CAR-T therapy, it is likely that many patients who have not been exposed to ≥4 lines of therapy, receive the commercial CAR-T [7]. Patients who are not penta-refractory or penta-exposed are also likely to have received this therapy. It is of great interest for the clinical community to study real-world utilization patterns and study its impact on outcomes. Real-world evidence can provide valuable insight into various treatment outcome parameters and hypothesis generation.

Q19a. SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF)

N/A

Q20. PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.

Inclusion: - All patients who received BCMA CAR-T therapy for myeloma Exclusion: - Age < 18 yrs
- Those who received CAR-T therapy directed at non_BCMA targets

Q21. Does this study include pediatric patients?

- No

Q21a. If this study does not include pediatric patients, please provide justification:

Multiple Myeloma is a disease affecting adults. All clinical trials and commercial approvals only include adults.

Q22. DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Data collection forms available at: http://www.cibmtr.org/DataManagement/DataCollectior Outline any supplementary data required. Additional data collection is extremely difficult and will make your proposal less feasible.

Demographics at time of collection
Age
Race (White, African American, Asian, Other)
Ethnicity (Hispanic/ Non-Hispanic)
Gender
CMI score
Karnofsky score
Comorbidities pre-infusion: (form 4000 R7.0)
Myeloma Characteristics
Disease (Myeloma, Myeloma-Light Chain, solitary plasmacytoma, other)
ISS at diagnosis M spike (IgG kappa, IgA kappa, IgG lambda, IgA lambda, kappa LC only, Lambda LC only, No bands, other)
Years since diagnosis
High-risk cytogenetics (yes vs no)
PET scan involvement of myeloma (extramedullary vs no)
Treatment of Myeloma At Collection:
Response to latest therapy (CCR, sCR, VGPR, PR, NR, PD)
Number of lines of therapy ( )
Prior systemic therapies used (Yes/no)
-Lenalidomide
-Pomalidomide
-Bortezomib
-Carfilzomib
-Daratumumab
-Isatuximab
-Selinexor
Chemotherapy (bendamustine or cisplatin-containing regimens)
Prior allogeneic transplant (yes/no) Prior Autologous transplant (yes/no)
Prior tandem autologous transplant (yes/no)
Prior salvage autologous transplant (yes/ no)
Prior BCMA-directed therapy (non-CART) (yes/no)
Prior BCMA CART (yes/no)
CAR-T therapy product (ide-cel / cilta-cel/ other)
CRS
CRS any grade (yes/no) Maximum grade (I, II, III, IV) Days to onset ___ Duration ___
Macrophage activating syndrome / HLH (yes/no)
Neurotoxicity: ICANS any grade (yes/no) Maximum grade (I, II, III, IV) Days from infusion to onset ___ Duration___
Treatment for CRS and ICANS:
Tocilizumab doses used (0,1, ≥2)
Anakinra (yes/no)
Siltuximab (yes/no)
Corticosteroids (yes/no)
Anti-epileptics (yes/no)
Outcomes: Form 4100 R6.0
100-day Outcomes :
Alive (yes/no)
Best response (CCR, CR, PR, No response, PD)
6- mo Outcomes:
Alive (yes/no)
Best response (CCR, CR, PR, No response, PD)
1-year Outcomes
Alive (yes/no)
Best response (CCR, CR, PR, No response, PD)

Q23. **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 specific to PROS.**

For additional information on what PRO measures have been collected and timepoints of collection, please reach out to the Late Effects and Quality of Life or Health Services Working Committee leadership: https://www.cibmtr.org/About/WhoWeAre/Com

None

Q24. **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 experience with the proposed assay systems. PIs should be encouraged to review the inventory details, sample types collected and reach out to research_repos@nmdp.org with any questions.**

More information can be found at: https://www.cibmtr.org/Samples/Inventory/Pages/index

None

Q25. NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required, i.e., neither database contains all the data required to answer the study question.

None

Q26. REFERENCES:

1. Gandhi, U.H., et al., Outcomes of patients with multiple myeloma refractory to CD38-targeted monoclonal antibody therapy. Leukemia, 2019. 33(9): p. 2266-2275.
2. Friedman, K.M., et al., Effective Targeting of Multiple B-Cell Maturation Antigen–Expressing Hematological Malignances by Anti-B-Cell Maturation Antigen Chimeric Antigen Receptor T Cells. Human Gene Therapy, 2018. 29(5): p. 585-601.
3. Neelapu, S.S., et al., Axicabtagene ciloleucel CAR T-cell therapy in refractory large B-cell lymphoma. New England Journal of Medicine, 2017. 377(26): p. 2531-2544.
4. Maude, S.L., et al., Tisagenlecleucel in children and young adults with B-cell lymphoblastic leukemia. New England Journal of Medicine, 2018. 378(5): p. 439-448.
5. Sharma, P., et al., FDA Approval Summary: Idecabtagene Vicleucel for Relapsed or Refractory Multiple Myeloma. Clinical Cancer Research, 2022. 28(9): p. 1759-1764.
6. Munshi, N.C., et al., Idecabtagene Vicleucel in Relapsed and Refractory Multiple Myeloma. New England Journal of Medicine, 2021. 384(8): p. 705-716.
7. Rajkumar, S.V., P. Richardson, and J.F. San Miguel, Guidelines for determination of the number of prior lines of therapy in multiple myeloma. Blood, 2015. 126(7): p. 921-922.

Q27. CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning:

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

N/A

Q27a. **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.**

N/A

BEFORE FINAL SUBMISSION, please review the PI checklist to ensure that you have completed all necessary steps. This will increase the likelihood of submitting a feasible and successful proposal.

Embedded Data:

N/A

Response Summary:

This form is intended to be completed by a physician/researcher for the purpose of proposing a study. Content should not include Personal Identifiable Information (PII) or Protected Health Information (PHI). If you are a patient, do not complete this form. Patients: Contact your healthcare provider immediately for reports of problems with your treatment or problems with products received for your treatment. The CIBMTR uses de-identified data and is unable to associate reported treatment problems, adverse events, or corrections of information with a center, clinical trial, or healthcare provider.

Q1. Study Title

Real-world evidence of safety and efficacy of idecabtagene vicleucel in patients with multiple myeloma

Q2. Key Words

ide-cel, myeloma

Q3. PRINCIPAL INVESTIGATOR

Provide the following information for each investigator:

Principal Investigator #1:

First and last name, degree(s):	Binod Dhakal
Email address:	bdhakal@mcw.edu
Institution name:	Medical College of Wisconsin
Academic rank:	Associate Professor of Medicine

Q4. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- No

Q5. Do you identify as an underrepresented/minority?

- Yes

Q6. Principal Investigator #2 (If applicable):

First and last name, degree(s):	N/A
Email address:	N/A
Institution name:	N/A
Academic rank:	N/A

Q7. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

N/A

Q8. Do you identify as an underrepresented/minority?

N/A

Q9. 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:

N/A

Q10. If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:

N/A

LETTER OF COMMITMENT:

Please note: *A letter of commitment will be signed by Lead and Last authors as it describes the expectations for filling that role. By signing the letter of commitment, the authors accept their responsibilities and will be held accountable for timely completion of all steps in the project. More details regarding author responsibilities can be found here:* *https://www.cibmtr.org/Studies/Observational/StudyManagement/p*

Q12. CURRENT ONGOING WORK WITH CIBMTR: Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.

I was involved in 3 CIBMTR studies for plasma cell disorders. One was looking at the transplant outcomes in plasma cell leukemia which was published in Leukemia (PMID 32313109), and the other one investigating the prognostic score after stem cell transplantation in myeloma (PMID 33094839). The third project looking at the role of bortezomib vs. lenalidomide maintenance which was an oral presentation at the last TCT meeting.

Q13. PROPOSED WORKING COMMITTEE:

- Plasma Cell Disorders

Q14. Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.

- Yes

Q14a. If you have already spoken with a scientific director or working committee chair regarding this study, then please specify who:

Marcelo Pasquini

Q15. RESEARCH QUESTION:

Chimeric antigen receptor T (CAR-T) cell therapy has shown unprecedented responses in patients with relapsed and/or refractory multiple myeloma (RRMM). Idecabtagene vicleucel (ide-cel) targeted against BCMA is the first CAR-T to be approved in RRMM. However, the real world evidence of safety and efficacy of this product is not known and needs further investigation.

Q16. RESEARCH HYPOTHESIS:

We hypothesize that the safety and efficacy of ide-cel, in real world, is comparable to what has been reported in clinical trials that led to its approval.

Q17. SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.) *Suggested word limit of 200 words:*

Efficacy (overall response rates, ORR)
Safety (cytokine release syndrome, CRS and immune effector cell associated neurotoxicity, ICANS)

Q18. SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.

The results of this study will help us understand the real world evidence of safety and efficacy of ide-cel in relapsed and/or refractory multiple myeloma. In addition, understanding the predictors of response and toxicities will inform further studies to identify and select patients that would benefit the most from this modality.

Q19. SCIENTIFIC JUSTIFICATION: Provide a background summary of previous related research and their strengths and weaknesses, justification of your research and why your research is still necessary.

Multiple myeloma (MM), a cancer of antibody producing plasma cells, has seen a sea change in the therapeutic landscape with the introduction of several novel agents (1,2). Management of MM is rapidly changing with the emergence of variety of immune based approaches (3). Among these chimeric antigen receptor T cell therapy (CAR-T) has shown considerable promise in the treatment of relapsed and or refractory MM (RRMM). B-cell maturation antigen has been the lead antigen target for these CAR-T products and several clinical trials against BCMA have shown unprecedented response rates in myeloma with heavily treated disease (4,5). As a matter of fact, given the very impressive safety and efficacy profile, FDA granted approval to idecabtagene vicleucel (ide-cel) which is an anti-BCMA CAR-T agent in MM patients with 4 or more lines of therapy including an ImID, PI and CD-38 antibody (5). This approval was based on a phase trial that included patients with median of 6 prior lines of treatment and resulted in overall response rate of 73% with a median progression free survival of 8.8 months (5). With the approval of this product, it is important to assess the efficacy and safety outcomes of this product in the real-world setting. Hence, in this study we seek to evaluate the safety and efficacy outcomes with commercial use of ide-cel using recently established cellular therapy registry.

References:1. Dhakal B, Girnius S, Hari P. Recent advances in understanding multiple myeloma. F1000Res. 2016;5; https://doi.org/10.12688/f1000research.8777.1
2. Kumar SK, Rajkumar V, Kyle RA, Van Duin M, Sonneveld P, Mateos MV, et al. Multiple myeloma. Nat Rev Dis Primers. 2017;3:17046. https://doi.org/10.1038/nrdp.2017.46
3. Neri P, Bahlis NJ, Lonial S. New strategies in multiple myeloma: immunotherapy as a novel approach to treat patients with multiple myeloma. Clin Cancer Res. 2016;22:5959–65.
4. Berdeja J, Madduri D, Usmani S et. al Ciltacabtagene autoleucel, a B-cell maturation antigen-directed chimeric antigen receptor T-cell therapy in patients with relapsed or refractory multiple myeloma (CARTITUDE-1): a phase 1b/2 open-label study. Lancet 398 (1027) (314-324)
5. Munshi et. al Idecabtagene Vicleucel in Relapsed and Refractory Multiple Myeloma; NEJM 2021

Q19a. SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF)

N/A

Q20. PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.

Patients who received idecabtagene vicleucel for an approved indication (RRMM) in the US or Canada and reported to CIBMTR will be included in the study. Inclusion criteria:
All MM patients who received idecabtagene vicleucel till data.
Exclusion criteria:
None

Q21. Does this study include pediatric patients?

- No

Q21a. If this study does not include pediatric patients, please provide justification:

NA

Q22. DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Data collection forms available at: http://www.cibmtr.org/DataManagement/DataCollectior Outline any supplementary data required. Additional data collection is extremely difficult and will make your proposal less feasible.

Patient-related:
- Age at cell therapy infusion
- Sex: male vs. female
- Karnofsky performance score: ≥80% vs. <80%
- Race: White vs. Black vs. Asian/pacific islander vs. Hispanic vs. others
- Hematopoietic cell transplantation co-morbidity index (HCT-CI) (≥3 vs. <3) (if available)
- International staging system (ISS)/ Durie Salmon Stage: I vs. II vs. III vs. Revised ISS (R-ISS) (if available)

Disease-related:
- Immunochemical subtype: IgG vs. IgA vs. light chain vs. non-secretory/others
- Prior therapies
- Triple class refractory
- Prior hematopoietic cell transplantation (autologous, allogeneic or both)

CAR-T related:
- Time of leukapheresis to infusion
- Time from diagnosis to cell therapy infusion
- Time of follow up since infusion
- CRS (grades, time to onset and median duration)
- ICANS (grades, time to onset and median duration)

Q23. 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 specific to PROS.

For additional information on what PRO measures have been collected and timepoints of collection, please reach out to the Late Effects and Quality of Life or Health Services Working Committee leadership: https://www.cibmtr.org/About/WhoWeAre/Com

N/A

Q24. 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 experience with the proposed assay systems. PIs should be encouraged to review the inventory details, sample types collected and reach out to research_repos@nmdp.org with any questions.

More information can be found at: https://www.cibmtr.org/Samples/Inventory/Pages/index

NA

Q25. NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required, i.e., neither database contains all the data required to answer the study question.

NA

Q26. REFERENCES:

1. Dhakal B, Girnius S, Hari P. Recent advances in understanding multiple myeloma. F1000Res. 2016;5; https://doi.org/10.12688/f1000research.8777.1
2. Kumar SK, Rajkumar V, Kyle RA, Van Duin M, Sonneveld P, Mateos MV, et al. Multiple myeloma. Nat Rev Dis Primers. 2017;3:17046. https://doi.org/10.1038/nrdp.2017.46
3. Neri P, Bahlis NJ, Lonial S. New strategies in multiple myeloma: immunotherapy as a novel approach to treat patients with multiple myeloma. Clin Cancer Res. 2016;22:5959–65.
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5. Munshi et. al Idecabtagene Vicleucel in Relapsed and/or Refractory Multiple myeloma; N Engl J Med 2021; 384:705-716

Q27. **CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning:**

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

- No, I do not have any conflicts of interest pertinent to this proposal

Q27a. **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.**

N/A

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Q1. Study Title

Real-world evidence of safety and efficacy of ciltacabtagene autoleucel in patients with multiple myeloma

Q2. Key Words

cilta-cabatgene autolceucel

Q3. PRINCIPAL INVESTIGATOR

Provide the following information for each investigator:

Principal Investigator #1:

First and last name, degree(s):	Binod Dhakal
Email address:	bdhakal@mcw.edu
Institution name:	Medical College of Wisconsin
Academic rank:	Associate Professor of Medicine

Q4. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- No

Q5. Do you identify as an underrepresented/minority?

- Yes

Q6. Principal Investigator #2 (If applicable):

First and last name, degree(s):	N/A
Email address:	N/A
Institution name:	N/A
Academic rank:	N/A

Q7. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

N/A

Q8. Do you identify as an underrepresented/minority?

N/A

Q9. 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:

N/A

Q10. If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:

N/A

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Q13. PROPOSED WORKING COMMITTEE:

- Plasma Cell Disorders

Q14. Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.

- Yes

Q14a. If you have already spoken with a scientific director or working committee chair regarding this study, then please specify who:

Marcelo Pasquini

Q15. RESEARCH QUESTION:

Chimeric antigen receptor T (CAR-T) cell therapy has shown unprecedented responses in patients with relapsed and/or refractory multiple myeloma (RRMM). Ciltacabtagene autoleucel (cilta-cel) targeted against BCMA is the first CAR-T to be approved in RRMM. However, the real world evidence of safety and efficacy of this product is not known and needs further investigation.

Q16. RESEARCH HYPOTHESIS:

We hypothesize that the safety and efficacy of cilta-cel, in real world, is comparable to what has been reported in clinical trials that led to its approval.

Q17. SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.) *Suggested word limit of 200 words:*

Primary:
Efficacy (overall response rates, ORR)
Safety (cytokine release syndrome, CRS and immune effector cell associated neurotoxicity, ICANS)
Secondary:
Progression free survival
Duration of response
Overall survival

Q18. SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.

The results of this study will help us understand the real world evidence of safety and efficacy of cilta-cel in relapsed and/or refractory multiple myeloma. In addition, understanding the predictors of response and toxicities will inform further studies to identify and select patients that would benefit the most from this modality.

Q19. SCIENTIFIC JUSTIFICATION: Provide a background summary of previous related research and their strengths and weaknesses, justification of your research and why your research is still necessary.

Multiple myeloma (MM), a cancer of antibody producing plasma cells, has seen a sea change in the therapeutic landscape with the introduction of several novel agents (1,2). Management of MM is rapidly changing with the emergence of variety of immune based approaches (3). Among these chimeric antigen receptor T cell therapy (CAR-T) has shown considerable promise in the treatment of relapsed and or refractory MM (RRMM). B-cell maturation antigen has been the lead antigen target for these CAR-T products and several clinical trials against BCMA have shown unprecedented response rates in myeloma with heavily treated disease (4,5). As a matter of fact, given the very impressive safety and efficacy profile, FDA granted approval 2 CAR-T products idecabtagene vicleucel (ide-cel) and ciltacabtagene autoleucel (cilta-cel) which is an anti-BCMA CAR-T agent in MM patients with 4 or more lines of therapy including an ImID, PI and CD-38 antibody (4, 5). This approval was based on a phase trial that included patients with median of 6 prior lines of treatment and resulted in overall response rate of 73% with a median progression free survival of 8.8 months (5). Simialry, cilta-cel approval was based on a phase Ib/II study that showed response rates of 97% with median PFS not reached (4)
With the approval of these products, it is important to assess the efficacy and safety outcomes of this product in the real-world setting. Hence, in this study we seek to evaluate the safety and efficacy outcomes with commercial use of cilta-cel using recently established cellular therapy registry.

Q19a. SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF)

N/A

Q20. PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.

Patients who received ciltacabtagene autoleucel for an approved indication (RRMM) in the US or Canada and reported to CIBMTR will be included in the study. Inclusion criteria:
All MM patients who received ciltacabtagene autoleucel till data.
Exclusion criteria:
None

Q21. Does this study include pediatric patients?

- No

Q21a. If this study does not include pediatric patients, please provide justification:

NA

Q22. DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Data collection forms available at: http://www.cibmtr.org/DataManagement/DataCollectior Outline any supplementary data required. Additional data collection is extremely difficult and will make your proposal less feasible.

Patient-related:
- Age at cell therapy infusion
- Sex: male vs. female
- Karnofsky performance score: ≥80% vs. <80%
- Race: White vs. Black vs. Asian/pacific islander vs. Hispanic vs. others
- Hematopoietic cell transplantation co-morbidity index (HCT-CI) (≥3 vs. <3) (if available)
- International staging system (ISS)/ Durie Salmon Stage: I vs. II vs. III vs. Revised ISS (R-ISS) (if available)

Disease-related:
- Immunochemical subtype: IgG vs. IgA vs. light chain vs. non-secretory/others
- Prior therapies
- Triple class refractory
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NA

Q24. **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 experience with the proposed assay systems. PIs should be encouraged to review the inventory details, sample types collected and reach out to research_repos@nmdp.org with any questions.**

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NA

Q25. NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required, i.e., neither database contains all the data required to answer the study question.

CAR-T cell viability
CAR-T cell dose

Q26. REFERENCES:

1. Dhakal B, Girnius S, Hari P. Recent advances in understanding multiple myeloma. F1000Res. 2016;5; https://doi.org/10.12688/f1000research.8777.1
2. Kumar SK, Rajkumar V, Kyle RA, Van Duin M, Sonneveld P, Mateos MV, et al. Multiple myeloma. Nat Rev Dis Primers. 2017;3:17046. https://doi.org/10.1038/nrdp.2017.46
3. Neri P, Bahlis NJ, Lonial S. New strategies in multiple myeloma: immunotherapy as a novel approach to treat patients with multiple myeloma. Clin Cancer Res. 2016;22:5959–65.
4. Berdeja J, Madduri D, Usmani S et. al Ciltacabtagene autoleucel, a B-cell maturation antigen-directed chimeric antigen receptor T-cell therapy in patients with relapsed or refractory multiple myeloma (CARTITUDE-1): a phase 1b/2 open-label study. Lancet 398 (1027) (314-324)
5. Munshi et. al Idecabtagene Vicleucel in Relapsed and/or Refractory Multiple myeloma; N Engl J Med 2021; 384:705-716

Q27. CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning:

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

- No, I do not have any conflicts of interest pertinent to this proposal

Q27a. 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.

N/A

BEFORE FINAL SUBMISSION, please review the PI checklist to ensure that you have completed all necessary steps. This will increase the likelihood of submitting a feasible and successful proposal.

Embedded Data:

N/A

Response Summary:

This form is intended to be completed by a physician/researcher for the purpose of proposing a study. Content should not include Personal Identifiable Information (PII) or Protected Health Information (PHI). If you are a patient, do not complete this form. Patients: Contact your healthcare provider immediately for reports of problems with your treatment or problems with products received for your treatment. The CIBMTR uses de-identified data and is unable to associate reported treatment problems, adverse events, or corrections of information with a center, clinical trial, or healthcare provider.

Q1. Study Title

Assessment of Feasibility, Safety, and Efficacy of anti-BCMA CAR T-cell Therapy in the Real-World Setting for Patients with Relapsed or Refractory Multiple Myeloma

Q2. Key Words

Multiple Myeloma; B-cell maturation antigen; Chimeric Antigen Receptor; idecabtagene vicleucel; ciltacabtagene autoleucel

Q3. PRINCIPAL INVESTIGATOR

Provide the following information for each investigator:

Principal Investigator #1:

First and last name, degree(s):	Christopher Ferreri, MD
Email address:	cjferreri@mdanderson.org
Institution name:	University of Texas MD Anderson Cancer Center
Academic rank:	Fellow in Hematology & Oncology

Q4. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- Yes

Q5. Do you identify as an underrepresented/minority?

- No

Q6. Principal Investigator #2 (If applicable):

First and last name, degree(s):	Krina Patel, MD, MSc
Email address:	KPatel1@mdanderson.org
Institution name:	UT MD Anderson Cancer Center
Academic rank:	Associate Professor

Q7. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- No

Q8. Do you identify as an underrepresented/minority?

- No

Q9. 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:

Christopher Ferreri

Q10. If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:

N/A

LETTER OF COMMITMENT:

Please note: *A letter of commitment will be signed by Lead and Last authors as it describes the expectations for filling that role. By signing the letter of commitment, the authors accept their responsibilities and will be held accountable for timely completion of all steps in the project. More details regarding author responsibilities can be found here:* *https://www.cibmtr.org/Studies/Observational/StudyManagement/p*

Q12. CURRENT ONGOING WORK WITH CIBMTR: Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.

N/A

Q13. PROPOSED WORKING COMMITTEE:

- Cellular Immunotherapy for Cancer

Q14. Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.

- No

Q15. RESEARCH QUESTION:

For patients with relapsed/refractory multiple myeloma who receive commercial CAR T-cell therapy (idecabtagene vicleucel or ciltacabtagene autoleucel), how do key safety and efficacy outcomes compare to those of patients treated with these CAR T-cell therapies on the respective registrational clinical trials?

Q16. RESEARCH HYPOTHESIS:

We hypothesize that the clinical safety and efficacy outcomes for patients receiving standard-of-care anti-BCMA CAR T-cell therapy will be similar to outcomes reported in clinical trials leading to regulatory approval, and that the clinical benefits will extend to patients who would not have met eligibility criteria to receive such therapy on clinical trial.

Q17. SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.)

Suggested word limit of 200 words:

1. Primary Objectives: To compare the infusion failure rate (patients unable to receive CAR T-cell infusion of those who underwent apheresis), safety outcomes regarding incidence and severity of cytokine release syndrome (CRS), immune effector cell-associated neurotoxicity syndrome (ICANS), hemophagocytic lymphohistiocytosis (HLH), CTCAE grade 3-4 adverse events, and non-relapse related mortality (NRM), and efficacy outcomes of objective response rate (ORR) further stratified to PR, VGPR, CR, sCR, and MRD-negative as per IMWG criteria for response assessment,[1] progression free survival (PFS), overall survival (OS), and duration of response (DOR) for patients receiving anti-BCMA CAR T-cell therapy in the real-world setting
2. Secondary Objectives: To assess whether the following patient and disease-specific variables are significantly associated with the aforementioned safety and efficacy outcomes: age, gender, ethnicity, performance status, renal insufficiency, disease burden measured by bone marrow clonal plasma cells prior to treatment, standard versus high-risk FISH disease, presence of extramedullary disease, number of prior lines of therapy, prior autologous stem cell transplant, prior CAR T-cell therapy, prior BCMA-targeted therapy, bridging therapy prior to CAR T-cell therapy, response to bridging therapy if given.

Q18. SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.

The clinical efficacy outcomes achieved with autologous anti-BCMA CAR T-cell therapies in the KarMMa and CARTITUDE-1 studies demonstrated a significant improvement in the treatment of triple-class refractory multiple myeloma compared to prior therapies used in this setting.[2,3] With the FDA approval of idecabtagene vicleucel in March 2021 and ciltacabtagene autoleucel in February 2022, a significant increase in the utilization of these autologous CAR T-cell therapies is anticipated for patients with relapsed/refractory myeloma over the next several years. While the results with anti-BCMA CAR T-cell therapies have been quite promising to date, the individual trials are of relatively small sample size and with considerable heterogeneity amongst patient populations treated and outcomes reported. Herein, we propose a registry analysis of patients who have received standard-of-care anti-BCMA CAR T-cell therapy (idecabtagene vicleucel or ciltacabtagene autoleucel) for relapsed/refractory multiple myeloma to evaluate how safety and efficacy outcomes compare to those of patients treated on the respective registrational trials.
Completion of the study will generate valuable data aimed at determining the extent of clinical benefit for patients receiving these CAR T-cell therapies who would not have been ineligible to receive them on a clinical trial. The expected large sample size will allow for analysis of covariates associated with safety and efficacy. As access to CAR T-cell therapy remains limited, results from this study should help further inform which patients are most likely to benefit from commercial CAR T-cell therapy.

Q19. 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.

B-cell maturation antigen (BCMA) has become a primary therapeutic target for the treatment of relapsed/refractory multiple myeloma (RRMM) given that its expression is limited to the cell membrane of late memory B cells committed to plasma cell differentiation, thus limiting off target effects.[4] Prior to the recent emergence of autologous anti-BCMA CAR T-cell therapies, FDA approved treatments for patients with triple-class refractory multiple myeloma (refractory to immunomodulatory drugs, proteasome inhibitors, and anti-CD38 monoclonal antibodies) were limited. Such available therapies included selinexor plus dexamethasone (ORR 26%, mPFS 3.7 months, mOS 8.6 months) and the anti-BCMA monoclonal antibody drug conjugate belantamab mafodotin (ORR 31%, mPFS 2.9 months).[5,6] Idecabtagene vicleucel (ide-cel) became the first autologous anti-BCMA CAR T-cell therapy to receive FDA approval based on results from the phase 2 KarMMa trial in which 128 heavily pretreated patients receiving ide-cel at a target dose of 150-450 x 10e6 CAR-T cells were noted to obtain impressive responses (ORR 73%, 33% CR or better, 26% MRD-negative) and with improved PFS and OS compared to the aforementioned therapies at 8.8 months and 19.4 months respectively.[2] In the phase 1b/2 CARTITUDE-1 study, 97 heavily pre-treated patients received ciltacabtagene autoleucel (cilta-cel) at the recommended phase 2 dose of 0.75 x 10e6 CAR-T cells. Unprecedented response rates (ORR 97%, sCR 67%) and survival outcomes (mPFS and mOS not reached, 12 month PFS 77%, 12 month OS 89%) were noted with cilta-cel.[3]

With an expected significant increase in the use of autologous anti-BCMA CAR T-cell therapies for patients with RRMM with ≥ 4 prior lines of therapy, further clinical characterization of efficacy and safety outcomes will be valuable. The published registrational clinical trials have had relatively small sample sizes and notable heterogeneity regarding patient and disease-related factors. This registry analysis of patients receiving standard-of-care therapies will allow for a larger sample size to assess for prognostic and predictive factors related to safety and efficacy outcomes. Unique toxicities such as HLH-MAS, delayed non-ICANS neurotoxicity (noted with cilta-cel), and the infectious sequelae of BCMA-targeted CAR T-cell therapy will benefit from further characterization with a larger sample size of patients. Additionally, the expanded access to this therapy for patients who might not have been eligible to receive such treatments on clinical trial will likely translate to meaningful clinical benefits. For example, a large multicenter retrospective study of patients receiving standard-of-care axicabtagene ciloleucel for relapsed or refractory large B-cell lymphoma noted that 43% of patients would not have met eligibility on the ZUMA-1 registrational study, yet safety and efficacy results from this retrospective cohort were comparable with those seen on the ZUMA-1 study.[7] This registry analysis will help to define the extent to which such clinical benefits will extend to patients who would have been excluded from the registrational anti-BCMA CAR T-cell trials, which will in turn help clinicians further inform future treatment decisions and help clinical investigators refine future research questions.

Q19a. SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF)

N/A

Q20. PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.

1. Adult patients (age ≥ 18) who underwent apheresis with intent to receive anti-BCMA CAR T-cell therapy for relapsed/refractory multiple myeloma in the standard-of-care setting (idecabtagene vicleucel or ciltacabtagene autoleucel) from date of first FDA approval (3/27/2021) through 12/31/2022
2. Any lymphodepletion chemotherapy regimen
3. Any bridging therapy leading up to CAR T-cell infusion

Q21. Does this study include pediatric patients?

- No

Q21a. If this study does not include pediatric patients, please provide justification:

N/A

Q22. DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Data collection forms available at: http://www.cibmtr.org/DataManagement/DataCollectior Outline any supplementary data required. Additional data collection is extremely difficult and will make your proposal less feasible.

Data will be captured through CIBMTR collection forms
Patient-specific variables:
- Age
- Gender
- Ethnicity
- Performance Status
- Moderate-severe hepatic and renal insufficiency

Disease-specific variables:
- Percentage of plasma cells in bone marrow biopsy prior to cell therapy
- Standard risk versus high risk FISH/cytogenetics
- Presence of extramedullary disease
- Number of prior lines of therapy
- Prior autologous stem cell transplant
- Prior cellular therapy
- Prior BCMA-targeted therapy (may need supplementary data for this)

Infusion-related variables:
- Need for bridging therapy
- Response to bridging therapy
- Cell dose at time of infusion

Q23. **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 specific to PROS.**

For additional information on what PRO measures have been collected and timepoints of collection, please reach out to the Late Effects and Quality of Life or Health Services Working Committee leadership: https://www.cibmtr.org/About/WhoWeAre/Com

N/A

Q24. **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 experience with the proposed assay systems. PIs should be encouraged to review the inventory details, sample types collected and reach out to research_repos@nmdp.org with any questions.**

More information can be found at: https://www.cibmtr.org/Samples/Inventory/Pages/index

N/A

Q25. NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required, i.e., neither database contains all the data required to answer the study question.

N/A

Q26. REFERENCES:

1. Kumar S, Paiva B, Anderson KC, et al. International Myeloma Working Group consensus criteria for response and minimal residual disease assessment in multiple myeloma. Lancet Oncol. 2016;17(8):e328-e346. doi:10.1016/S1470-2045(16)30206-6
2. Munshi NC, Anderson LD, Shah N, et al. Idecabtagene Vicleucel in Relapsed and Refractory Multiple Myeloma. N Engl J Med. 2021;384(8):705-716. doi:10.1056/NEJMoa2024850
3. Berdeja JG, Madduri D, Usmani SZ, et al. Ciltacabtagene autoleucel, a B-cell maturation antigen-directed chimeric antigen receptor T-cell therapy in patients with relapsed or refractory multiple myeloma (CARTITUDE-1): a phase 1b/2 open-label study. Lancet. 2021;398(10297):314-324. doi:10.1016/S0140-6736(21)00933-8
4. Cho SF, Anderson KC, Tai YT. Targeting B cell maturation antigen (BCMA) in multiple myeloma: Potential uses of BCMA-based immunotherapy. Front Immunol. 2018;9(AUG). doi:10.3389/fimmu.2018.01821
5. Chari A, Vogl DT, Gavriatopoulou M, et al. Oral Selinexor–Dexamethasone for Triple-Class Refractory Multiple Myeloma. N Engl J Med. 2019;381(8):727-738. doi:10.1056/nejmoa1903455
6. Lonial S, Lee HC, Badros A, et al. Belantamab mafodotin for relapsed or refractory multiple myeloma (DREAMM-2): a two-arm, randomised, open-label, phase 2 study. Lancet Oncol. 2020;21(2):207-221. doi:10.1016/S1470-2045(19)30788-0
7. Nastoupil LJ, Jain MD, Feng L, et al. Standard-of-care axicabtagene ciloleucel for relapsed or refractory large B-cell lymphoma: Results from the US lymphoma CAR T consortium. J Clin Oncol. 2020;38(27):3119-3128. doi:10.1200/JCO.19.02104

Q27. **CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning:**

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

- No, I do not have any conflicts of interest pertinent to this proposal

Q27a. **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.**

N/A

BEFORE FINAL SUBMISSION, please review the PI checklist to ensure that you have completed all necessary steps. This will increase the likelihood of submitting a feasible and successful proposal.

Embedded Data:

N/A

Response Summary:

This form is intended to be completed by a physician/researcher for the purpose of proposing a study. Content should not include Personal Identifiable Information (PII) or Protected Health Information (PHI). If you are a patient, do not complete this form. Patients: Contact your healthcare provider immediately for reports of problems with your treatment or problems with products received for your treatment. The CIBMTR uses de-identified data and is unable to associate reported treatment problems, adverse events, or corrections of information with a center, clinical trial, or healthcare provider.

Q1. Study Title

Real World Experience of Abecma, Chimeric Antigen Receptor (CAR) T-Cells Targeting BCMA in Patients with Multiple Myeloma (MM)

Q2. Key Words

BCMA-targeted CAR-T therapy, ABECMA, Real-world data

Q3. PRINCIPAL INVESTIGATOR

Provide the following information for each investigator:

Principal Investigator #1:

First and last name, degree(s):	Aimaz Afrough, M.D.
Email address:	aimaz.afrough@utsouthwestern.edu
Institution name:	UT Southwestern Medical Center
Academic rank:	Assistant Professor

Q4. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- Yes

Q5. Do you identify as an underrepresented/minority?

- No

Q6. Principal Investigator #2 (If applicable):

First and last name, degree(s):	Larry D. Anderson, Jr. , M.D, Ph.D.
Email address:	larry.anderson@utsouthwestern.edu
Institution name:	UT Southwestern Medical Center
Academic rank:	Professor

Q7. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- No

Q8. Do you identify as an underrepresented/minority?

- No

Q9. 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:

N/A

Q10. If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:

N/A

LETTER OF COMMITMENT:

Please note: *A letter of commitment will be signed by Lead and Last authors as it describes the expectations for filling that role. By signing the letter of commitment, the authors accept their responsibilities and will be held accountable for timely completion of all steps in the project. More details regarding author responsibilities can be found here:* https://www.cibmtr.org/Studies/Observational/StudyManagement/

Q12. CURRENT ONGOING WORK WITH CIBMTR: Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.

N/A

Q13. PROPOSED WORKING COMMITTEE:

- Cellular Immunotherapy for Cancer

Q14. Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.

- No

Q15. RESEARCH QUESTION:

Safety and efficacy data of ABECMA in real world setting

Q16. RESEARCH HYPOTHESIS:

The primary hypothesis of this study is that ABECMA is safe and efficacious in relapsed or refractory multiple myeloma in a real-world setting, despite having broader eligibility criteria compared to the pivotal KarMMa trial.

Q17. SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.)

Suggested word limit of 200 words:

1. To evaluate early safety and efficacy outcomes of commercial ABECMA in the real-world setting
2. To evaluate the safety and efficacy of ABECMA in sequence with other BCMA-targeted therapy
3. To evaluate the incidence and severity of cytokine release syndrome (CRS), immune effector cell–associated neurotoxicity syndrome (ICANS), Secondary Hemophagocytic lymphohistiocytosis / Macrophage activation syndrome (HLH/MAS), cytopenias and hematologic recovery post-CAR-T infusion
4. To evaluate clinical outcomes including overall response rate (ORR), duration of response (DOR), time to progression (TTP), progression-free survival (PFS), overall survival (OS) in the real-world setting

Q18. SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.

The data obtained from this study will provide real-world evidence in BCMA-targeted CAR-T treatment and can form the basis of a future clinical trial and provide practical insight into this setting for daily clinical practice.

Q19. 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.

Due to the specificity of B cell maturation antigen (BCMA) in multiple myeloma (MM), currently, multiple BCMA-targeted therapies including antibody-drug conjugate (ADC), bispecific antibody, T cell engager (BiTE), and CAR-T therapy are under investigation in either preclinical or clinical trials, with at least 2 of them already approved by FDA in the relapsed and refractory (R/R) setting.

On March 26, 2021, the US FDA approved the first BCMA-directed chimeric antigen receptor (CAR) T cell product (ABECMA, idecabtagene vicleucel) for treatment of the adult with relapsed or refractory multiple myeloma (MM) in the 5th or later lines of therapy[1].

The pivotal CAR-T trial, KarMMa, excluded patients with history of a CNS disease, requiring ongoing treatment with a chronic immunosuppressant, creatinine clearance ≤45 mL/minute, alanine aminotransferase >2.5 times upper limit of normal (ULN), and left ventricular ejection fraction <45%, absolute neutrophil count <1000 cells/mm3 and platelet count <50,000/m3, and history of prior BCMA targeted therapy[2], however, FDA issued no contraindication for ABECMA administration.

Therefore, given the current availability of multiple BCMA-targeted therapies, and less strict eligibility criteria for ABECMA administration, evaluating the safety and efficacy of this commercially approved CAR-T product outside of a clinical trial context is crucial.

Q19a. SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF)

N/A

Q20. PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.

Inclusion criteria:
1. Patient with R/R MM who received ABECMA after 3/26/21
2. At least 3 months of follow-up post-CAR-T therapy
3. Age greater than or equal to 18 years
4. Both genders
5. All races

Exclusion criteria:
1. Participant in KarMMa trial, or other ongoing BMCA-CAR-T clinical trial

Q21. Does this study include pediatric patients?

- No

Q21a. If this study does not include pediatric patients, please provide justification:

Multiple myeloma is rare in pediatric population, with only approximately 0.3% of cases diagnosed before the age of 30.

Q22. DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Data collection forms available at: http://www.cibmtr.org/DataManagement/DataCollectior Outline any supplementary data required. Additional data collection is extremely difficult and will make your proposal less feasible.

1. Baseline patient characteristics
a. Age at diagnosis
b. Age at infusion
c. Gender
d. Race/Ethnicity
e. Date of multiple myeloma diagnosis
f. Disease type (IgG, IgA, IgM, IgD, IgE, light chain only, non-secretory)
g. Light chain type (kappa, lambda, ...)
h. Disease status at the time of infusion
i. Comorbidities/comorbidity Index score
j. Cytogenetic by karyotype (conventional)
k. Cytogenetic by FISH
l. International Staging System (ISS)
m. Revised ISS
n. History of autologous or allogeneic hematopoietic stem cell transplantation (HCT)
o. Date of HCT
2. Treatments prior to CAR-T infusion
a. Type of treatment
b. line of treatment
c. Number of cycles

d. Date therapy started
e. Date therapy stopped
f. Best response to line of therapy
g. Relapse/progress following line of therapy
h. Date to relapse/progression
i. Disease status at the last evaluation prior to CAR-T infusion
3. Laboratory value
a. At the time of infusion (and prior to initiation of chemodepletion)
i. WBC
ii. Hemoglobin
iii. Platelet
iv. Plasma cells in bone marrow aspirate and biopsy or unknown source
v. Serum albumin
vi. Serum beta 2 microglobulin
vii. Serum calcium
viii. Serum creatinine
ix. Creatinine clearance
x. Serum monoclonal Ig (M-spike)
xi. Serum immunofixation
xii. Urinary monoclonal light chains
xiii. Urine immunofixation
xiv. Serum free light changes (kappa, lambda, ratio)
xv. LDH and upper limit of normal for LDH
xvi. Quantitative immunoglobulins (IgG, IgA, IgM)
xvii. MRD status, and method of MRD assessment
xviii. Viability of cell %
xix. Method of testing cell viability
4. Outcome data
a. Incidence and severity of cytokine release syndrome (CRS)
b. Incidence and severity of immune effector cell–associated neurotoxicity syndrome
c. Hematologic recovery (neutrophils and platelets), date ANC ≥500/mm3, date platelets ≥ 20 x 109/L
d. Response at 100 days, 6 months, 1 year, 2 years, >2 years (if available)
e. Best response to CAR-T therapy
f. Overall response rate (ORR)
g. Duration of response (DOR)
h. Event-free survival (EFS)
i. Progression-free survival (PFS)
j. Overall survival (OS)
a. MRD status when available
b. Incidence of Secondary primary malignancy
c. Relapse or disease progression
d. Site of progression
e. Date of progression
f. Date of death
g. Cause of death
5. Maintenance treatment post CAR-T treatment (if applicable)
a. Type of maintenance treatment
b. Dose of medication
c. Number of cycles of maintenance
d. Date maintenance started
e. Date maintenance stopped
f. Cause of maintenance discontinuation
g. Type of toxicity
h. Best response to maintenance treatment with date of evaluation

Q23. **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 specific to PROS.**

For additional information on what PRO measures have been collected and timepoints of collection, please reach out to the Late Effects and Quality of Life or Health Services Working Committee leadership: https://www.cibmtr.org/About/WhoWeAre/Com

not applicable

Q24. **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 experience with the proposed assay systems. PIs should be encouraged to review the inventory details, sample types collected and reach out to research_repos@nmdp.org with any questions.**

More information can be found at: https://www.cibmtr.org/Samples/Inventory/Pages/index

Not applicable

Q25. NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required, i.e., neither database contains all the data required to answer the study question.

Not applicable

Q26. REFERENCES:

1. FDA, ABECMA package insert 2021.
2. Munshi, N.C., et al., Idecabtagene Vicleucel in Relapsed and Refractory Multiple Myeloma. N Engl J Med, 2021. 384(8): p. 705-716.

Q27. CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning:

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

- No, I do not have any conflicts of interest pertinent to this proposal

Q27a. 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.

AA has received honoraria from OncLive.
LDA Jr has received honoraria/consulting fees from and served on advisory boards for Celgene, BMS, Amgen, GSK, Janssen, Karyopharm, Beigene, AbbVie, Cellectar, and Sanofi

BEFORE FINAL SUBMISSION, please review the PI checklist to ensure that you have completed all necessary steps. This will increase the likelihood of submitting a feasible and successful proposal.

Embedded Data:

N/A

Response Summary:

This form is intended to be completed by a physician/researcher for the purpose of proposing a study. Content should not include Personal Identifiable Information (PII) or Protected Health Information (PHI). If you are a patient, do not complete this form. Patients: Contact your healthcare provider immediately for reports of problems with your treatment or problems with products received for your treatment. The CIBMTR uses de-identified data and is unable to associate reported treatment problems, adverse events, or corrections of information with a center, clinical trial, or healthcare provider.

Q1. Study Title

Characteristics and management of post-CAR T cell therapy toxicities in the real world for relapsed refractory multiple myeloma

Q2. Key Words

CAR T cell therapy, toxicities, relapsed refractory, multiple myeloma

Q3. PRINCIPAL INVESTIGATOR

Provide the following information for each investigator:

Principal Investigator #1:

First and last name, degree(s):	Hamza Hashmi, M.D.
Email address:	hashmih@musc.edu
Institution name:	Medical University of South Carolina
Academic rank:	Assistant Professor

Q4. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- Yes

Q5. Do you identify as an underrepresented/minority?

- Yes

Q6. Principal Investigator #2 (If applicable):

First and last name, degree(s):	Saad Usmani, M.D.
Email address:	usmanis@mskcc.org
Institution name:	Memorial Sloan Kettering
Academic rank:	Professor

Q7. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- No

Q8. Do you identify as an underrepresented/minority?

- Yes

Q9. 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:

N/A

Q10. If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:

N/A

LETTER OF COMMITMENT:

Please note: *A letter of commitment will be signed by Lead and Last authors as it describes the expectations for filling that role. By signing the letter of commitment, the authors accept their responsibilities and will be held accountable for timely completion of all steps in the project. More details regarding author responsibilities can be found here:* *https://www.cibmtr.org/Studies/Observational/StudyManagement/p*

Q12. CURRENT ONGOING WORK WITH CIBMTR: Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.

-CIBMTR Study Proposal: Development of comorbidity scores that could impact the treatment related mortality and overall survival in patients receiving CD19 directed CAR T-cell therapy; proposal selected for full study ASTCT 2020-manuscript in preparation
-CIBMTR Study Proposal: Role of CD19 directed CAR T cell therapy for CNS lymphoma; proposal selected for full study ASTCT 2022-manuscript in preparation
-Outcomes of autologous hematopoietic cell transplantation for Light Chain Deposition Disease- proposal selected by the Plasma Cell Disorders and Adult Solid Tumors Working Committee leadership for full study on the annual meeting of the Plasma Cell Disorders Working Committee of the CIBMTR in 2022
-Outcomes of autologous hematopoietic cell transplantation for Multiple Myeloma with plasmacytomas and Macrofocal Multiple Myeloma- selected by the Plasma Cell Disorders and Adult Solid Tumors Working Committee leadership for presentation on the annual meeting of the Plasma Cell Disorders Working Committee of the CIBMTR
-Early versus delayed autologous hematopoietic cell transplantation for Multiple Myeloma patients- selected by the Plasma Cell Disorders and Adult Solid Tumors Working Committee leadership for presentation on the annual meeting of the Plasma Cell Disorders Working Committee of the CIBMTR

Q13. PROPOSED WORKING COMMITTEE:

- Plasma Cell Disorders

Q14. Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.

- No

Q15. RESEARCH QUESTION:

Determine the safety of CAR T cell therapy in relapsed refractory multiple myeloma in the real world

Q16. RESEARCH HYPOTHESIS:

With the use of appropriate mitigation strategies and supportive care measures, CAR T cell therapy can be safely administered to patients with relapsed refractory multiple myeloma who may be at excessive risk of toxicities

Q17. SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.)

Suggested word limit of 200 words:

• Determine the patterns of post CAR T CRS, ICANS, cytopenias, hypogammaglobinemia, and infections [incidence, onset, duration, severity, predictors of toxicities]
• Determine the impact of tocilizumab and corticosteroids for post CAR -T CRS and/or ICANS [prophylactic/preemptive versus treatment] on safety and efficacy of CAR T-cell therapy
• Determine the patterns of use of growth factors, TPO agonists, IVIG, stem cell boosts for the management of post CAR T cytopenias and hypogammaglobinemia [incidence, onset, duration/doses, effectiveness]

Q18. SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.

Given limited evidence available from clinical trials, the study will be valuable contribution to the literature. The study will help identify patient, disease and CAR -T therapy related factors that impact safety of CAR T-cell therapy. The study will inform patient selection and counseling for CAR T cell therapy for RRMM as well as help develop mitigation strategies for high risk patient populations.

Q19. 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.

In real-world experience of CAR T (Hansen et al ASCO 2022), more patients had extra medullary myeloma, penta-refractory disease, and worse performance status when compared to patients enrolled in KarMMa trial. However, these patients appeared to have incidence of any grade and grade 3+ CRS and ICANS similar to that seen in KarMMa trial. Whether that is related to more frequent or earlier use of tocilizumab [real world versus clinical trial: 72% versus 50%] and/or corticosteroids [real world versus clinical trial: 25% versus 15%] remains unknown. Similarly, post CAR -T cytopenias constitute a significant clinical challenge in both clinical trial and the real-world settings with little known about the patterns of use of supportive care in the KarMMa trial. Potential predictors of cytopenias [prior number of lines of therapy, bone marrow cellularity, prior alkylating agents, severe CRS/ICANS, use of corticosteroids] have not been established. Similarly, a better understanding of the patterns of the use of supportive care with growth factors, TPO agonists, IVIG, and stem cell boosts in the real-world settings will help improve the safety profile of commercial CAR T-cell therapy.

Q19a. SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF)

N/A

Q20. PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.

Patient with relapsed refractory multiple myeloma having received either idecabtagene vicleucel or ciltacabtagene autoleucel

Q21. Does this study include pediatric patients?

- No

Q21a. If this study does not include pediatric patients, please provide justification:

Multiple Myeloma is not seen in pediatric patient population

Q22. DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Data collection forms available at: http://www.cibmtr.org/DataManagement/DataCollectior Outline any supplementary data required. Additional data collection is extremely difficult and will make your proposal less feasible.

Patient related:
• Age at CAR T-cell therapy
• Gender: male vs. female
• Race: Caucasian vs. African American vs. vs. Hispanic
• Ethnicity: Hispanic or Latino vs. Non-Hispanic or non-Latino vs. non-resident of the U.S.
• ECOG Performance status: 0 vs 1-2 vs 3+
• renal function [GFR 30-60, GFR 15-30, GFR less than 15, ESRD on hemodialysis]
Disease-related:
• Myeloma subtype: IgG versus IgA versus IgM versus light chain [kappa versus lambda] vs non- secretory
• Diagnosis of plasma cell leukemia: primary vs secondary
• Secondary involvement with AL amyloidosis
• High risk disease [del 17, 4; 14, 14; 16]
• R-ISS at CAR-T infusion
• Number of prior lines of chemotherapy
• Response to prior therapy [lenalidomide, pomalidomide, bortezomib, carfilzomib, daratumumab]: Exposed versus refractory
• Prior autologous transplant
• Extramedullary disease at referral
• Bone marrow plasma cell percentage prior to infusion
• Disease status at referral
• Disease status prior to infusion
• Baseline markers of inflammation (ferritin, CRP) prior to infusion
CAR T-cell therapy related:
• Time from diagnosis to infusion
• Time from leukapheresis to infusion
• Use of bridging therapy
• Type of bridging therapy: Chemotherapy versus radiotherapy versus both chemo and radiotherapy
• Bridging chemotherapy regimen
• CAR-T cell dose
• CRS: grade, onset, duration
• ICANS: grade, onset, duration
• Use of tocilizumab
• Use of corticosteroids
• Persistent cytopenias at day +30 and day +90
• Use of G-CSF
• Use of TPO agonists
• Response at 1 month, 3-month, 6 months, 9 months, 12 months
• Time from infusion to progression
• Date of Death
• Cause of death
• Date of last contact

Q23. **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 specific to PROS.**

For additional information on what PRO measures have been collected and timepoints of collection, please reach out to the Late Effects and Quality of Life or Health Services Working Committee leadership: https://www.cibmtr.org/About/WhoWeAre/Com

NA

Q24. **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 experience with the proposed assay systems. PIs should be encouraged to review the inventory details, sample types collected and reach out to research_repos@nmdp.org with any questions.**

More information can be found at: https://www.cibmtr.org/Samples/Inventory/Pages/index

NA

Q25. NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required, i.e., neither database contains all the data required to answer the study question.

NA

Q26. REFERENCES:

Munshi NC, Anderson LD, Jr., Shah N, et al: Idecabtagene Vicleucel in Relapsed and Refractory Multiple Myeloma. N Engl J Med 384:705-716, 2021

Raje N, Berdeja J, Lin Y, et al: Anti-BCMA CAR T-Cell Therapy bb2121 in Relapsed or Refractory Multiple Myeloma. N Engl J Med 380:1726-17

Lee DW, Santomasso BD, Locke FL, et al: ASTCT Consensus Grading for Cytokine Release Syndrome and Neurologic Toxicity Associated with Immune Effector Cells. Biol Blood Marrow Transplant 25:625-638, 2019

Berdeja JG, Madduri D, Usmani SZ, et al: Ciltacabtagene autoleucel, a B-cell maturation antigen-directed chimeric antigen receptor T-cell therapy in patients with relapsed or refractory multiple myeloma (CARTITUDE-1): a phase 1b/2 open-label study. Lancet 398:314-324, 2021

Martin T, Usmani SZ, Berdeja JG, et al: Ciltacabtagene Autoleucel, an Anti-B-cell Maturation Antigen Chimeric Antigen Receptor T-Cell Therapy, for Relapsed/Refractory Multiple Myeloma: CARTITUDE-1 2-Year Follow-Up. J Clin Oncol:Jco2200842, 2022

Q27. CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning:

1. Employment (such as an independent contractor, consultant or providing expert testimony)?

2. Relationships (such as executive and advisory committee positions, medical consultant, speaker's bureau)?

3. Ownership (such as equity, ownership or financial interests)?

4. Transactions (such as honoraria, patents, royalties and licenses)?

5. Legal (such as pending or current arbitration or legal proceedings)?

- No, I do not have any conflicts of interest pertinent to this proposal

Q27a. **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.**

N/A

BEFORE FINAL SUBMISSION, please review the PI checklist to ensure that you have completed all necessary steps. This will increase the likelihood of submitting a feasible and successful proposal.

Embedded Data:

N/A

Response Summary:

This form is intended to be completed by a physician/researcher for the purpose of proposing a study. Content should not include Personal Identifiable Information (PII) or Protected Health Information (PHI). If you are a patient, do not complete this form. Patients: Contact your healthcare provider immediately for reports of problems with your treatment or problems with products received for your treatment. The CIBMTR uses de-identified data and is unable to associate reported treatment problems, adverse events, or corrections of information with a center, clinical trial, or healthcare provider.

Q1. Study Title

Real world outcomes with BCMA directed CAR-T cell therapy in multiple myeloma

Q2. Key Words

CAR-T therapy, real-world, myeloma

Q3. PRINCIPAL INVESTIGATOR

Provide the following information for each investigator:

Principal Investigator #1:

First and last name, degree(s):	Surbhi Sidana, MD
Email address:	surbhi.sidana@stanford.edu
Institution name:	Stanford University
Academic rank:	Assistant Professor

Q4. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- Yes

Q5. Do you identify as an underrepresented/minority?

- No

Q6. Principal Investigator #2 (If applicable):

First and last name, degree(s):	Doris Hansen, MD
Email address:	Doris.Hansen@moffitt.org
Institution name:	Moffitt Cancer Center
Academic rank:	Assistant Professor

Q7. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- Yes

Q8. Do you identify as an underrepresented/minority?

- No

Q9. 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:

Surbhi Sidana, MD

Q10. If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:

N/A

LETTER OF COMMITMENT:

Please note: *A letter of commitment will be signed by Lead and Last authors as it describes the expectations for filling that role. By signing the letter of commitment, the authors accept their responsibilities and will be held accountable for timely completion of all steps in the project. More details regarding author responsibilities can be found here:* *https://www.cibmtr.org/Studies/Observational/StudyManagement/p*

Q12. CURRENT ONGOING WORK WITH CIBMTR: Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.

Evaluating optimal maintenance in high-risk multiple myeloma patients. Last author (Manuscript revision in review)

Q13. PROPOSED WORKING COMMITTEE:

- Plasma Cell Disorders

Q14. Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.

- No

Q15. RESEARCH QUESTION:

To evaluate real world outcomes including safety and efficacy with BCMA directed CAR-T cell therapy in patients with relapsed/refractory MM receiving standard of care (SOC) CAR-T therapy

Q16. RESEARCH HYPOTHESIS:

BCMA CAR-T therapy has similar efficacy and toxicity profile in patients with relapsed multiple myeloma when used in the real-world as it did in a highly selected population of patients treated on clinical trial.
BCMA CAR-T therapies to include idecabtagene vicleucel (ide-cel) and if data available, ciltacabtagene autoleucel (cilta-cel)

Q17. SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.)

Suggested word limit of 200 words:

Primary:
1a. To evaluate response rates after SOC ide-cel
1b. To evaluate response rates after SOC cilta-cel (if data available)
Secondary
2. To evaluate progression free survival and overall survival after ide-cel and if data available, after cilta-cel.
3. To evaluate safety (CRS, neurotoxicity, cytopenias) after SOC ide-cel and if data available, after cilta-cel.
4. Compare efficacy and safety of SOC ide-cel and cilta-cel after matching for baseline patient characteristics (if data available)

Q18. SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.

This data will provide valuable insights on real-world efficacy of CAR-T therapy in myeloma. Clinical trials often require patients to meet several criteria and are not representative of a general patient population.
In consortium real-world experience that has been presented by the authors of this proposal (Hansen, Sidana et al, IMS 2022 meeting), we observed similar efficacy and safety with ide-cel, despite over 70% patients not meeting eligibility criteria for KarMMa. This CIBMTR study aims to validate this finding in the largest cohort of BCMA CAR-T cell therapy patients reported to date.

Q19. 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 authors of this CIBMTR proposal have presented the results from real-world data with ide-cel from an academic US consortium with over 150 patients treated with ide-cel. (Hansen, Sidana et al. IMS 2022 meeting) This study will serve to expand the patient population and confirm or refute our results, which show similar efficacy and safety of ide-cel when used as SOC therapy.
As cilta-cel was FDA approved in Feb 2022, this study also provides the first opportunity to look at real world data with cilta-cel and compare outcomes with ide-cel after adjusting for baseline patient characteristics.
This study will provide impactful and actionable data for clinical practice.
Advantages of CIBMTR:
-Significantly more number of patients
-Patients in the consortium study with ide-cel were from high volume academic centers. This study will include all ide-cel patients and present a more 'real-world' insight into outcomes with ide-cel
-First look at cilta-cel data in real world (if data available)
-First and very impactful comparison of safety and efficacy of ide-cel and cilta-cel (if data available for cilta-cel)

Q19a. SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF)

N/A

Q20. PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.

1. Adult patients who have received standard of care BCMA directed CAR-T cell therapy.
For this study, we would like to include all patients receiving ide-cel CAR-T therapy and if data is available, all patients receiving cilta-cel CAR-T cell therapy. By the time of presentation, cilta-cel would have been FDA approved for 1 year.

Q21. Does this study include pediatric patients?

- No

Q21a. If this study does not include pediatric patients, please provide justification:

Myeloma is a disease of adults

Q22. DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Data collection forms available at: http://www.cibmtr.org/DataManagement/DataCollectior Outline any supplementary data required. Additional data collection is extremely difficult and will make your proposal less feasible.

1. Patient Related
-Age
-Sex
-Comorbidity index
-Renal function i.e creatinine and eGFR
- Race
-Performance Status
2. Disease Related
- Number and details of prior lines of therapy
- FISH abnormalities (high risk vs standard risk)
- Immunochemical subtype: IgG vs. IgA vs. Light chain vs. Non-secretory
- ISS stage - Response rates prior to CAR-T by IMWG criteria
3. CAR-T related
- Response rate to CAR-T therapy (day 30, day 90 and best response)
- Rates and severity of cytokine release syndrome
- Rates and severity of immune effector cell associated neurotoxicity syndrome
- Progression free survival and overall survival after CAR-T therapy
- Cytopenias at day 90

Q23. **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 specific to PROS.**

For additional information on what PRO measures have been collected and timepoints of collection, please reach out to the Late Effects and Quality of Life or Health Services Working Committee leadership: https://www.cibmtr.org/About/WhoWeAre/Com

None

Q24. **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 experience with the proposed assay systems. PIs should be encouraged to review the inventory details, sample types collected and reach out to research_repos@nmdp.org with any questions.**

More information can be found at: https://www.cibmtr.org/Samples/Inventory/Pages/index

None

Q25. NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required, i.e., neither database contains all the data required to answer the study question.

None

Q26. REFERENCES:

1. Munshi et al. NEJM 2021.
2. Raje et al. NEJM 2019
3. Berdeja et al. The Lancet 2021
4. Martin et al. JCO 2022
3. Hansen, Sidana et al. IMS 2022 meeting abstract

Q27. CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning:

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

- Yes, I have conflicts of interest pertinent to this proposal

Q27a. 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.

Advisory board/consulting for BMS and Janssen

BEFORE FINAL SUBMISSION, please review the PI checklist to ensure that you have completed all necessary steps. This will increase the likelihood of submitting a feasible and successful proposal.

Embedded Data:

N/A

Response Summary:

This form is intended to be completed by a physician/researcher for the purpose of proposing a study. Content should not include Personal Identifiable Information (PII) or Protected Health Information (PHI). If you are a patient, do not complete this form. Patients: Contact your healthcare provider immediately for reports of problems with your treatment or problems with products received for your treatment. The CIBMTR uses de-identified data and is unable to associate reported treatment problems, adverse events, or corrections of information with a center, clinical trial, or healthcare provider.

Q1. Study Title

BCMA CAR-T for Multiple Myeloma: Real World Evidence and Identifying Predictors of toxicity and Efficacy

Q2. Key Words

Multiple Myeloma, CAR-T

Q3. PRINCIPAL INVESTIGATOR

Provide the following information for each investigator:

Principal Investigator #1:

First and last name, degree(s):	Lohith Gowda
Email address:	Lohith.gowda@yale.edu
Institution name:	Yale Cancer Center
Academic rank:	Assistant Professor

Q4. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- No

Q5. Do you identify as an underrepresented/minority?

N/A

Q6. Principal Investigator #2 (If applicable):

First and last name, degree(s):	Sayeef Mirza
Email address:	abu-sayeef.mirza@yale.edu
Institution name:	Yale Cancer Center
Academic rank:	Fellow in Hematology and Oncology

Q7. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- Yes

Q8. Do you identify as an underrepresented/minority?

- No

Q9. 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:

N/A

Q10. If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:

N/A

LETTER OF COMMITMENT:

Please note: *A letter of commitment will be signed by Lead and Last authors as it describes the expectations for filling that role. By signing the letter of commitment, the authors accept their responsibilities and will be held accountable for timely completion of all steps in the project. More details regarding author responsibilities can be found here:* *https://www.cibmtr.org/Studies/Observational/StudyManagement/p*

Q12. CURRENT ONGOING WORK WITH CIBMTR: Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.

N/A

Q13. PROPOSED WORKING COMMITTEE:

- Cellular Immunotherapy for Cancer

Q14. Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.

- No

Q15. RESEARCH QUESTION:

1) What is the toxicity and efficacy profile 2 FDA approved CAR-T products for multiple myeloma (MM) in real world.
2) What are the predictors of efficacy (response rate, progression free survival, overall survival) and toxicity (cytokine release syndrome- CRS, neurotoxicity, movement disorders, HLH, cytopenia)

Q16. RESEARCH HYPOTHESIS:

1) Response rates, survival with Ciltacabtagene autoleucel (cilatcel) is superior compared to Idecabtagene Vicleucel (Idecel)
2) Ciltacabtagene autoleucel (cilatcel) has a favorable toxicity profile (rates of cytokine release syndromes, neurotoxicty, duration of cytopenia, risk of developing HLH) compared to Idecabtagene Vicleucel (Idecel) in real world

Q17. SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.)

Suggested word limit of 200 words:

1. Primary aim: Characterize overall response rates with 2 FDA approved CAR-T products for MM in real world
2. Secondary aims:

a. Evaluate progression free survival (PFS) and overall survival (OS) for patients with MM receiving 2 different CAR-T cell therapy and using patient, disease, and product variables to build a predictive model

b. Evaluate the risk of cytokine release syndromes, neurotoxicty, HLH, cytopenias, movement disorder for the 2 different products and using patient, disease, and product variables to build a predictive model

c. Evaluate impact of the need for bridging therapies on toxicity and efficacy

d. Evaluate the impact of pre-existing comorbidities, functional status on post CAR-T relapse and non-relapse mortality

Q18. SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.

In the absence of randomization choosing appropriate CAR-T for different disease risk group MM can be challenging. Based on limited samples in registration trials identifying predictors of toxicity and efficacy is challenging, for which real world data is of critical importance.

Q19. 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.

According to SEER statistics, approximately 35000 new cases of multiple myeloma (MM) are diagnosed per year with 1 in 3 of them dying due to active disease. Over the last decade there has been an explosion of newer drugs approved to treat relapsed refractory (r/r) MM. Generally, outcomes are poor for patients who have failed IMIDs, Proteosome inhibitors and CD 38 antibodies. Recently BCMA targeting CAR-T cells have shown remarkable response rates in highly refractory MM in both KARMMA (phase 2) and CARTITUDE (phase ½) studies. With this Idecabtagene Vicleucel (Idecel) and Ciltacabtagene autoleucel (cilatcel) were FDA approved recently. A quick summary of the 2 studies suggests ORR (overall response rates), median PFS (progression free survival), median OS (overall survival), median time to best response, median duration of response is superior with ciltacel compared to idacel. However, representation of patients with extramedullary disease, high risk cytogenetics and need for bridging therapy was relatively higher in those enrolled in idacel study compared to ciltacel study. Comparing toxicity profile, while CRS grades were similar between the 2 products, median time to CRS (7 vs 1 day) and neurotoxicty (8 vs 2 days) was later with ciltacel. Ciltacel has also been reported to have cranial nerve disorders, movement disorder more frequently than its counterparts and some have proposed a possible benefit for early steroids for non- ICANS neurotoxicty. In the absence of randomized study between the 2 products and limited number of patients reported from clinical trials (< 250 patients combined included in both trials), the choice of CAR-T selection has become complicated. Hence, real world data could be a major boost to drive future practice. Also it is yet not well known what are the predictors of toxicity and efficacy in real world with these products

Q19a. SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF)

N/A

Q20. PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.

Any patient (any age) with the diagnosis of MM receiving 2 FDA approved CAR-T for MM.

Q21. Does this study include pediatric patients?

- Yes

Q22. DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Data collection forms available at: http://www.cibmtr.org/DataManagement/DataCollectior Outline any supplementary data required. Additional data collection is extremely difficult and will make your proposal less feasible.

would be censored at the time of last contact.

Patient-related:

- Age at CAR-T
- Gender
- Karnofsky performance status at infusion: < 90% vs. ≥ 90%
- HCT comorbidity index at infusion: 0, 1, 2, and ≥ 3
- ABO blood group
- CMV status

Disease-related:

- Diagnosis: multiple myeloma
- Disease risk index (ISS, R-ISS)
- High risk cytogenetics: yes vs.no
- Number of prior therapies (before infusion): 1 vs. 2 vs. ≥ 3
- Type of prior therapies (chemo vs radiation vs other)
- Sites of disease
- Tumor size/bulk (in cm)
- Dose/fraction of radiation (2 Gy vs 3-Gy vs 4-Gy vs other)
- Field of radiation
- Sites of radiation
- Proximity of disease sites to crucial/essential structures/tissues
- Timing of radiation prior to apheresis
- Timing of radiation prior to CAR-T
- Time from diagnosis to CAR-T (<12 mo vs > 12 mo)
- Name of salvage therapies (including number of cycles and number of lines)
- History of local radiation prior to bridging therapy
- Disease status at the time of each salvage therapy: complete remission vs partial response vs. stable disease vs progressive disease
- CNS involvement at diagnosis and prior to CAR-T infusion
- Response to First line therapy
- Therapies given before HCT
- Remission status prior to HCT
- cytogenetics/fish, ISS stage
- Treatment: First line therapy (Dara based vs carfilzomib based- doublets, triplets, and quadruplets) and those who get VCD or VRD,
- Melphalan dose at transplant.
- Change (%) in M spike pre (i.e. post induction) and post-transplant, changes in light chain ratio, maintenance drug (type and duration)
- Best response prior to CAR-T
- Drugs used pre apheresis and post apheresis awaiting infusion

CAR-T related:

- CAR-T product
- Date from disease relapse to CART apheresis.
- Time for apheresis to CART infusion
- Cell dose
- Disease status at time of infusion
- CRP and Ferritin at infusion
- lymphodepletion prior to CAR-T (Y/N)
- Response to CAR-T
- CRS (Y/N and grade) and duration
- CRES/Neurotoxicity (Y/N and grade)
- Cytopenias
- Infectious complications

Q23. **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 specific to PROS.**

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N/A

Q24. **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 experience with the proposed assay systems. PIs should be encouraged to review the inventory details, sample types collected and reach out to research_repos@nmdp.org with any questions.**

More information can be found at: https://www.cibmtr.org/Samples/Inventory/Pages/index

N/A

Q25. **NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required, i.e., neither database contains all the data required to answer the study question.**

N/A

Q26. **REFERENCES:**

N/A

Q27. **CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning:**

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

- No, I do not have any conflicts of interest pertinent to this proposal

Q27a. **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.**

N/A

BEFORE FINAL SUBMISSION, please review the PI checklist to ensure that you have completed all necessary steps. This will increase the likelihood of submitting a feasible and successful proposal.

Embedded Data:

N/A

Table. Patients who received first CAR-T infusion between 2016 - 2022 for Multiple Myeloma, with follow-up reported to CIBMTR

Characteristic	N (%)
No. of patients[1]	786
No. of centers	73
Age at infusion, yrs - median (min-max)	64 (29-86)
Age at infusion, by category #1 - no. (%)	
20 - 29 years	2 (0)
30 - 39 years	13 (2)
40 - 49 years	58 (7)
50 - 59 years	200 (25)
60 - 69 years	330 (42)
70+ years	183 (23)
Age at infusion, by category #2 - no. (%)	
18 - 39	15 (2)
40 - 65	407 (52)
65+	364 (46)
Age at Infusion, by category #3 - no. (%)	
>=18 years	786 (100)
Age at infusion, by category #4 - no. (%)	
0 - 64	422 (54)
65+	364 (46)
Gender - no. (%)	
Male	468 (60)
Female	314 (40)
Not reported	4 (1)
Recipient race - no. (%)	
White	624 (79)
Black or African American	102 (13)
Asian	20 (3)
Native Hawaiian or other Pacific Islander	1 (0)
American Indian or Alaska Native	3 (0)
Other	5 (1)
More than one race	11 (1)
Not reported	20 (3)
Recipient ethnicity - no. (%)	
Hispanic or Latino	51 (6)
Not Hispanic or Latino	710 (90)

Characteristic	N (%)
Non-resident of the U.S.	12 (2)
Unknown	13 (2)
Country - no. (%)	
US	765 (97)
Other	21 (3)
Karnofsky performance score prior to CT - no. (%)	
90-100	291 (37)
80	268 (34)
< 80	147 (19)
Not reported	80 (10)
ECOG performance status prior to CT - no. (%)	
0 - Asymptomatic	291 (37)
1 - Symptomatic but completely ambulatory	382 (49)
2 - Symptomatic, < 50% in bed during the day	29 (4)
3 - Symptomatic, > 50% in bed, but not bedbound	3 (0)
4 - Bedbound	1 (0)
Not reported	80 (10)
Body mass index (BMI) category at infusion - no. (%)	
< 18.5 - Underweight	14 (2)
>= 18.5 to < 25 - Normal	224 (28)
>= 25 to < 30 - Overweight	288 (37)
>= 30 - Obese	238 (30)
Not reported	22 (3)
Sub-disease for CT - no. (%)	
Multiple myeloma, NOS	501 (64)
Plasma cell leukemia	11 (1)
Multiple myeloma - IgG	54 (7)
Multiple myeloma - IgA	23 (3)
Multiple myeloma - light chain only	180 (23)
Multiple myeloma - non-secretory	17 (2)
Diagnosis	
Age at initial diagnosis - median (min-max)	57 (25-85)
ISS stage at diagnosis - no. (%)	
1 (beta2-mic < 3.5, albumin >= 3.5)	202 (26)
2 (Not fitting stage 1 or 3)	170 (22)
3 (beta2-mic >= 5.5, regardless of albumin)	160 (20)
Not reported	254 (32)
R-ISS stage at diagnosis - no. (%)	

Characteristic	N (%)
1 (ISS stage I and standard-risk abnormalities by iFISH and normal LDH)	62 (8)
2 (Not R-ISS stage I or III)	188 (24)
3 (ISS stage III and either high-risk chromosomal abnormalities by iFISH or high LDH)	78 (10)
Not reported	458 (58)
Serum creatinine at diagnosis, value - median (min-max)	1 (0-1493)
Time from initial diagnosis to CT - no. (%)	
Median (min-max)	66 (0-324)
>= 0 to < 12 months	39 (5)
>= 12 to < 36 months	131 (17)
>= 36 to < 60 months	185 (24)
>= 60 months	431 (55)
Lymphodepleting regimen - no. (%)	
Yes	779 (99)
Lymphodepleting chemotherapy: bendamustine	3 (0)
Lymphodepleting chemotherapy: cyclophosphamide	3 (0)
Lymphodepleting chemotherapy: cyclophosphamide + Lymphodepleting chemotherapy: cytarabine + Lymphodepleting chemotherapy: fludarabine	1 (0)
Lymphodepleting chemotherapy: cyclophosphamide + Lymphodepleting chemotherapy: fludarabine	761 (97)
Lymphodepleting chemotherapy: cyclophosphamide + Lymphodepleting chemotherapy: fludarabine + Lymphodepleting chemotherapy: other	4 (1)
Lymphodepleting chemotherapy: cyclophosphamide + Lymphodepleting chemotherapy: thiotepa	1 (0)
Lymphodepleting chemotherapy: fludarabine	3 (0)
Lymphodepleting chemotherapy: other	1 (0)
None specified	2 (0)
No	7 (1)
Commercial vs. noncommercial CAR-T product - no. (%)	

Characteristic	N (%)
Commercial	501 (64)
Noncommercial	285 (36)
Clinical trial - no. (%)	
No	499 (63)
Yes	287 (37)
CAR-T Product type (Other - specify) - no. (%)	
Abecma	468 (60)
Carvykti	33 (4)
Other	285 (36)
Non-commercial Idecabtagene vicleucel	84 (11)
Non-commercial Ciltacabtagene autoleucel	14 (2)
Non-commercial Orvacabtagene autoleucel	1 (0)
Non-commercial - No product name	9 (1)
Non-commercial - Other product	94 (12)
Non-commercial - Product name not reported	83 (11)
Prior transplants and therapies	
Types of prior HCTs - no. (%)	
No	78 (10)
Yes	707 (90)
Prior allo-HCT	8 (1)
Prior auto-HCT	668 (85)
Prior auto and allo-HCT	23 (3)
Not reported	8 (1)
Unknown	1 (0)
Total number of prior HCTs - no. (%)	
0	78 (10)
1	508 (65)
2	139 (18)
3	17 (2)
4	1 (0)
Not reported	43 (5)
Prior CT - no. (%)	
No	766 (97)
Yes	20 (3)
CT infusion counting number - no. (%)	
1	777 (99)
2	8 (1)
3	1 (0)

Characteristic	N (%)
Time from prior HCT to CT, months - median (min-max)	
No prior HCT	NE
Prior allo-HCT	36 (9-176)
Prior auto-HCT	46 (0-250)
Prior auto and allo-HCT	51 (5-159)
Time from the latest prior HCT to current CT, days - median (min-max)	1407 (14-7601)
Clinically significant co-existing diseases or organ impairment	
Clinically significant comorbidity prior to CT - no. (%)	
No	256 (33)
Yes	526 (67)
Comorbidity: Arrhythmia, any history	83 (11)
Comorbidity: Cardiac, any history	94 (12)
Comorbidity: Cerebrovascular disease, any history	23 (3)
Comorbidity: Diabetes requiring non-diet treatment, in the last 4 week	93 (12)
Comorbidity: Heart valve disease	19 (2)
Comorbidity: Hepatic disease (mild), any history or at the time of infusion	38 (5)
Comorbidity: Hepatic disease (moderate/severe), any history or at the time of infusion	12 (2)
Comorbidity: Infection requiring antimicrobial treatment, continuation after day 0	36 (5)
Comorbidity: Inflammatory bowel disease, any history	2 (0)
Comorbidity: Obesity, during pre-infusion work-up period	86 (11)
Comorbidity: Peptic ulcer, any history	11 (1)
Comorbidity: Psychiatric disturbance requiring consult/treatment, in the last 4 weeks	124 (16)
Comorbidity: Pulmonary disease (moderate), at the time of infusion	127 (16)
Comorbidity: Pulmonary disease (severe), at the time of infusion	80 (10)

Characteristic	N (%)
Comorbidity: Renal disease (moderate/severe), at the time of infusion or prior renal transplant	31 (4)
Comorbidity: Rheumatologic disease, any history	10 (1)
Comorbidity: Prior malignancy, treated at any time in the past	116 (15)
Comorbidity: Breast cancer	22 (3)
Comorbidity: Central nervous system malignancy	1 (0)
Comorbidity: Genitourinary malignancy	36 (5)
Comorbidity: Leukemia (including acute or chronic leukemia)	4 (1)
Comorbidity: Lung cancer	1 (0)
Comorbidity: Lymphoma (including Hodgkin & non-Hodgkin lymphoma)	1 (0)
Comorbidity: MDS/MPN	1 (0)
Comorbidity: Melanoma	11 (1)
Comorbidity: Multiple myeloma/plasma cell disorder (PCD)	4 (1)
Comorbidity: Oropharyngeal cancer	1 (0)
Comorbidity: Sarcoma	2 (0)
Comorbidity: Thyroid cancer	6 (1)
Comorbidity: Other skin malignancy (basal cell, squamous)	38 (5)
Comorbidity: Other solid tumor	1 (0)
Not reported	4 (1)
Disease/indication - no. (%)	
Malignant hematologic disorder	786 (100)
Disease status prior to infusion - no. (%)	
Stringent complete response	3 (0)
Complete response (CR)	8 (1)
Very good partial response (VGPR)	53 (7)
Partial response (PR)	84 (11)
No response (NR) / stable disease (SD)	124 (16)
Progressive disease (PD)	493 (63)
Relapse from CR (Rel) (untreated)	14 (2)
Not reported	7 (1)
Year of CT - no. (%)	

Characteristic	N (%)
2016	1 (0)
2017	3 (0)
2018	59 (8)
2019	72 (9)
2020	91 (12)
2021	331 (42)
2022	229 (29)
Serum creatinine at the time of best response since infusion, value - median (min-max)	1 (0-8)
Time from receiving H4000 baseline form to infusion, days - median (min-max)	29 (-5-1116)
No. of patients with follow-up	786
Follow-up - median (range)	9 (1-53)

[1] Note: Excluded cases with Amyloidosis, Solitary plasmacytoma, Light chain deposition disease, Smoldering myeloma, Plasma cell myeloma, Plasma cell proliferative disorder, and missing sub-disease data (n=22)

Response Summary:

This form is intended to be completed by a physician/researcher for the purpose of proposing a study. Content should not include Personal Identifiable Information (PII) or Protected Health Information (PHI). If you are a patient, do not complete this form. Patients: Contact your healthcare provider immediately for reports of problems with your treatment or problems with products received for your treatment. The CIBMTR uses de-identified data and is unable to associate reported treatment problems, adverse events, or corrections of information with a center, clinical trial, or healthcare provider.

Q1. Study Title

Utility of urine testing in post-ASCT response assessments in multiple myeloma

Q2. Key Words

Multiple myeloma, autologous stem cell transplantation, urine immunofixation, urine protein electrophoresis

Q3. PRINCIPAL INVESTIGATOR

Provide the following information for each investigator:

Principal Investigator #1:

First and last name, degree(s):	Rahul Banerjee, MD, FACP
Email address:	rahulban@uw.edu
Institution name:	University of Washington
Academic rank:	Assistant Professor

Q4. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- Yes

Q5. Do you identify as an underrepresented/minority?

- No

Q6. Principal Investigator #2 (If applicable):

First and last name, degree(s):	Nina Shah, MD
Email address:	nina.shah@ucsf.edu
Institution name:	UCSF
Academic rank:	Full professor (volunteer)

Q7. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- No

Q8. Do you identify as an underrepresented/minority?

- No

Q9. We encourage a maximum of two Principal Investigators per study. If more than one author is listed, please indicate who will be identified as the corresponding PI below:

Dr. Banerjee as corresponding PI, with Dr. Shah as senior mentor

Q10. If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:

N/A

LETTER OF COMMITMENT:

Please note: *A letter of commitment will be signed by Lead and Last authors as it describes the expectations for filling that role. By signing the letter of commitment, the authors accept their responsibilities and will be held accountable for timely completion of all steps in the project. More details regarding author responsibilities can be found here:* *https://www.cibmtr.org/Studies/Observational/StudyManagement/p*

Q12. CURRENT ONGOING WORK WITH CIBMTR: Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.

Member, Plasma Cell Disorders Working Committee

Q13. PROPOSED WORKING COMMITTEE:

- Plasma Cell Disorders

Q14. Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.

- Yes

Q14a. If you have already spoken with a scientific director or working committee chair regarding this study, then please specify who:

Anita D'Souza, Nina Shah; also presented at the 2022 meeting

Q15. RESEARCH QUESTION:

Does 24-hour urine testing collected for pre-ASCT response assessments affect the prognostic value of CIBMTR response criteria with regard to progression-free survival?

Q16. RESEARCH HYPOTHESIS:

Firstly: the presence versus absence of pre-ASCT urine immunofixation results will not significantly impact PFS. Secondly: A simplified set of CIBMTR response criteria that omits all urine testing (urine-free CIBMTR) will perform similarly to traditional CIBMTR response criteria in terms of predicting progression-free survival (PFS) based on pre-ASCT values.

Q17. SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.)

Suggested word limit of 200 words:

1. PRIMARY: The prognostic value of pre-ASCT urine immunofixation results (reported versus missing) on PFS, as analyzed by Cox regression using interaction testing
2. PRIMARY: The prognostic value of urine-free versus traditional pre-ASCT response criteria on PFS among patients with complete data, as analyzed by log-rank testing for PFS
3. PRIMARY: The prognostic value of urine-free versus traditional pre-ASCT response criteria on PFS among all patients, as analyzed by log-rank testing for PFS

Q18. SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.

Currently, 24-hour urine assessments are required as a component of CIBMTR response assessments prior to transplantation. From a practical perspective, these assessments are awkward for patients to collect and add to the complexity of pre-ASCT testing. Unpublished CIBMTR data presented at this working group's meeting in April 2022 (personal communication, N Estrada-Merly, 2022) show that 60% of patients have missing values for pre-ASCT urine immunofixation, which highlights the impracticality of these tests. If our analysis demonstrates that urine-free CIBMTR assessments perform similarly to traditional CIBMTR assessments, patients will benefit immediately from streamlined testing algorithms that omit the need for urine testing.

Q19. 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.

To our knowledge, two groups have specifically investigated the impact of urine testing on peri-ASCT outcomes using secondary analyses of European trial data. Dejoie et al (Blood 2016, PMID 27729323) analyzed outcomes from the French IFM2009 trial and found that serum free light chain (SFLC) testing provided more discriminatory power than urine assessments. Lahuerta et al (Blood 2019, PMID 31010846) analyzed outcomes from the Spanish GEM2012MENOS65 trial and found no difference in outcomes between patients who achieved a complete response (CR) and those who achieved an 'uncertain' CR (meeting criteria for CR but missing urine immunofixation). However, these studies only analyzed trial-enrolled patients and only investigated specific components of response assessments (SFLC versus urine testing and CR versus uncertain CR, respectively).

More recently, our group has preliminarily analyzed real-world data from two sources. Firstly, at the CIBMTR Plasma Cell Working Group meeting in April 2022, we presented CIBMTR data (courtesy of N Estrada-Merly) showing that 60% of patients (4187/6935) had missing pre-ASCT urine immunofixation results. In comparison, only 38% had missing SFLC and 18% had missing serum protein electrophoresis results. Secondly, unpublished data from our group submitted to the 2022 ASH meeting (K Natsuhara et al, 2022) transplanted at a single center showed that urine-free response criteria changed pre-ASCT response depths in only 4% of patients (11/281).

Being able to analyze the CIBMTR's full breadth of data will build on our modest single-site analysis substantially in terms of a much larger sample size, which will allow us to discern any small contributions of urine testing toward post-ASCT outcomes. We also hope to benefit from the expertise of the CIBMTR Plasma Cell Working Committee in terms of adjudicating missing data (e.g., urine protein electrophoresis results with missing urine immunofixation) and biostatistical expertise for specific hypothesis testing. If our analysis demonstrates that 24-hour urine testing is not needed as a component of pre-ASCT response assessments, the result will be immediately practice-changing in terms of supporting discontinuation of this testing requirement. Conversely, if our data demonstrate that urine testing provides value to PFS prediction, our analysis will provide an impetus to improve the current 60% non-completion rate of urine testing based on current CIBMTR data.

Q19a. SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF)

N/A

Q20. PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.

Inclusion criteria: All patients with multiple myeloma, including patients with urinary involvement at diagnosis.
Exclusion criteria:
- Patients with concurrent AL amyloidosis (rationale: urine protein assessments remain a critical tool as a component of renal response evaluation).
- Patients with non-secretory MM (rationale: pre-ASCT and post-ASCT urine testing would not be helpful in these patients regardless).

Q21. Does this study include pediatric patients?

- No

Q21a. If this study does not include pediatric patients, please provide justification:

Not relevant to MM

Q22. DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Data collection forms available at: http://www.cibmtr.org/DataManagement/DataCollectior Outline any supplementary data required. Additional data collection is extremely difficult and will make your proposal less feasible.

• Patient-specific or center-specific variables: Age, gender, race/ethnicity, urban vs rural (as suggested at 2022 CIBMTR working committee meeting), proportion of patients at that center with reported pre-ASCT urine immunofixation values (≥50% vs <50% of patients at that center, as suggested at 2022 CIBMTR working committee meeting)
• Disease-specific variables (at both pre-ASCT and post-ASCT timepoints): Serum protein electrophoresis, serum immunofixation, serum free light chains, urine protein electrophoresis, urine immunofixation, imaging assessments.
• Transplant-specific variables: Overall survival and progression-free survival

Q23. **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 specific to PROS.**

For additional information on what PRO measures have been collected and timepoints of collection, please reach out to the Late Effects and Quality of Life or Health Services Working Committee leadership: https://www.cibmtr.org/About/WhoWeAre/Com

None

Q24. **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 experience with the proposed assay systems. PIs should be encouraged to review the inventory details, sample types collected and reach out to research_repos@nmdp.org with any questions.**

More information can be found at: https://www.cibmtr.org/Samples/Inventory/Pages/index

None

Q25. NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required, i.e., neither database contains all the data required to answer the study question.

None

Q26. REFERENCES:

1. Dejoie T, Corre J, Caillon H, et al. Serum free light chains, not urine specimens, should be used to evaluate response in light-chain multiple myeloma. Blood. 2016;128(25):2941-2948.
2. Lahuerta J, Jiménez-Ubieto A, Paiva B, et al. Role of urine immunofixation in the complete response assessment of MM patients other than light-chain-only disease. Blood. 2019;133(25):2664-2668.
3. Schavgoulidze A, Lauwers-Cances V, Perrot A, et al. The Discriminatory Ability of the R-ISS Is Equivalent to the ISS in a Large Cohort of Newly Diagnosed Multiple Myeloma (NDMM) Patients. Blood. 2020;136(Supplement 1): 46-47.

Q27. CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning:

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

- No, I do not have any conflicts of interest pertinent to this proposal

Q27a. 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.

N/A

BEFORE FINAL SUBMISSION, please review the PI checklist to ensure that you have completed all necessary steps. This will increase the likelihood of submitting a feasible and successful proposal.

Embedded Data:

N/A

Table 1. Characteristics of Multiple Myeloma patients, transplanted in the US from 2008 to 2019, CRF

Characteristic	Known UIFE	Unknown UIFE	Total
No. of patients	2748	4187	6935
No. of centers	101	130	131
Median age (range) - median (min-max)	61 (26-82)	60 (20-80)	61 (20-82)
Age at transplant, years - no. (%)			
18-39	76 (3)	118 (3)	194 (3)
40-49	309 (11)	568 (14)	877 (13)
50-59	826 (30)	1421 (34)	2247 (32)
60-69	1208 (44)	1731 (41)	2939 (42)
70+	329 (12)	349 (8)	678 (10)
Gender - no. (%)			
Male	1464 (53)	2393 (57)	3857 (56)
Female	1284 (47)	1794 (43)	3078 (44)
Region - no. (%)			
US	2748 (100)	4187 (100)	6935 (100)
Race - no. (%)			
White	1426 (52)	2703 (65)	4129 (60)
Black or African-American	1102 (40)	1207 (29)	2309 (33)
Asian	106 (4)	133 (3)	239 (3)
Native Hawaiian or other Pacific islander	5 (0)	10 (0)	15 (0)
American Indian or Alaska Native	31 (1)	32 (1)	63 (1)
More than one race	20 (1)	16 (0)	36 (1)
Missing	58 (2)	86 (2)	144 (2)
Karnofsky score - no. (%)			
>= 90	1337 (49)	2256 (54)	3593 (52)
< 90	1356 (49)	1805 (43)	3161 (46)
Missing	55 (2)	126 (3)	181 (3)
HCT-CI - no. (%)			
0	624 (23)	1317 (31)	1941 (28)
1	376 (14)	644 (15)	1020 (15)
2	498 (18)	655 (16)	1153 (17)
3+	1231 (45)	1558 (37)	2789 (40)
Missing	19 (1)	13 (0)	32 (0)
Bone marrow plasma cells at diagnosis - no. (%)			
<10%	262 (10)	423 (10)	685 (10)

Characteristic	Known UIFE	Unknown UIFE	Total
>=10%	2200 (80)	3013 (72)	5213 (75)
Missing	286 (10)	751 (18)	1037 (15)
ISS stage at diagnosis - no. (%)			
ISS stage I	857 (31)	1284 (31)	2141 (31)
ISS stage II	759 (28)	1125 (27)	1884 (27)
ISS stage III	496 (18)	884 (21)	1380 (20)
Missing	636 (23)	894 (21)	1530 (22)
Lines of chemotherapy - no. (%)			
1	1953 (71)	2697 (64)	4650 (67)
>=2	739 (27)	1177 (28)	1916 (28)
Missing	56 (2)	313 (7)	369 (5)
Chemotherapy - no. (%)			
VTD	20 (1)	159 (4)	179 (3)
VRD	1714 (62)	1742 (42)	3456 (50)
VCD	430 (16)	513 (12)	943 (14)
VD	148 (5)	553 (13)	701 (10)
RD	166 (6)	501 (12)	667 (10)
TD	3 (0)	170 (4)	173 (2)
Carfilzomib	11 (0)	6 (0)	17 (0)
Pomalidomide	0 (0)	1 (0)	1 (0)
KRD	73 (3)	32 (1)	105 (2)
Daratumumab	111 (4)	43 (1)	154 (2)
Others	16 (0)	154 (3)	170 (2)
Missing	56 (2)	313 (7)	369 (5)
Immunochemical subtype - no. (%)			
IgG	1603 (58)	2404 (57)	4007 (58)
IgA	511 (19)	814 (19)	1325 (19)
IgD	14 (1)	26 (1)	40 (1)
IgE	3 (0)	2 (0)	5 (0)
IgM	11 (0)	13 (0)	24 (0)
Light chain	580 (21)	793 (19)	1373 (20)
Non-secretory	26 (1)	54 (1)	80 (1)
Unknown Type	0 (0)	81 (2)	81 (1)
Hemoglobin prior to transplant - no. (%)			
< 10 g/dl	578 (21)	957 (23)	1535 (22)
>= 10 g/dl	2169 (79)	3160 (75)	5329 (77)
Missing	1 (0)	70 (2)	71 (1)

Characteristic	Known UIFE	Unknown UIFE	Total
Serum creatinine prior to transplant, mg/dl - no. (%)			
< 2 mg/dl	2593 (94)	3878 (93)	6471 (93)
>= 2 mg/dl	149 (5)	227 (5)	376 (5)
Missing	6 (0)	82 (2)	88 (1)
Conditioning regimen - no. (%)			
Melphalan only	2748 (100)	4187 (100)	6935 (100)
Melphalan dose in conditioning regimen, mg/m - no. (%)			
MEL 140	778 (28)	1195 (29)	1973 (28)
MEL 200	1970 (72)	2992 (71)	4962 (72)
Disease status prior to transplant - no. (%)			
sCR/CR	477 (17)	596 (14)	1073 (15)
VGPR	1093 (40)	1394 (33)	2487 (36)
PR	992 (36)	1769 (42)	2761 (40)
SD	128 (5)	264 (6)	392 (6)
PD/Relapse	49 (2)	138 (3)	187 (3)
Missing	9 (0)	26 (1)	35 (1)
Total urinary protein excretion (g/24hr) at Time of HCT - no. (%)			
Known	1903 (69)	207 (5)	2110 (30)
Unknown	845 (31)	3980 (95)	4825 (70)
Urinary monoclonal protein (M-spike)(g/24hr) at Time of HCT - no. (%)			
Known	2051 (75)	155 (4)	2206 (32)
Unknown	697 (25)	4032 (96)	4729 (68)
Serum free light chains — Kappa at HCT - no. (%)			
Known	2696 (98)	1563 (37)	4259 (61)
Unknown	52 (2)	2624 (63)	2676 (39)
Serum free light chains — Lambda at HCT - no. (%)			
Known	2703 (98)	1568 (37)	4271 (62)
Unknown	45 (2)	2619 (63)	2664 (38)
Urinary monoclonal immu result pr - no. (%)			
No	1621 (59)	0 (0)	1621 (23)
Yes	1127 (41)	0 (0)	1127 (16)
Unknown	0 (0)	4187 (100)	4187 (60)
Urinary new mono bands pr - no. (%)			
No	1017 (37)	0 (0)	1017 (15)
Yes	87 (3)	0 (0)	87 (1)
Unknown	1644 (60)	4187 (100)	5831 (84)

Characteristic	Known UIFE	Unknown UIFE	Total
Urinary original mono bands pr - no. (%)			
No	71 (3)	0 (0)	71 (1)
Yes	1032 (38)	0 (0)	1032 (15)
Unknown	1645 (60)	4187 (100)	5832 (84)
Time from diagnosis to transplant - median (min-max)	7 (1-210)	8 (0-295)	7 (0-295)
Time from diagnosis to transplant - no. (%)			
< 6 months	964 (35)	1181 (28)	2145 (31)
6 - 12 months	1295 (47)	1990 (48)	3285 (47)
12 - 24 months	314 (11)	611 (15)	925 (13)
>= 24 months	174 (6)	405 (10)	579 (8)
Missing	1 (0)	0 (0)	1 (0)
Year of transplant - no. (%)			
2008	6 (0)	801 (19)	807 (12)
2009	3 (0)	292 (7)	295 (4)
2010	10 (0)	225 (5)	235 (3)
2011	5 (0)	311 (7)	316 (5)
2012	22 (1)	287 (7)	309 (4)
2013	133 (5)	463 (11)	596 (9)
2014	267 (10)	234 (6)	501 (7)
2015	353 (13)	299 (7)	652 (9)
2016	406 (15)	296 (7)	702 (10)
2017	381 (14)	272 (6)	653 (9)
2018	834 (30)	414 (10)	1248 (18)
2019	317 (12)	202 (5)	519 (7)
2020	11 (0)	91 (2)	102 (1)
Post-HCT therapy - no. (%)			
No	492 (18)	1318 (31)	1810 (26)
Yes	2085 (76)	2622 (63)	4707 (68)
Missing	171 (6)	247 (6)	418 (6)
Total urinary protein excretion (g/24hr) at Time of Best response - no. (%)			
Known	757 (28)	341 (8)	1098 (16)
Unknown	1991 (72)	3846 (92)	5837 (84)
Urinary monoclonal protein (M-spike)(g/24hr) at Time of Best response - no. (%)			
Known	797 (29)	327 (8)	1124 (16)
Unknown	1951 (71)	3860 (92)	5811 (84)

Characteristic	Known UIFE	Unknown UIFE	Total
Serum free light chains — Kappa at Best response - no. (%)			
Known	1998 (73)	2791 (67)	4789 (69)
Unknown	750 (27)	1396 (33)	2146 (31)
Serum free light chains — Lambda at Best response - no. (%)			
Yes	2007 (73)	2777 (66)	4784 (69)
Unknown	741 (27)	1410 (34)	2151 (31)
Specify monoclonal immunoglobulin result at Best response - no. (%)			
No	694 (25)	789 (19)	1483 (21)
Yes	307 (11)	442 (11)	749 (11)
Unknown	1747 (64)	2956 (71)	4703 (68)
New monoclonal (or oligoclonal) bands at Best response - no. (%)			
No	262 (10)	390 (9)	652 (9)
Yes	43 (2)	45 (1)	88 (1)
Unknown	2443 (89)	3752 (90)	6195 (89)
Original monoclonal bands at Best response - no. (%)			
No	26 (1)	22 (1)	48 (1)
Yes	279 (10)	411 (10)	690 (10)
Unknown	2443 (89)	3754 (90)	6197 (89)
Follow-up - median (range)	37 (3-147)	72 (3-157)	54 (3-157)

Table2.1 Crosstab frequencies where UIFE is missing

Serum Kappa at HCT	Serum Lambda at HCT	Serum M-Spike at HCT	Frequency	Percent	Cumulative Frequency	Cumulative Percent
Known	Known	Known	1309	31.26	1309	31.26
Known	Known	Unknown	249	5.95	1558	37.21
Known	Unknown	Known	2	0.05	1560	37.26
Known	Unknown	Unknown	3	0.07	1563	37.33
Unknown	Known	Known	5	0.12	1568	37.45
Unknown	Known	Unknown	5	0.12	1573	37.57
Unknown	Unknown	Known	1842	43.99	3415	81.56
Unknown	Unknown	Unknown	772	18.44	4187	100

Table2.2 Crosstab frequencies where UIFE is known

Serum Kappa at HCT	Serum Lambda at HCT	Serum M-Spike at HCT	Frequency	Percent	Cumulative Frequency	Cumulative Percent
Known	Known	Known	2491	90.65	2491	90.65
Known	Known	Unknown	201	7.31	2692	97.96
Known	Unknown	Known	3	0.11	2695	98.07
Known	Unknown	Unknown	1	0.04	2696	98.11
Unknown	Known	Known	10	0.36	2706	98.47
Unknown	Known	Unknown	1	0.04	2707	98.51
Unknown	Unknown	Known	36	1.31	2743	99.82
Unknown	Unknown	Unknown	5	0.18	2748	100

Response Summary:

This form is intended to be completed by a physician/researcher for the purpose of proposing a study. Content should not include Personal Identifiable Information (PII) or Protected Health Information (PHI). If you are a patient, do not complete this form. Patients: Contact your healthcare provider immediately for reports of problems with your treatment or problems with products received for your treatment. The CIBMTR uses de-identified data and is unable to associate reported treatment problems, adverse events, or corrections of information with a center, clinical trial, or healthcare provider.

Q1. Study Title

Impact of renal impairment on the safety and outcomes CAR T-cell therapy in multiple myeloma patients

Q2. Key Words

CAR-T, renal impairment, relapsed myeloma

Q3. PRINCIPAL INVESTIGATOR

Provide the following information for each investigator:

Principal Investigator #1:

First and last name, degree(s):	Binod Dhakal
Email address:	bdhakal@mcw.edu
Institution name:	Medical College of Wisconsin
Academic rank:	Associate Professor of Medicine

Q4. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- No

Q5. Do you identify as an underrepresented/minority?

- Yes

Q6. Principal Investigator #2 (If applicable):

First and last name, degree(s):	N/A
Email address:	N/A
Institution name:	N/A
Academic rank:	N/A

Q7. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

N/A

Q8. Do you identify as an underrepresented/minority?

N/A

Q9. 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:

N/A

Q10. If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:

N/A

LETTER OF COMMITMENT:

Please note: *A letter of commitment will be signed by Lead and Last authors as it describes the expectations for filling that role. By signing the letter of commitment, the authors accept their responsibilities and will be held accountable for timely completion of all steps in the project. More details regarding author responsibilities can be found here:* *https://www.cibmtr.org/Studies/Observational/StudyManagement/p*

Q12. CURRENT ONGOING WORK WITH CIBMTR: Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.

I was involved in 3 CIBMTR studies for plasma cell disorders. One was looking at the transplant outcomes in plasma cell leukemia which was published in Leukemia (PMID 32313109), and the other one investigating the prognostic score after stem cell transplantation in myeloma (PMID 33094839). The third project looking at the role of bortezomib vs. lenalidomide maintenance was presented at the last TCT meeting.

Q13. PROPOSED WORKING COMMITTEE:

- Plasma Cell Disorders

Q14. Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.

- Yes

Q14a. If you have already spoken with a scientific director or working committee chair regarding this study, then please specify who:

Marcelo Pasquini

Q15. RESEARCH QUESTION:

CAR-T cell treatment against BCMA has shown impressive efficacy and safety profile in patients with RRMM leading to the approval of 2 BCMA-targeted CARTs, designated idecabtagene vicleucel (ide-cel, ABECMA) and ciltacabtagene autoleucel (cilta-cel, CARVYKTI), in patients with 4 or more lines of prior therapy. The role of allo-HCT, despite being a potentially curative option in MM, is limited to selective young high-risk patients preferably in the context of clinical trials. There is limited data on the safety and efficacy in renal impaired patients receiving CAR-T therapies as these patients were excluded from the clinical trials.

Q16. RESEARCH HYPOTHESIS:

We hypothesize that CAR-t cell therapy is safe and results in superior efficacy in patients with renal impairment.

Q17. SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.) *Suggested word limit of 200 words:*

Primary outcomes:
1.Safety outcomes included the incidence and severity of adverse events (AEs). AEs were graded using National Cancer Institute Common Terminology Criteria for Adverse Events version 5.0 (NCI-CTCAE 5.0). Cytokine release syndrome (CRS) and immune effector associated neurotoxicity syndrome (ICANS) were graded as per the ASTCT criteria.
2. Efficacy outcomes included overall response rates as per the IMWG criteria.
Secondary outcomes:
Duration of response
Progression free survival
Overall survival

Q18. SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.

The results of the study will help determine whether BCMA CAR-T in patients with renal impairment will be safe and provide deep and durable disease control in heavily treated MM. As renal impairment is present in significant portion of patients with multiple myeloma, this data will be informative for clinical practice.

Q19. SCIENTIFIC JUSTIFICATION: Provide a background summary of previous related research and their strengths and weaknesses, justification of your research and why your research is still necessary.

Multiple myeloma (MM), a cancer of antibody producing plasma cells, has seen a sea change in the therapeutic landscape with the introduction of several novel agents (1,2). Management of MM is rapidly changing with the emergence of variety of immune based approaches (3). Among these chimeric antigen receptor T cell therapy (CAR-T) has shown considerable promise in the treatment of relapsed and or refractory MM (RRMM). B-cell maturation antigen has been the lead antigen target for these CAR-T products and several clinical trials against BCMA have shown unprecedented response rates in myeloma with heavily treated disease (4,5). As a matter of fact, given the very impressive safety and efficacy profile, FDA granted approval 2 CAR-T products idecabtagene vicleucel (ide-cel) and ciltacabtagene autoleucel (cilta-cel) which is an anti-BCMA CAR-T agent in MM patients with 4 or more lines of therapy including an ImID, PI and CD-38 antibody (4, 5). This approval was based on a phase trial that included patients with median of 6 prior lines of treatment and resulted in overall response rate of 73% with a median progression free survival of 8.8 months (5). Similarly, cilta-cel approval was based on a phase Ib/II study that showed response rates of 97% with median PFS not reached (4). Both these trials excluded patients with renal impairment (defined as CrCl <40 ml/min including those on dialysis). Hence, safety and efficacy of CAR-T in these patients are limited and need further investigation from the real world studies.

Q19a. SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF)

N/A

Q20. PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.

Patients who received commercial BCMA CAR (idecabtagene vicleucel and ciltacabtagene autoleucel) and had renal impairment (defined as creatinine clearance of <40 ml/min) at the time of infusion.

Q21. Does this study include pediatric patients?

- No

Q21a. If this study does not include pediatric patients, please provide justification:

NA

Q22. DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Data collection forms available at: http://www.cibmtr.org/DataManagement/DataCollectior Outline any supplementary data required. Additional data collection is extremely difficult and will make your proposal less feasible.

NA

Q23. **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 specific to PROS.**

For additional information on what PRO measures have been collected and timepoints of collection, please reach out to the Late Effects and Quality of Life or Health Services Working Committee leadership: https://www.cibmtr.org/About/WhoWeAre/Com

NA

Q24. **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 experience with the proposed assay systems. PIs should be encouraged to review the inventory details, sample types collected and reach out to research_repos@nmdp.org with any questions.**

More information can be found at: https://www.cibmtr.org/Samples/Inventory/Pages/index

NA

Q25. NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required, i.e., neither database contains all the data required to answer the study question.

NA

Q26. REFERENCES:

1. Dhakal B, Girnius S, Hari P. Recent advances in understanding multiple myeloma. F1000Res. 2016;5; https://doi.org/10.12688/f1000research.8777.1
2. Kumar SK, Rajkumar V, Kyle RA, Van Duin M, Sonneveld P, Mateos MV, et al. Multiple myeloma. Nat Rev Dis Primers. 2017;3:17046. https://doi.org/10.1038/nrdp.2017.46
3. Neri P, Bahlis NJ, Lonial S. New strategies in multiple myeloma: immunotherapy as a novel approach to treat patients with multiple myeloma. Clin Cancer Res. 2016;22:5959–65.
4. Berdeja J, Madduri D, Usmani S et. al Ciltacabtagene autoleucel, a B-cell maturation antigen-directed chimeric antigen receptor T-cell therapy in patients with relapsed or refractory multiple myeloma (CARTITUDE-1): a phase 1b/2 open-label study. Lancet 398 (1027) (314-324)
5. Munshi et. al Idecabtagene Vicleucel in Relapsed and/or Refractory Multiple myeloma; N Engl J Med 2021; 384:705-716

Q27. CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning:

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

- No, I do not have any conflicts of interest pertinent to this proposal

Q27a. **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.**

N/A

BEFORE FINAL SUBMISSION, please review the PI checklist to ensure that you have completed all necessary steps. This will increase the likelihood of submitting a feasible and successful proposal.

Embedded Data:

N/A

Response Summary:

This form is intended to be completed by a physician/researcher for the purpose of proposing a study. Content should not include Personal Identifiable Information (PII) or Protected Health Information (PHI). If you are a patient, do not complete this form. Patients: Contact your healthcare provider immediately for reports of problems with your treatment or problems with products received for your treatment. The CIBMTR uses de-identified data and is unable to associate reported treatment problems, adverse events, or corrections of information with a center, clinical trial, or healthcare provider.

Q1. Study Title

Outcomes of elderly patients receiving B-Cell Maturation Antigen (BCMA)-directed Chimeric Antigen Receptor (CAR) T-cell Therapy in the standard of care setting

Q2. Key Words

Hematologic neoplasms, Multiple Myeloma, Chimeric antigen receptor T-cell therapy, adoptive

Q3. PRINCIPAL INVESTIGATOR

Provide the following information for each investigator:

Principal Investigator #1:

First and last name, degree(s):	Doris K. Hansen
Email address:	Doris.Hansen@moffitt.org
Institution name:	Moffitt Cancer Center
Academic rank:	Assistant Professor/Member

Q4. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- Yes

Q5. Do you identify as an underrepresented/minority?

- Yes

Q6. Principal Investigator #2 (If applicable):

First and last name, degree(s):	Surbhi Sidana
Email address:	Surbhi.Sidana@stanford.edu
Institution name:	Stanford University
Academic rank:	Assistant Professor

Q7. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- Yes

Q8. Do you identify as an underrepresented/minority?

- Yes

Q9. 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:

Doris K. Hansen

Q10. If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:

- Yes, I am a junior investigator and would like assistance identifying a senior mentor for my project

LETTER OF COMMITMENT:

Please note: *A letter of commitment will be signed by Lead and Last authors as it describes the expectations for filling that role. By signing the letter of commitment, the authors accept their responsibilities and will be held accountable for timely completion of all steps in the project. More details regarding author responsibilities can be found here:* *https://www.cibmtr.org/Studies/Observational/StudyManagement/p*

Q12. CURRENT ONGOING WORK WITH CIBMTR: Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.

I currently have no ongoing CIBMTR projects

Q13. PROPOSED WORKING COMMITTEE:

- Cellular Immunotherapy for Cancer

Q14. Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.

- No

Q15. RESEARCH QUESTION:

Do elderly patients receiving commercial B-cell maturation antigen (BCMA)-directed Chimeric Antigen Receptor (CAR) T-cell therapy have similar toxicity and efficacy as younger patients?

Q16. RESEARCH HYPOTHESIS:

We hypothesize that elderly myeloma patients (age ≥ 65 years) achieve similar response rates in addition to similar incidence and severity of cytokine release syndrome (CRS) and neurologic toxicity (NT) after receiving anti-BCMA CAR-T compared to younger patients.

Q17. SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.)

Suggested word limit of 200 words:

Primary aim: Evaluate cumulative incidence, severity, median time to onset, and duration of CRS and neurologic toxicity in elderly patients receiving BCMA-directed CAR T-cell therapy.
Secondary aims (stratified by age/elderly adults):
- Evaluate response rates to include ORR, PR, VGPR, CR, sCR, and clearance of MRD
- Evaluate progression free survival (PFS) and overall survival (OS)
- Evaluate incidence of relapse and non-relapse mortality (NRM)
- Identify patterns of end organ damage, hospital stay length, need for intensive care, pre-infusion comorbidities between elderly and younger patients
- Identify pattern of post CAR-T cytopenias, infections, use of growth factor, and immunoglobulin support
- Compare pre- and post- infusion inflammatory markers (ferritin and C-reactive protein) and their contribution to toxicity and response
- Observe differences in renal function (creatinine clearance), fludarabine or other conditioning regimen dosing, and timing of hematologic recovery
- Identify differences in disease biology between different age groups and their contribution to response rates and survival
- Identify cardiovascular and pulmonary complications
- Identify cause of death in all patients

Q18. SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.

Results from this study will assist in informing appropriate selection for patients receiving anti-BCMA CAR-T for multiple myeloma. With increasing life span in the western world, the prevalence of elderly patients with RRMM continues to rise and safe application of CAR-T therapy is of critical importance. In the event that anti-BCMA CAR-T is associated with a worsened toxicity profile or poor outcomes, this study will assist in refining ongoing clinical trials and pre-emptive therapies to reduce immune-mediated toxicities in addition to informing better counseling options. In standing with current evidence, the rate of infections, cytopenias, and use of growth factor and immunoglobulin support has not been well studied in this specific cohort in addition to rate of cardiovascular and pulmonary complications. We remain optimistic that our study will help eliminate current age-based biases that exist in clinical practice and CAR-T clinical trials for multiple myeloma in order to better care for this growing population.

Q19. 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.

Patients with relapsed/refractory multiple myeloma (RRMM) who have had disease progression following ≥ 4 lines of therapy to include immunomodulatory agent (IMiD), proteasome inhibitor (PI), and anti-CD38 monoclonal antibody have poor outcomes with infrequent complete responses. In this heavily treated population, the median progression free survival is 3 to 4 months and median overall survival is approximately 8-9 months [1-5]. CAR T-cell therapy for RRMM has shown excellent responses in such historically chemotherapy resistant populations. Based on pivotal KarMMa trial which led to Food and Drug Administration (FDA) approval of idecabtagene vicleucel, this heavily pretreated population achieved an ORR of 73%, with 33% having achieved a CR, and 26% clearance of MRD at a median follow-up of 13.3 months [6]. Although B-cell maturation antigen (BCMA)-targeted CAR T-cell therapy has yielded success for myeloma patients, there is an under representation of elderly patients in the pivotal trials (KarMMa 1, CARTITUDE-1)[6,7]. Patients with RRMM have a median age at diagnosis of 69 years with over two-thirds of new cases diagnosed beyond 65 years of age [8]. However, data available is derived from clinical trials conducted in younger patients. Prior studies suggest age to be an important factor in making high intensity chemotherapy decisions with historically worse outcomes in the elderly compared to younger populations [9]. Elderly patients also have difficulty tolerating high dose chemotherapy due to increased comorbidities and aggressive tumor biology [10].

In the registrational KarMMa trial, the median age was 61 years with nearly double the numbers of responders aged < 65 years [6]. In phase 1 trial, LEGEND-2 using LCAR-B38M, a novel CAR construct that consists of two BCMA single-domain antibodies, the median age of treated population was 54 years with only 19% aged ≥ 65 years [7,11]. In phase 1b/2 study of ciltacabtagene autoleucel (cilta-cel), CARTITUDE-1, median age was 61 years, similar to KarMMa [7]. A small subgroup analysis of ZUMA for large B-cell lymphoma revealed that axicabtagene-ciloleucel induced high rate of durable responses in elderly patients (≥65 years) with increased rates of some neurologic event-associated symptoms including grade > 3 delirium and encephalopathy [12]. Another limited study by Zetler et al reported differences in CRS and neurotoxicity patterns querying FDA Adverse Events Reporting System (FAERS) among relapsed or refractory large B-cell lymphoma patients > 60 years of age, however, risk factors, comorbidities, and outcomes were not studied [13]. A recent study by Reyes et al did not demonstrate an increase in toxicity or efficacy in patients aged ≥ 70 years and treated with anti-BCMA CAR-T, albeit, limited by small sample size and likely selection bias in favor of healthier-functioning older adults [14].

We have performed a preliminary analysis of 21 consecutive patients > 30 days from commercial ide-cel at Moffitt Cancer Center and consented to an IRB approved protocol. Patients were classified into two age groups, < 65 years (N=10, 47.6%) and ≥ 65 years (N=11, 52.4%). There were no statistically significant differences in demographics, disease characteristics, renal function, and lymphodepletion effect as demonstrated by comparable lymphocyte count pre and post CAR-T infusion based on age. Patients ≥ 65 years demonstrated no significant difference in day 30 overall response rate (ORR; 67% vs. 50% respectively, P = 0.6) and incidence of CRS and ICANS compared to patients younger than 65 (Figure 1). There was one death experienced in the ≥ 65-year cohort despite supportive measures (tocilizumab, dexamethasone), and it was attributed to grade 5 CRS.

To evaluate whether age impacts treatment outcomes and toxicity in patients treated with anti-BCMA CAR-T, further studies from larger multi-centered cohorts are warranted. In this study, we aim to evaluate the impact of age on safety and efficacy of commercial anti-BCMA CAR-T in RRMM patients. Given that data is limited in the elderly myeloma population and the fact that there are toxicity concerns due to associated comorbidities, our study seeks to develop a deeper understanding of this patient population.

Q19a. SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF)

[Click here]

Q20. PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.

Inclusion Criteria:

• Adult patients (age ≥ 18) with the diagnosis of RRMM receiving commercial anti-BCMA CAR-T cell therapy

No exclusions

Q21. Does this study include pediatric patients?

- No

Q21a. If this study does not include pediatric patients, please provide justification:

Anti-BCMA directed therapies have not been approved for pediatric patients.

Q22. DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Data collection forms available at: http://www.cibmtr.org/DataManagement/DataCollectior Outline any supplementary data required. Additional data collection is extremely difficult and will make your proposal less feasible.

Patient-related factors:
• Age at CAR-T (< 65, 65-74, 75- 85 and > 85 years)
• Gender: male vs female
• Race: Caucasian vs African American vs. Hispanic vs. Asian/Pacific vs other
• ECOG performance status at CAR-T: < 90% vs. ≥ 90%
• HCT-CI comorbidity index pre-infusion 0, 1, 2, and ≥ 3
• Creatinine clearance at baseline
• Comorbidities
Disease-related factors:
• Heavy and light chain subtypes
• Disease stage: ISS and/or R-ISS – I, II, and III
• High risk cytogenetics: yes vs. no including high risk: del 17p, t(4:14), t(14;16), gain/amp 1q
• Number of prior antimyeloma therapies
• Type of prior therapies (chemotherapy vs radiation vs other)
• Previous autologous HCT: yes vs no, > 1 transplant: yes vs no
• Extramedullary disease: yes vs no
• Bone marrow involvement by disease/tumor burden pre CAR-T (< 50 or ≥ 50% CD 138+ plasma cells)
• Disease status at the time of CAR-T and best response to each line of therapy: sCR, CR, VGPR, PR, and clearance of MRD as per IMWG response consensus criteria
• Circulating plasma cells prior to CAR-T infusion: yes vs no
• CNS involvement prior to CAR-T infusion: yes vs no
• Chemotherapy exposed vs refractory disease (identify exposed and refractory status to IMiD, PI, and anti-CD38 monoclonal antibodies) (identify if double-refractory, triple-refractory or penta-refractory or exposed)
CAR-T related factors:
• Specific BCMA CAR-T product
• Time from disease relapse to CAR-T apheresis
• Time from apheresis to CAR-T infusion
• Outpatient vs inpatient infusion
• CAR-T Cell dose
• Bridging therapy: yes vs no. If yes, type of bridging chemotherapy
• Lymphodepleting chemotherapy doses and if any dose reductions
• Baseline and peak CRP, ferritin, and LDH
• CRS: yes vs no, grade, and duration
• Neurotoxicity: yes vs no, grade, and duration
• Response to CAR-T therapy
• Cytopenias post CAR-T
• Infections post CAR-T
• Use of growth factor and IVIG support
• Hospitalizations and length including ICU stay
• Toxicity management including utilization of steroids (yes vs no), tocilizumab (yes vs no), anakinra (yes vs no)
• Cardiovascular and cardiopulmonary complications
Outcomes:
• Overall response rate (ORR), complete response rates (CR, sCR) and clearance of MRD: as defined by the International Myeloma Working Group (IMWG) response criteria [16].
• Overall survival (OS): Time from CAR-T to death due to any cause. Surviving patients will be censored at the time of last follow up.
• Progression-free survival (PFS): Time from CAR-T to death or relapse. Patients will be censored at the time of last follow up.
• Relapse/ Progression: Progressive or recurrent disease as defined by the IMWG be counted as an event. Those who survive without recurrence or progression to be censored at the date of last follow-up.
• Non-relapse mortality (NRM): Death without relapse or progression, where relapse or progression would be competing risks. Those who survive without recurrence or progression would be censored at the time of last contact.

Q23. **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 specific to PROS.**

For additional information on what PRO measures have been collected and timepoints of collection, please reach out to the Late Effects and Quality of Life or Health Services Working Committee leadership: https://www.cibmtr.org/About/WhoWeAre/Com

Not needed

Q24. **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 experience with the proposed assay systems. PIs should be encouraged to review the inventory details, sample types collected and reach out to research_repos@nmdp.org with any questions.**

More information can be found at: https://www.cibmtr.org/Samples/Inventory/Pages/index

None needed

Q25. NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required, i.e., neither database contains all the data required to answer the study question.

No external data source is required

Q26. REFERENCES:

1. Raje N, Berdeja J, Lin Y, et al: Anti-BCMA CAR T-Cell Therapy bb2121 in Relapsed or Refractory Multiple Myeloma. N Engl J Med 380:1726-1737, 2019
2. Chari A, Vogl DT, Gavriatopoulou M, et al: Oral Selinexor-Dexamethasone for Triple-Class Refractory Multiple Myeloma. N Engl J Med 381:727-738, 2019
3. Fulciniti M, Munshi NC, Martinez-Lopez J: Deep Response in Multiple Myeloma: A Critical Review. Biomed Res Int 2015:832049, 2015
4. Gandhi UH, Cornell RF, Lakshman A, et al: Outcomes of patients with multiple myeloma refractory to CD38-targeted monoclonal antibody therapy. Leukemia 33:2266-2275, 2019
5. Mikhael J: Treatment Options for Triple-class Refractory Multiple Myeloma. Clin Lymphoma Myeloma Leuk 20:1-7, 2020
6. Munshi NC, Anderson LD, Jr., Shah N, et al: Idecabtagene Vicleucel in Relapsed and Refractory Multiple Myeloma. N Engl J Med 384:705-716, 2021
7. Berdeja JG, Madduri D, Usmani SZ, et al: Ciltacabtagene autoleucel, a B-cell maturation antigen-directed chimeric antigen receptor T-cell therapy in patients with relapsed or refractory multiple myeloma (CARTITUDE-1): a phase 1b/2 open-label study. Lancet 398:314-324, 2021
8. SEER Cancer Stat Facts: Myeloma. Bethesda, MD: National Cancer Institute; 2020. Available from: https://seer.cancer.gov/statfacts/html/mulmy.html.
9. Diamond E, Lahoud OB, Landau H: Managing multiple myeloma in elderly patients. Leuk Lymphoma 59:1300-1311, 2018
10. Palumbo A, Bringhen S, Mateos MV, et al: Geriatric assessment predicts survival and toxicities in elderly myeloma patients: an International Myeloma Working Group report. Blood 125:2068-74, 2015
11. Zhao WH, Liu J, Wang BY, et al: A phase 1, open-label study of LCAR-B38M, a chimeric antigen receptor T cell therapy directed against B cell maturation antigen, in patients with relapsed or refractory multiple myeloma. J Hematol Oncol 11:141, 2018
12. Neelapu SS, Jacobson CA, Oluwole OO, et al: Outcomes of older patients in ZUMA-1, a pivotal study of axicabtagene ciloleucel in refractory large B-cell lymphoma. Blood 135:2106-2109, 2020
13. Zettler ME, Feinberg BA, Phillips EG, Jr., et al: Real-world adverse events associated with CAR T-cell therapy among adults age ≥ 65 years. J Geriatr Oncol 12:239-242, 2021
14. Reyes K, Huang C-Y, Lo M, et al: OAB-008: Efficacy and safety of BCMA-targeted CAR-T therapy in elderly patients with multiple myeloma. Clinical Lymphoma Myeloma and Leukemia 22:S5, 2022
15. Lee DW, Gardner R, Porter DL, et al: Current concepts in the diagnosis and management of cytokine release syndrome. Blood 124:188-95, 2014
16. Kumar S, Paiva B, Anderson KC, et al: International Myeloma Working Group consensus criteria for response and minimal residual disease assessment in multiple myeloma. Lancet Oncol 17:e328-e346, 2016

Q27. **CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning:**

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

- No, I do not have any conflicts of interest pertinent to this proposal

Q27a. **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.**

N/A

BEFORE FINAL SUBMISSION, please review the PI checklist to ensure that you have completed all necessary steps. This will increase the likelihood of submitting a feasible and successful proposal.

Embedded Data:

N/A

Response Summary:

This form is intended to be completed by a physician/researcher for the purpose of proposing a study. Content should not include Personal Identifiable Information (PII) or Protected Health Information (PHI). If you are a patient, do not complete this form. Patients: Contact your healthcare provider immediately for reports of problems with your treatment or problems with products received for your treatment. The CIBMTR uses de-identified data and is unable to associate reported treatment problems, adverse events, or corrections of information with a center, clinical trial, or healthcare provider.

Q1. Study Title

Safety and efficacy of CAR T-cell therapy in areas of unmet need for relapsed refractory multiple myeloma

Q2. Key Words

Safety, efficacy, CAR T-cell therapy, relapsed refractory, multiple myeloma

Q3. PRINCIPAL INVESTIGATOR

Provide the following information for each investigator:

Principal Investigator #1:

First and last name, degree(s):	Hamza Hashmi, M.D.
Email address:	hashmih@musc.edu
Institution name:	Medical University of South Carolina
Academic rank:	Assistant Professor

Q4. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- Yes

Q5. Do you identify as an underrepresented/minority?

- Yes

Q6. Principal Investigator #2 (If applicable):

First and last name, degree(s):	Saad Usamni
Email address:	usmanis@mskcc.org
Institution name:	Memorial Sloan Kettering
Academic rank:	Professor

Q7. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- No

Q8. Do you identify as an underrepresented/minority?

- Yes

Q9. 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:

N/A

Q10. If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:

- Yes, I am a junior investigator and would like assistance identifying a senior mentor for my project

LETTER OF COMMITMENT:

Please note: *A letter of commitment will be signed by Lead and Last authors as it describes the expectations for filling that role. By signing the letter of commitment, the authors accept their responsibilities and will be held accountable for timely completion of all steps in the project. More details regarding author responsibilities can be found here:* *https://www.cibmtr.org/Studies/Observational/StudyManagement/p*

Q12. CURRENT ONGOING WORK WITH CIBMTR: Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.

-CIBMTR Study Proposal: Development of comorbidity scores that could impact the treatment related mortality and overall survival in patients receiving CD19 directed CAR T-cell therapy; proposal selected for full study ASTCT 2020-manuscript in preparation
-CIBMTR Study Proposal: Role of CD19 directed CAR T cell therapy for CNS lymphoma; proposal selected for full study ASTCT 2022-manuscript in preparation
-Outcomes of autologous hematopoietic cell transplantation for Light Chain Deposition Disease- proposal selected by the Plasma Cell Disorders and Adult Solid Tumors Working Committee leadership for full study on the annual meeting of the Plasma Cell Disorders Working Committee of the CIBMTR in 2022
-Outcomes of autologous hematopoietic cell transplantation for Multiple Myeloma with plasmacytomas and Macrofocal Multiple Myeloma- selected by the Plasma Cell Disorders and Adult Solid Tumors Working Committee leadership for presentation on the annual meeting of the Plasma Cell Disorders Working Committee of the CIBMTR
-Early versus delayed autologous hematopoietic cell transplantation for Multiple Myeloma patients- selected by the Plasma Cell Disorders and Adult Solid Tumors Working Committee leadership for presentation on the annual meeting of the Plasma Cell Disorders Working Committee of the CIBMTR

Q13. PROPOSED WORKING COMMITTEE:

- Plasma Cell Disorders

Q14. Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.

- No

Q15. RESEARCH QUESTION:

Determine the safety and efficacy of CAR T-cell therapy for relapsed refractory multiple myeloma in areas of unmet need

Q16. RESEARCH HYPOTHESIS:

CAR T cell therapy is both safe and effective in patients with relapsed refractory multiple myeloma in areas of unmet needs including impaired renal function, plasma cell leukemia, myeloma with secondary AL amyloidosis, non-secretory myeloma and elderly/frail patients

Q17. SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.)

Suggested word limit of 200 words:

Determine the safety and efficacy of CAR T-cell therapy for the following RRMM patient populations:

- Patients with impaired renal function [GFR 30-60, GFR 15-30, GFR less than 15, ESRD on hemodialysis]
- Plasma cell leukemia
- Multiple myeloma with secondary AL amyloidosis involvement
- Non-secretory multiple myeloma
- Frail patients [ECOG performance status 2+]

Q18. SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.

Given limited evidence available from clinical trials, the study will be valuable contribution to the literature. The study will help identify patient, disease and CAR -T therapy related factors that impact both safety and efficacy of CAR T-cell therapy in these areas of unmet need. The study will inform patient selection and counseling for CAR T cell therapy for RRMM.

Q19. 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.

Patient with plasma cell leukemia and secondary amyloidosis have been excluded from clinical trials due to aggressive nature of the disease and concerns for excessive toxicities related to CAR T-cell therapy. Patient with non-secretory multiple myeloma have been excluded from clinical trials as response assessment can be challenging. Similarly, patients with impaired renal function and borderline performance status have been excluded from clinical trials for CAR T-cell therapy due to concerns for excessive related toxicities. In both clinical trials and real-world settings, frail patients that are not deemed candidates for autologous stem cell transplant have been administered CAR T-cell therapy. Little is known in literature about the safety and efficacy of CAR T-cell therapy for these patient populations.
The study will not only be a valuable contribution to the limited existing literature but also identify patient, disease and CAR -T therapy related factors that impact both safety and efficacy of CAR T-cell therapy in these areas of unmet need.

Q19a. SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF)

N/A

Q20. PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.

Patient with relapsed refractory multiple myeloma having received either idecabtagene vicleucel or ciltacabtagene autoleucel

Q21. Does this study include pediatric patients?

- No

Q21a. If this study does not include pediatric patients, please provide justification:

Multiple Myeloma is not seen in pediatric patient population

Q22. DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Data collection forms available at: http://www.cibmtr.org/DataManagement/DataCollectior Outline any supplementary data required. Additional data collection is extremely difficult and will make your proposal less feasible.

Patient related:
• Age at CAR T-cell therapy
• Gender: male vs. female
• Race: Caucasian vs. African American vs. vs. Hispanic
• Ethnicity: Hispanic or Latino vs. Non-Hispanic or non-Latino vs. non-resident of the U.S.
• ECOG Performance status: 0 vs 1-2 vs 3+
• renal function [GFR 30-60, GFR 15-30, GFR less than 15, ESRD on hemodialysis]
Disease-related:
• Myeloma subtype: IgG versus IgA versus IgM versus light chain [kappa versus lambda] vs non- secretory
• Diagnosis of plasma cell leukemia: primary vs secondary
• Secondary involvement with AL amyloidosis
• High risk disease [del 17, 4; 14, 14; 16]
• R-ISS at CAR-T infusion
• Number of prior lines of chemotherapy
• Response to prior therapy [lenalidomide, pomalidomide, bortezomib, carfilzomib, daratumumab]: Exposed versus refractory
• Prior autologous transplant
• Extramedullary disease at referral
• Bone marrow plasma cell percentage prior to infusion
• Disease status at referral
• Disease status prior to infusion
• Baseline markers of inflammation (ferritin, CRP) prior to infusion
• Exposure to BCMA agent (commercial versus trial)
CAR T-cell therapy related:
• Time from diagnosis to infusion
• Time from leukapheresis to infusion
• Use of bridging therapy
• Type of bridging therapy: Chemotherapy versus radiotherapy versus both chemo and radiotherapy
• Bridging chemotherapy regimen
• CAR-T cell dose
• CRS: grade, onset, duration
• ICANS: grade, onset, duration
• Use of tocilizumab
• Use of corticosteroids
• Persistent cytopenias at day +30 and day +90
• Use of G-CSF
• Use of TPO agonists
• Response at 1 month, 3-month, 6 months, 9 months, 12 months
• Time from infusion to progression
• Date of Death
• Cause of death
• Date of last contact

Q23. **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 specific to PROS.**

For additional information on what PRO measures have been collected and timepoints of collection, please reach out to the Late Effects and Quality of Life or Health Services Working Committee leadership: https://www.cibmtr.org/About/WhoWeAre/Com

NA

Q24. **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 experience with the proposed assay systems. PIs should be encouraged to review the inventory details, sample types collected and reach out to research_repos@nmdp.org with any questions.**

More information can be found at: https://www.cibmtr.org/Samples/Inventory/Pages/index

NA

Q25. NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required, i.e., neither database contains all the data required to answer the study question.

NA

Q26. REFERENCES:

Munshi NC, Anderson LD, Jr., Shah N, et al: Idecabtagene Vicleucel in Relapsed and Refractory Multiple Myeloma. N Engl J Med 384:705-716, 2021

Raje N, Berdeja J, Lin Y, et al: Anti-BCMA CAR T-Cell Therapy bb2121 in Relapsed or Refractory Multiple Myeloma. N Engl J Med 380:1726-17

Lee DW, Santomasso BD, Locke FL, et al: ASTCT Consensus Grading for Cytokine Release Syndrome and Neurologic Toxicity Associated with Immune Effector Cells. Biol Blood Marrow Transplant 25:625-638, 2019

Berdeja JG, Madduri D, Usmani SZ, et al: Ciltacabtagene autoleucel, a B-cell maturation antigen-directed chimeric antigen receptor T-cell therapy in patients with relapsed or refractory multiple myeloma (CARTITUDE-1): a phase 1b/2 open-label study. Lancet 398:314-324, 2021

Martin T, Usmani SZ, Berdeja JG, et al: Ciltacabtagene Autoleucel, an Anti-B-cell Maturation Antigen Chimeric Antigen Receptor T-Cell Therapy, for Relapsed/Refractory Multiple Myeloma: CARTITUDE-1 2-Year Follow-Up. J Clin Oncol:Jco2200842, 2022

Q27. CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning:

1. Employment (such as an independent contractor, consultant or providing expert testimony)?

2. Relationships (such as executive and advisory committee positions, medical consultant, speaker's bureau)?

3. Ownership (such as equity, ownership or financial interests)?

4. Transactions (such as honoraria, patents, royalties and licenses)?

5. Legal (such as pending or current arbitration or legal proceedings)?

- No, I do not have any conflicts of interest pertinent to this proposal

Q27a. **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.**

N/A

BEFORE FINAL SUBMISSION, please review the PI checklist to ensure that you have completed all necessary steps. This will increase the likelihood of submitting a feasible and successful proposal.

Embedded Data:

N/A

Response Summary:

This form is intended to be completed by a physician/researcher for the purpose of proposing a study. Content should not include Personal Identifiable Information (PII) or Protected Health Information (PHI). If you are a patient, do not complete this form. Patients: Contact your healthcare provider immediately for reports of problems with your treatment or problems with products received for your treatment. The CIBMTR uses de-identified data and is unable to associate reported treatment problems, adverse events, or corrections of information with a center, clinical trial, or healthcare provider.

Q1. Study Title

Impact of obesity on outcomes following B-Cell Maturation Antigen (BCMA)-directed Chimeric Antigen Receptor (CAR) T cell therapy in the standard of care setting

Q2. Key Words

Hematologic neoplasms, Multiple Myeloma, Chimeric antigen receptor T-cell therapy, adoptive

Q3. PRINCIPAL INVESTIGATOR

Provide the following information for each investigator:

Principal Investigator #1:

First and last name, degree(s):	Doris K. Hansen
Email address:	Doris.Hansen@moffitt.org
Institution name:	Moffitt Cancer Center
Academic rank:	Assistant Professor

Q4. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- Yes

Q5. Do you identify as an underrepresented/minority?

- No

Q6. Principal Investigator #2 (If applicable):

First and last name, degree(s):	Ciara Freeman
Email address:	Ciara.Freeman@moffitt.org
Institution name:	Moffitt Cancer Center
Academic rank:	Assistant Professor

Q7. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- Yes

Q8. Do you identify as an underrepresented/minority?

- No

Q9. 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:

Doris Hansen

Q10. If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:

N/A

LETTER OF COMMITMENT:

Please note: *A letter of commitment will be signed by Lead and Last authors as it describes the expectations for filling that role. By signing the letter of commitment, the authors accept their responsibilities and will be held accountable for timely completion of all steps in the project. More details regarding author responsibilities can be found here:* *https://www.cibmtr.org/Studies/Observational/StudyManagement/p*

Q12. CURRENT ONGOING WORK WITH CIBMTR: Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.

None

Q13. PROPOSED WORKING COMMITTEE:

- Cellular Immunotherapy for Cancer

Q14. Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.

- No

Q15. RESEARCH QUESTION:

Do overweight and obese patients receiving commercial B-cell maturation antigen (BCMA)-directed Chimeric Antigen Receptor (CAR) T-cell therapy have similar toxicity and efficacy as underweight and healthy weight patients?

Q16. RESEARCH HYPOTHESIS:

We hypothesize that overweight (body mass index, BMI 25 – 29.99 kg/m2) and obese (BMI ≥ 30 kg/m2) patients will experience similar response rates but increased incidence and severity of immune-mediated toxicities after receiving commercial BCMA CAR-T cell therapy relative to underweight (BMI < 18.5 kg/m2) and healthy weight (BMI 18.5 – 24.9 kg/m2) patients.

Q17. SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.)

Suggested word limit of 200 words:

Primary Aim: Evaluate the cumulative incidence, severity, median time to onset, and duration of cytokine release syndrome (CRS) and immune effector cell associated neurologic syndrome (ICANS) as stratified by obesity status
Secondary Aims (stratified by obesity status):

- Evaluate response rates to include ORR, PR, VGPR, CR, sCR, and clearance of MRD
- Evaluate progression free survival (PFS) and overall survival (OS)
- Identify incidence of relapse and non-relapse mortality (NRM)
- Identify distribution of CAR-T cell dose per body weight
- Identify total delivered cyclophosphamide and fludarabine doses per body surface area (BSA) and BMI
- Compare lymphodepletion and CAR-T effects based on absolute lymphocyte count post CAR-T
- Identify patterns of pre-infusion comorbidities (HCT-CI), length of hospital stay, need for intensive care, incidence of infections, and use of growth factor and immunoglobulin support
- Compare pre- and post- infusion inflammatory markers (ferritin, CRP, LDH) and their contribution to toxicity and efficacy
- Observe differences in renal function and hematologic recovery (WBC/ANC, Hgb, and Platelets)
- Compare differences in tocilizumab, steroid, and anakinra use for CRS and/or ICANS
- Identify cardiovascular and pulmonary complications post CAR-T by body weight
- Identify cause of death

Q18. SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.

Results from this study will inform appropriate management of overweight and obese patients receiving anti-BCMA CAR-T for multiply relapsed multiple myeloma. With increasing prevalence of obesity in the western world, safe application of CAR T-cell therapy remains of critical importance. This study will assist with refining future clinical trials in overweight and obese patients. We will evaluate distribution of total delivered lymphodepleting chemotherapy, cyclophosphamide and fludarabine, per body surface area and body mass index to assess its contribution to success or failure of CAR T-cell therapy. Ultimately, our study will inform LD chemotherapy dosing patterns and its effect on efficacy and toxicity of CAR-T. In standing with current evidence, the rate, severity, onset, and duration of CRS, neurotoxicity, cytopenias, incidence of infections, length of hospital stay, need for intensive care, and the role of inflammatory markers have not been well described in the overweight and obese anti-BCMA CAR-T populations. We remain optimistic that a large multi-center cohort analysis will establish the significance of obesity and body weight on clinical outcomes and toxicity after BCMA directed CAR T-cell therapy.

Q19. 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.

B cell maturation antigen (BCMA) CAR T-cell therapy has revolutionized the treatment armamentarium of relapsed/refractory multiple myeloma with excellent response rates in a difficult to treat population (1-6). The impact of obesity on efficacy and safety of commercially treated anti-BCMA CAR-T patients has not yet been described. Obesity remains a public health concern in the United States with a prevalence that has increased from 30.5% to 42.4% from 1999 – 2018 with an increase in severe obesity from 4.7% to 9.2% (7). Obesity is a metabolic disorder which leads to a state of chronic low-grade inflammation and is an important contributor to many disease states including cancer. Obesity impacts the immune system and is hypothesized to impact efficacy of chemotherapy and immunotherapy. Several studies have shown that body weight and BMI are important factors that influence chemotherapy dosing in clinical practice. In overweight and obese patients, chemotherapy dose reduction, capped dosing, and adjustment to an ideal body weight are commonly used strategies to minimize excessive chemotherapy-associated toxicities (8). Study by Bouleftour et al. has demonstrated that the practice of dose reduction based on BMI may negatively impact efficacy and quality of care in cancer patients (9).

Cortellini et al have demonstrated increased survival in obese patients treated with immunotherapies (10). However, obesity is associated with a pro-inflammatory state and immune dysregulation, features which have been associated with worse outcomes following CAR-T in lymphoma as described by Jain et al. Obesity is also associated with increased transplant-related mortality, worse survival, and higher incidence of acute graft versus host disease (GVHD) in allogeneic hematopoietic stem-cell transplant (HCT) recipients (12). Recent study by Wudhikarn et al., demonstrated no association between obesity and CAR-T efficacy, survival, and immune-mediated toxicities in patients treated with axicabtagene ciloleucel in the standard of care setting (11).

We performed a retrospective analysis of 21 consecutive patients > 30 days from commercial ide-cel consented to an IRB approved protocol. Patient and clinical characteristics were assessed by body mass index (BMI) (non-overweight/obese: < 25, overweight/obese: ≥ 25 kg/m2) using Kruskal-Wallis rank sum or Fisher's exact tests. The correlation of dosing of lymphodepleting chemotherapy (LD), described as total dose per m^2 of body surface area and actual delivered dose to standard dose ratio, with BMI was estimated. We also investigated overall response rate at day 30 and cumulative incidence of CRS and ICANS by BMI. Lymphodepletion effect was measured by lymphocyte count at and post CAR-T infusion.

Of the 21 patients, 15 (71%) were overweight/obese and 6 (29%) non-overweight/obese, with characteristics presented in Table 1. There was a positive correlation between total dose of cyclophosphamide (P=0.0003) and fludarabine (P=0.0047) delivered as stratified by BMI (Figure 1). Overweight/obese compared to non-overweight/obese received a higher median total dose of cyclophosphamide (610 mg vs. 495 mg, respectively; P = 0.004) and fludarabine (60 mg vs. 47.5 mg, respectively; P = 0.048). There were no differences in baseline serum ferritin or CRP by BMI. After ide-cel infusion, median maximum C-reactive protein (CRP) was higher in overweight/obese (5.4 mg/dL, range 3.8 – 9.7 mg/dL) relative to non-overweight/obese (1.4 mg/dL, range 0.8 – 1.6 mg/dL) (P < 0.001). There was no difference in overall response rate at day 30, incidence and severity of CRS or ICANS, renal function, or lymphodepletion effect by BMI.

In our small cohort, we did not find that obesity associated with day 30 response or toxicities following commercial ide-cel. Obesity was associated with absolute dose of lymphodepleting chemotherapy and increased peak CRP level post CAR-T infusion. To evaluate whether obesity impacts outcomes and toxicity in patients treated with anti-BCMA CAR-T, further studies from larger multi-centered cohorts are warranted to include longer follow-up and correlative studies on CAR-T kinetics. In the proposed study, we aim to identify the impact of obesity on efficacy, immune-mediated toxicities, and lymphodepleting chemotherapy dosing patterns following anti-BCMA CAR T-cell therapy in multiple myeloma.

Q19a. SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF)

[Click here]

Q20. PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.

Inclusion Criteria:
• Adult patients (age ≥ 18) with the diagnosis of multiple myeloma receiving commercial anti-BCMA CAR T-cell therapy
No exclusion criteria

Q21. Does this study include pediatric patients?

- No

Q21a. If this study does not include pediatric patients, please provide justification:

Ide-cel is not approved in the pediatric population.

Q22. DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Data collection forms available at: http://www.cibmtr.org/DataManagement/DataCollectior Outline any supplementary data required. Additional data collection is extremely difficult and will make your proposal less feasible.

Variables: The following variables will be analyzed
Patient-Related:
• BMI at CAR-T (< 18.5, 18.5 – 24.9, 25 – 29.9, 30 – 40, and 40.0 kg/m2)
• Weight at CAR-T (< 100 and 100 kg)
• Age at CAR-T: continuous and categorical by decade
• Race: Caucasian vs African American vs Hispanic vs Asian/Pacific vs other
• Gender: male vs female
• Karnofsky or ECOG performance status at CAR-T infusion (< 90% vs 90%)
• Creatinine clearance at baseline (60. 50.0 – 59.9, ≤ 49.9 mL/min)
• HCT comorbidity index pre infusion (0, 1, 2 and 3)
Disease-Related:
• Heavy and light chain subtypes
• Disease status: ISS, and/or R-ISS
• High risk cytogenetics: yes vs no including high risk: del 17p, t(4;14), t(14;16)
• Number of prior anti-myeloma therapies
• Types of prior therapies (chemotherapy vs radiation vs other)
• Best response to each line of therapy as per IMWG response criteria
• Previous autologous hematopoietic stem-cell transplant: yes vs no; > 1 transplant: yes vs no
• Extramedullary disease: yes vs no
• Bone marrow involvement by disease/tumor burden (< 50% or ≥ 50% CD138 positive plasma cells)
• Disease status at the time CAR-T: relapsed vs refractory; doubling time of paraprotein
• Circulating plasma cells: yes vs no
• CNS involvement prior to CAR-T infusion: yes vs no
• Chemotherapy exposed vs refractory status (identify status to immunomodulatory agent, proteasome inhibitor, anti-CD38 monoclonal antibody) (identify if double-refractory, triple-refractory or penta-refractory vs exposed)
CAR-T Related:
• Specific BCMA CAR-T product
• Time from disease relapse to CAR-T apheresis
• Time from apheresis to CAR-T infusion
• CAR-T Cell dose per body weight
• Bridging therapy: yes vs no. If yes, type of bridging chemotherapy
• Lymphodepleting chemotherapy doses per BSA and if any dose reductions
• Absolute lymphocyte count pre and post CAR-T infusion
• Baseline and peak CRP, ferritin, and LDH
• CRS (yes vs no), maximum grade, onset, and duration
• Neurotoxicity (ICANS) (yes vs no), maximum grade, onset, and duration
• Response to CAR-T therapy
• Infections post CAR-T therapy
• Use of growth factor and IVIG support
• Length of hospitalization(s) including ICU stay
• Toxicity management including utilization of tocilizumab (yes vs no), corticosteroids (yes vs no), and anakinra (yes vs no)
• Cardiovascular and pulmonary complications
Outcomes:
• Overall response rate (ORR), complete response rates (CR, sCR) and clearance of MRD: as defined by the International Myeloma Working Group (IMWG) response criteria.
• Overall survival (OS): Time from CAR-T to death due to any cause. Surviving patients will be censored at the time of last follow up.
• Progression-free survival (PFS): Time from CAR-T to death or relapse. Patients will be censored at the time of last follow up.
• Relapse/Progression: Progressive or recurrent disease as defined by the IMWG be counted as an event. Those who survive without recurrence or progression to be censored at the date of last follow-up.
• Non-relapse mortality (NRM): Death without relapse or progression, where relapse or progression would be competing risks. Those who survive without recurrence or progression would be censored at the time of last contact.

Q23. **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 specific to PROS.**

For additional information on what PRO measures have been collected and timepoints of collection, please reach out to the Late Effects and Quality of Life or Health Services Working Committee leadership: https://www.cibmtr.org/About/WhoWeAre/Com

No PRO data required

Q24. **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 experience with the proposed assay systems. PIs should be encouraged to review the inventory details, sample types collected and reach out to research_repos@nmdp.org with any questions.**

More information can be found at: https://www.cibmtr.org/Samples/Inventory/Pages/index

No sample requirements

Q25. NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required, i.e., neither database contains all the data required to answer the study question.

No external DataSource is needed

Q26. REFERENCES:

1. Raje N, Berdeja J, Lin Y, Siegel D, Jagannath S, Madduri D, et al. Anti-BCMA CAR T-Cell Therapy bb2121 in Relapsed or Refractory Multiple Myeloma. N Engl J Med. 2019;380(18):1726-37.
2. Chari A, Vogl DT, Gavriatopoulou M, et al. Oral selinexor-dexamethasone for triple-class refractory multiple myeloma. N Engl J Med 2019; 381: 727-38.
3. Fulciniti M, Munshi NC, Martinez-Lopez J. Deep response in multiple myeloma: a critical review. Biomed Res Int 2015;2015: 832049.
4. Gandhi UH, Cornell RF, Lakshman A, et al. Outcomes of patients with multiple myeloma refractory to CD38-targeted monoclonal antibody therapy. Leukemia 2019; 33: 2266-75.
5. Mikhael J. Treatment options for triple class refractory multiple myeloma. Clin Lymphoma Myeloma Leuk 2020; 20: 1-7.
6. Munshi NC, Anderson LD, Shah N, Madduri D, Berdeja J, Lonial S, et al. Idecabtagene Vicleucel in Relapsed and Refractory Multiple Myeloma. N Engl J Med. 2021;384(8):705-16.
7. Hales CM, Carroll MD, Fryar CD, Ogden CL. Prevalence of obesity and severe obesity among adults: United States, 2017–2018. NCHS Data Brief, no 360. Hyattsville, MD: National Center for Health Statistics. 2020
8. Woodall MJ, Neumann S, Campbell K, Pattison ST, Young SL. The effects of obesity on anti-cancer immunity and cancer immunotherapy. Cancers. 2020;12:1230–33.
9. Bouleftour W, Mery B, Chanal E, Rowinski E, Viard A, Forges F, et al. Obesity and chemotherapy administration: between empiric and mathematic method review. Acta Oncol. 2019;58:880–7.
10. Cortellini A, Bersanelli M, Buti S, Cannita K, Santini D, Perrone F, et al. A multicenter study of body mass index in cancer patients treated with anti-PD-1/PD-L1 immune checkpoint inhibitors: when overweight becomes favorable. J Immunother Cancer. 2019;7:57. doi: 10.1186/s40425-019-0527-y.
11. Wudhikarn, K., Bansal, R., Khurana, A. et al. The impact of obesity and body weight on the outcome of patients with relapsed/refractory large B-cell lymphoma treated with axicabtagene ciloleucel. Blood Cancer J. 11, 124 (2021). https://doi.org/10.1038/s41408-021-00515-2
12. Berdeja JG, Madduri D, Usmani SZ, Jakubowiak A, Agha M, Cohen AD, et al. Ciltacabtagene autoleucel, a B-cell maturation antigen-directed chimeric antigen receptor T-cell therapy in patients with relapsed or refractory multiple myeloma (CARTITUDE-1): a phase 1b/2 open-label study. Lancet. 2021.
13. Kumar S, Paiva B, Anderson KC, et al. International Myeloma Working Group consensus criteria for response and minimal residual disease assessment in multiple myeloma. Lancet Oncol 2016; 17(8):e328-e346.
14. Lee DW, Gardner R, Porter DL, et al. Current concepts in the diagnosis and management of cytokine release syndrome. Blood 2014; 124: 188-95.
15. Mikkilineni L, Kochenderfer JN. CAR T cell therapies for patients with multiple myeloma. Nat Rev Clin Oncol. 2021;18(2):71-84.
16. Turtle CJ, Hanafi LA, Berger C, Gooley TA, Cherian S, Hudecek M, et al. CD19 CAR-T cells of defined CD4+:CD8+ composition in adult B cell ALL patients. J Clin Invest. 2016;126:2123–38.

Q27. **CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning:**

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

- No, I do not have any conflicts of interest pertinent to this proposal

Q27a. **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.**

N/A

BEFORE FINAL SUBMISSION, please review the PI checklist to ensure that you have completed all necessary steps. This will increase the likelihood of submitting a feasible and successful proposal.

Embedded Data:

N/A

Response Summary:

This form is intended to be completed by a physician/researcher for the purpose of proposing a study. Content should not include Personal Identifiable Information (PII) or Protected Health Information (PHI). If you are a patient, do not complete this form. Patients: Contact your healthcare provider immediately for reports of problems with your treatment or problems with products received for your treatment. The CIBMTR uses de-identified data and is unable to associate reported treatment problems, adverse events, or corrections of information with a center, clinical trial, or healthcare provider.

Q1. Study Title

Safety and Efficacy of anti-BCMA CAR-T Therapy in Older Adults with Multiple Myeloma: An Analysis of Real-World Outcomes from the Center for International Blood and Marrow Transplant Research (CIBMTR) and Cellular Therapy Registry

Q2. Key Words

Multiple Myeloma; Chimeric-antigen receptor therapy; Anti-BCMA CAR-T therapy; Older Adults

Q3. PRINCIPAL INVESTIGATOR

Provide the following information for each investigator:

Principal Investigator #1:

First and last name, degree(s):	Othman Salim Akhtar, MBBS
Email address:	Othman.akhtar@moffitt.org
Institution name:	H Lee Moffitt Cancer Center, Tampa, FL
Academic rank:	Fellow, Blood and Marrow Transplantation and Cellular Immunotherapy

Q4. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- Yes

Q5. Do you identify as an underrepresented/minority?

- No

Q6. Principal Investigator #2 (If applicable):

First and last name, degree(s):	Ciara Louise Freeman, MD, PhD
Email address:	ciara.freeman@moffitt.org
Institution name:	H Lee Moffitt Cancer Center, Tampa, FL
Academic rank:	Assistant Professor

Q7. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- No

Q8. Do you identify as an underrepresented/minority?

- No

Q9. 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:

N/A

Q10. If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:

- Yes, I am a junior investigator and would like assistance identifying a senior mentor for my project

LETTER OF COMMITMENT:

Please note: *A letter of commitment will be signed by Lead and Last authors as it describes the expectations for filling that role. By signing the letter of commitment, the authors accept their responsibilities and will be held accountable for timely completion of all steps in the project. More details regarding author responsibilities can be found here:* *https://www.cibmtr.org/Studies/Observational/StudyManagement/p*

Q12. CURRENT ONGOING WORK WITH CIBMTR: Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.

N/A

Q13. PROPOSED WORKING COMMITTEE:

- Cellular Immunotherapy for Cancer

Q14. Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.

- No

Q15. RESEARCH QUESTION:

A. How does the clinical efficacy of BCMA CAR-T cell therapy in older adults (age≥70 years) compare to younger patients (age <70 years)?
B. How do the rates of immune-mediated toxicity following BCMA CAR-T cell therapy in older adults (age≥70 years) compare to younger patients (age <70 years)?

Q16. RESEARCH HYPOTHESIS:

Older adults receiving anti-BCMA CAR-T therapy will have inferior survival outcomes and higher rates of immune-mediated toxicity compared to younger patients.

Q17. SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.)

Suggested word limit of 200 words:

- Overall Response Rate
- Complete Response Rate
- Cytokine Release Syndrome (CRS) – all grades and grade ≥3
- Immune-effector cell associated neurotoxicity syndrome (ICANS) - all grades and grade ≥3
- Length of Stay
- Non-relapse mortality at 100 days and 1 year
- Overall survival
- Progression-free survival

Q18. SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.

Anti-BCMA CAR-T therapy is now approved for treatment of relapse/refractory multiple myeloma after 4 lines of therapy, but data on outcomes in older patients (age≥70 years) is limited. The current proposal aims to address this critical knowledge gap. These data will help determine the clinical benefit of anti-BCMA CAR-T therapy in older adults in a real-world setting, identify risk factors for poor outcomes, and help inform strategies to improve outcomes in this heterogenous patient population.

Q19. 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.

Anti-BCMA chimeric antigen receptor T-cell (CAR-T) therapies are transforming care in multiple myeloma (MM). Based on results from the KarMMA and CARTITUDE-1 trials, the food and drug administration (FDA) approved idecabtagene vicleucel (ide-cel) and ciltacabtagene autoleucel (cilta-cel) respectively, for treatment of relapsed/refractory MM after >4 lines of therapy.1,2 Unfortunately, older adults were significantly under-represented in these trials. The median age at diagnosis for MM is 69 years, and approximately 65% of newly diagnosed patients are ≥65 years. In comparison, the median age of patients was 61 years in both the KarMMA and CARTITUDE-1 trials.1,2 In the KarMMA trial, only 35% (45/128) of patients were age≥65 years, and 16% (20/128) were age ≥70 years.3 In a subgroup analysis of the KarMMA trial, older adults in both these subgroups (age≥65 years and ≥70 years) had comparable response rates to the overall cohort.3 However, there were numerically higher rates of cytokine release syndrome (CRS) and immune-effector cell associated neurotoxic syndrome (ICANS).3 In patients above the age of 70 years, ICANS of any grade was reported in 30% of patients versus 18% in overall cohort. Additionally, all patients who developed grade 3 ICANS (n=4) were above the age of 65 years.3 It is important to note that the number of these patients was small and statistical significance was not reported. In the CARTITUDE-1 trial, older adults appear to have comparable efficacy to younger patients but a subgroup analysis describing toxicity has not been reported yet. In addition to differences in age distribution, the patient population in both trials were not necessarily representative of real-world clinical practice due to several comorbidity-related exclusions. Most patients had excellent performance status with an ECOG PS of 0-1 in 98% of patients in the KarMMA trial and 96% in the CARTITUDE-1.2,3

Real-world outcomes of CAR-T patients appear to differ from those in clinical trials. For example, in a CIBMTR analysis of patients receiving axicabtagene ciloleucel for NHL there was a significantly higher risk of all grade and grade ≥3 immune-mediated toxicities (both CRS and ICANS) in patients older than 65 years.4 Similarly, patients with poor PS (≥2), (often excluded in clinical trials), had higher rates of ICANS.4 These toxicities are associated with significant morbidity, resulting in prolonged length of stay and increased cost of care.5

Since both ide-cel and cilta-cel are now part of the treatment paradigm in MM, understanding outcomes in older adults who make up more than half of the patients seen in the real-world is critical. It is essential to identify risk factors associated with toxicities such as CRS and ICANS in these patients and the impact these have on outcomes such as length of stay and overall survival.

Q19a. SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF)

N/A

Q20. PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.

Inclusion Criteria:
• Patients with MM age ≥18 years of age undergoing anti-BCMA CAR-T therapy with idecabtagene vicleucel or ciltacabtagene autoleucel outside of a clinical trial.
Exclusion criteria:
• Patients receiving allogeneic anti-BCMA CAR-T therapy

Q21. Does this study include pediatric patients?

- No

Q21a. If this study does not include pediatric patients, please provide justification:

Multiple Myeloma is predominantly a disease of adults, and particularly older adults.

Q22. DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Data collection forms available at: http://www.cibmtr.org/DataManagement/DataCollectior Outline any supplementary data required. Additional data collection is extremely difficult and will make your proposal less feasible.

Patient related:
• Age at time of CAR-T: as a continuous variable, and categorical <70 years and ≥70 years, and by decade
• Gender: male vs. female
• Race: Caucasian vs. African American vs. Asian/Pacific Islander vs. Hispanic vs. Others vs. Missing
• Geographical region: USA vs other
Disease-related:
• Disease stage at diagnosis: ISS I/II vs III
• LDH elevated at diagnosis
• Cytogenetics (No abnormality/High risk/standard risk/unknown)
• Presence of extra-medullary disease
• Number of lines of therapy prior to CAR-T: ≤3 vs 4 or more
• Prior proteasome inhibitor use (yes/no)
• Prior immunomodulator use (yes/no)
• Prior anti-CD38 inhibitor use (yes/no)
• Prior autologous stem cell transplant
Prior to CAR-T:
• ECOG Performance status/Karnofsky Performance scale
• Height and weight
• Number of lines of therapy prior to CAR-T: ≤3 vs 4 or more
• Bridging therapy use immediately prior to CAR-T
• Disease status prior to CAR-T: % BM burden
• LDH (prior to CAR-T): normal vs >upper limit normal
• CRP (prior to CAR-T): continuous variable, and as categorical (normal vs >upper limit)
• Ferritin (prior to CAR-T): continuous variable , and as categorical (normal vs >upper limit)
• HCT-CI score: 0, 1, 2, ≥3
• Affected: Cardiac, cardiovascular, neurologic, pulmonary, renal
• Pre-CART GFR < 45ml/min (will examine continuous and categorical by CKD grouping)
• Pre-CART ejection fraction (categorical split >=50%/41-49%/<=40%)
• Use of prophylaxis for CRS or ICANS
CAR-T related:
• Specific product
• Conditioning regimen used
• Inpatient vs outpatient administration
• Date of administration
• Number of cells administered
• Date of post-CAR-T relapse
• Date of death
• Cause of death
Post CAR-T
• CRS occurred (maximum grade)
• ICANS occurred (maximum grade)
• Tocilizumab administered (Y/N)
• Steroids administered (Y/N)
• Anakinra administered (Y/N)
• Infection (<30 days post CAR-T, maximum grade)
• Day 30 cytopenia present (Y/N)
• MRD method (NGS vs NGF)

Patient- and disease- related factors will be compared between the two age-based cohorts (age <70 years versus ≥70 years) using the Chi-square test for categorical and the Kruskal-Wallis test for continuous variables. OS and PFS probabilities will be estimated by the Kaplan-Meier method. Comparison of survival curves will be performed with the log-rank test.

Multivariate analysis [MVA] of OS, PFS and relapse/progression will be performed using Cox proportional hazards model. Variables to be examined in the multivariate analysis will be tested in a forward stepwise approach. The final model will include covariates associated with the outcome at a level of 0.05. Tests for interactions may be considered. Risk factors for developing CRS/ICANs will also be interrogated.

Q23. **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 specific to PROS.**

For additional information on what PRO measures have been collected and timepoints of collection, please reach out to the Late Effects and Quality of Life or Health Services Working Committee leadership: https://www.cibmtr.org/About/WhoWeAre/Com

Not Applicable

Q24. **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 experience with the proposed assay systems. PIs should be encouraged to review the inventory details, sample types collected and reach out to research_repos@nmdp.org with any questions.**

More information can be found at: https://www.cibmtr.org/Samples/Inventory/Pages/index

Not Applicable

Q25. NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required, i.e., neither database contains all the data required to answer the study question.

Not Applicable

Q26. REFERENCES:

1 Munshi, N. C. et al. Idecabtagene Vicleucel in Relapsed and Refractory Multiple Myeloma. N Engl J Med 384, 705-716, doi:10.1056/NEJMoa2024850 (2021).
2 Berdeja, J. G. et al. Ciltacabtagene autoleucel, a B-cell maturation antigen-directed chimeric antigen receptor T-cell therapy in patients with relapsed or refractory multiple myeloma (CARTITUDE-1): a phase 1b/2 open-label study. Lancet 398, 314-324, doi:10.1016/s0140-6736(21)00933-8 (2021).
3 Berdeja, J. G. et al. Efficacy and Safety of Idecabtagene Vicleucel (ide-cel, bb2121) in Elderly Patients with Relapsed and Refractory Multiple Myeloma: KarMMa Subgroup Analysis. Blood 136, 16-17, doi:https://doi.org/10.1182/blood-2020-134322 (2020).
4 Locke, F. L. et al. Real-World Outcomes of Axicabtagene Ciloleucel (Axi-cel) for the Treatment of Large B-Cell Lymphoma (LBCL): Impact of Age and Specific Organ Dysfunction. Blood 138, 530-530, doi:10.1182/blood-2021-149679 (2021).
5 Siddiqi, T. et al. Estimation of the Resource Utilization and Costs of Cytokine Release Syndrome Observed in the Transcend-NHL Clinical Trial: A Micro-Costing Study. Blood 132, 319-319, doi:10.1182/blood-2018-99-112214 (2018).

Q27. CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning:

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

- No, I do not have any conflicts of interest pertinent to this proposal

Q27a. 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.

N/A

BEFORE FINAL SUBMISSION, please review the PI checklist to ensure that you have completed all necessary steps. This will increase the likelihood of submitting a feasible and successful proposal.

Embedded Data:

N/A

Table. Patients who received first CAR-T infusion between 2016 - 2022 for Multiple Myeloma, with follow-up reported to CIBMTR

Characteristic	N (%)
No. of patients[1]	786
No. of centers	73
Age at infusion, yrs - median (min-max)	64 (29-86)
Age at infusion, by category #1 - no. (%)	
20 - 29 years	2 (0)
30 - 39 years	13 (2)
40 - 49 years	58 (7)
50 - 59 years	200 (25)
60 - 69 years	330 (42)
70+ years	183 (23)
Age at infusion, by category #2 - no. (%)	
18 - 39	15 (2)
40 - 65	407 (52)
65+	364 (46)
Age at Infusion, by category #3 - no. (%)	
>=18 years	786 (100)
Age at infusion, by category #4 - no. (%)	
0 - 64	422 (54)
65+	364 (46)
Gender - no. (%)	
Male	468 (60)
Female	314 (40)
Not reported	4 (1)
Recipient race - no. (%)	
White	624 (79)
Black or African American	102 (13)
Asian	20 (3)
Native Hawaiian or other Pacific Islander	1 (0)
American Indian or Alaska Native	3 (0)
Other	5 (1)
More than one race	11 (1)
Not reported	20 (3)
Recipient ethnicity - no. (%)	
Hispanic or Latino	51 (6)
Not Hispanic or Latino	710 (90)

Characteristic	N (%)
Non-resident of the U.S.	12 (2)
Unknown	13 (2)
Country - no. (%)	
US	765 (97)
Other	21 (3)
Karnofsky performance score prior to CT - no. (%)	
90-100	291 (37)
80	268 (34)
< 80	147 (19)
Not reported	80 (10)
ECOG performance status prior to CT - no. (%)	
0 - Asymptomatic	291 (37)
1 - Symptomatic but completely ambulatory	382 (49)
2 - Symptomatic, < 50% in bed during the day	29 (4)
3 - Symptomatic, > 50% in bed, but not bedbound	3 (0)
4 - Bedbound	1 (0)
Not reported	80 (10)
Body mass index (BMI) category at infusion - no. (%)	
< 18.5 - Underweight	14 (2)
>= 18.5 to < 25 - Normal	224 (28)
>= 25 to < 30 - Overweight	288 (37)
>= 30 - Obese	238 (30)
Not reported	22 (3)
Sub-disease for CT - no. (%)	
Multiple myeloma, NOS	501 (64)
Plasma cell leukemia	11 (1)
Multiple myeloma - IgG	54 (7)
Multiple myeloma - IgA	23 (3)
Multiple myeloma - light chain only	180 (23)
Multiple myeloma - non-secretory	17 (2)
Diagnosis	
Age at initial diagnosis - median (min-max)	57 (25-85)
ISS stage at diagnosis - no. (%)	
1 (beta2-mic < 3.5, albumin >= 3.5)	202 (26)
2 (Not fitting stage 1 or 3)	170 (22)
3 (beta2-mic >= 5.5, regardless of albumin)	160 (20)
Not reported	254 (32)
R-ISS stage at diagnosis - no. (%)	

Characteristic	N (%)
1 (ISS stage I and standard-risk abnormalities by iFISH and normal LDH)	62 (8)
2 (Not R-ISS stage I or III)	188 (24)
3 (ISS stage III and either high-risk chromosomal abnormalities by iFISH or high LDH)	78 (10)
Not reported	458 (58)
Serum creatinine at diagnosis, value - median (min-max)	1 (0-1493)
Time from initial diagnosis to CT - no. (%)	
Median (min-max)	66 (0-324)
>= 0 to < 12 months	39 (5)
>= 12 to < 36 months	131 (17)
>= 36 to < 60 months	185 (24)
>= 60 months	431 (55)
Lymphodepleting regimen - no. (%)	
Yes	779 (99)
Lymphodepleting chemotherapy: bendamustine	3 (0)
Lymphodepleting chemotherapy: cyclophosphamide	3 (0)
Lymphodepleting chemotherapy: cyclophosphamide + Lymphodepleting chemotherapy: cytarabine + Lymphodepleting chemotherapy: fludarabine	1 (0)
Lymphodepleting chemotherapy: cyclophosphamide + Lymphodepleting chemotherapy: fludarabine	761 (97)
Lymphodepleting chemotherapy: cyclophosphamide + Lymphodepleting chemotherapy: fludarabine + Lymphodepleting chemotherapy: other	4 (1)
Lymphodepleting chemotherapy: cyclophosphamide + Lymphodepleting chemotherapy: thiotepa	1 (0)
Lymphodepleting chemotherapy: fludarabine	3 (0)
Lymphodepleting chemotherapy: other	1 (0)
None specified	2 (0)
No	7 (1)
Commercial vs. noncommercial CAR-T product - no. (%)	

Characteristic	N (%)
Commercial	501 (64)
Noncommercial	285 (36)
Clinical trial - no. (%)	
No	499 (63)
Yes	287 (37)
CAR-T Product type (Other - specify) - no. (%)	
Abecma	468 (60)
Carvykti	33 (4)
Other	285 (36)
Non-commercial Idecabtagene vicleucel	84 (11)
Non-commercial Ciltacabtagene autoleucel	14 (2)
Non-commercial Orvacabtagene autoleucel	1 (0)
Non-commercial - No product name	9 (1)
Non-commercial - Other product	94 (12)
Non-commercial - Product name not reported	83 (11)
Prior transplants and therapies	
Types of prior HCTs - no. (%)	
No	78 (10)
Yes	707 (90)
Prior allo-HCT	8 (1)
Prior auto-HCT	668 (85)
Prior auto and allo-HCT	23 (3)
Not reported	8 (1)
Unknown	1 (0)
Total number of prior HCTs - no. (%)	
0	78 (10)
1	508 (65)
2	139 (18)
3	17 (2)
4	1 (0)
Not reported	43 (5)
Prior CT - no. (%)	
No	766 (97)
Yes	20 (3)
CT infusion counting number - no. (%)	
1	777 (99)
2	8 (1)
3	1 (0)

Characteristic	N (%)
Time from prior HCT to CT, months - median (min-max)	
No prior HCT	NE
Prior allo-HCT	36 (9-176)
Prior auto-HCT	46 (0-250)
Prior auto and allo-HCT	51 (5-159)
Time from the latest prior HCT to current CT, days - median (min-max)	1407 (14-7601)
Clinically significant co-existing diseases or organ impairment	
Clinically significant comorbidity prior to CT - no. (%)	
No	256 (33)
Yes	526 (67)
Comorbidity: Arrhythmia, any history	83 (11)
Comorbidity: Cardiac, any history	94 (12)
Comorbidity: Cerebrovascular disease, any history	23 (3)
Comorbidity: Diabetes requiring non-diet treatment, in the last 4 week	93 (12)
Comorbidity: Heart valve disease	19 (2)
Comorbidity: Hepatic disease (mild), any history or at the time of infusion	38 (5)
Comorbidity: Hepatic disease (moderate/severe), any history or at the time of infusion	12 (2)
Comorbidity: Infection requiring antimicrobial treatment, continuation after day 0	36 (5)
Comorbidity: Inflammatory bowel disease, any history	2 (0)
Comorbidity: Obesity, during pre-infusion work-up period	86 (11)
Comorbidity: Peptic ulcer, any history	11 (1)
Comorbidity: Psychiatric disturbance requiring consult/treatment, in the last 4 weeks	124 (16)
Comorbidity: Pulmonary disease (moderate), at the time of infusion	127 (16)
Comorbidity: Pulmonary disease (severe), at the time of infusion	80 (10)

Characteristic	N (%)
Comorbidity: Renal disease (moderate/severe), at the time of infusion or prior renal transplant	31 (4)
Comorbidity: Rheumatologic disease, any history	10 (1)
Comorbidity: Prior malignancy, treated at any time in the past	116 (15)
Comorbidity: Breast cancer	22 (3)
Comorbidity: Central nervous system malignancy	1 (0)
Comorbidity: Genitourinary malignancy	36 (5)
Comorbidity: Leukemia (including acute or chronic leukemia)	4 (1)
Comorbidity: Lung cancer	1 (0)
Comorbidity: Lymphoma (including Hodgkin & non-Hodgkin lymphoma)	1 (0)
Comorbidity: MDS/MPN	1 (0)
Comorbidity: Melanoma	11 (1)
Comorbidity: Multiple myeloma/plasma cell disorder (PCD)	4 (1)
Comorbidity: Oropharyngeal cancer	1 (0)
Comorbidity: Sarcoma	2 (0)
Comorbidity: Thyroid cancer	6 (1)
Comorbidity: Other skin malignancy (basal cell, squamous)	38 (5)
Comorbidity: Other solid tumor	1 (0)
Not reported	4 (1)
Disease/indication - no. (%)	
Malignant hematologic disorder	786 (100)
Disease status prior to infusion - no. (%)	
Stringent complete response	3 (0)
Complete response (CR)	8 (1)
Very good partial response (VGPR)	53 (7)
Partial response (PR)	84 (11)
No response (NR) / stable disease (SD)	124 (16)
Progressive disease (PD)	493 (63)
Relapse from CR (Rel) (untreated)	14 (2)
Not reported	7 (1)
Year of CT - no. (%)	

Characteristic	N (%)
2016	1 (0)
2017	3 (0)
2018	59 (8)
2019	72 (9)
2020	91 (12)
2021	331 (42)
2022	229 (29)
Serum creatinine at the time of best response since infusion, value - median (min-max)	1 (0-8)
Time from receiving H4000 baseline form to infusion, days - median (min-max)	29 (-5-1116)
No. of patients with follow-up	786
Follow-up - median (range)	9 (1-53)

[1] Note: Excluded cases with Amyloidosis, Solitary plasmacytoma, Light chain deposition disease, Smoldering myeloma, Plasma cell myeloma, Plasma cell proliferative disorder, and missing sub-disease data (n=22)

Response Summary:

This form is intended to be completed by a physician/researcher for the purpose of proposing a study. Content should not include Personal Identifiable Information (PII) or Protected Health Information (PHI). If you are a patient, do not complete this form. Patients: Contact your healthcare provider immediately for reports of problems with your treatment or problems with products received for your treatment. The CIBMTR uses de-identified data and is unable to associate reported treatment problems, adverse events, or corrections of information with a center, clinical trial, or healthcare provider.

Q1. Study Title

Predictors of efficacy and safety of CAR T-cell therapy in patients with relapsed refractory multiple myeloma

Q2. Key Words

efficacy, safety, CAR T-cell therapy, relapsed refractory, multiple myeloma

Q3. PRINCIPAL INVESTIGATOR

Provide the following information for each investigator:

Principal Investigator #1:

First and last name, degree(s):	Hamza Hashmi, M.D.
Email address:	hashmih@musc.edu
Institution name:	Medical University of South Carolina
Academic rank:	Assistant Professor

Q4. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- Yes

Q5. Do you identify as an underrepresented/minority?

- Yes

Q6. Principal Investigator #2 (If applicable):

First and last name, degree(s):	Saad Usmani, M.D.
Email address:	usmanis@mskcc.org
Institution name:	Memorial Sloan Kettering
Academic rank:	Professor

Q7. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- No

Q8. Do you identify as an underrepresented/minority?

- Yes

Q9. 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:

N/A

Q10. If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:

N/A

LETTER OF COMMITMENT:

Please note: *A letter of commitment will be signed by Lead and Last authors as it describes the expectations for filling that role. By signing the letter of commitment, the authors accept their responsibilities and will be held accountable for timely completion of all steps in the project. More details regarding author responsibilities can be found here:* https://www.cibmtr.org/Studies/Observational/StudyManagement/p

Q12. CURRENT ONGOING WORK WITH CIBMTR: Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.

-CIBMTR Study Proposal: Development of comorbidity scores that could impact the treatment related mortality and overall survival in patients receiving CD19 directed CAR T-cell therapy; proposal selected for full study ASTCT 2020-manuscript in preparation
-CIBMTR Study Proposal: Role of CD19 directed CAR T cell therapy for CNS lymphoma; proposal selected for full study ASTCT 2022-manuscript in preparation
-Outcomes of autologous hematopoietic cell transplantation for Light Chain Deposition Disease- proposal selected by the Plasma Cell Disorders and Adult Solid Tumors Working Committee leadership for full study on the annual meeting of the Plasma Cell Disorders Working Committee of the CIBMTR in 2022
-Outcomes of autologous hematopoietic cell transplantation for Multiple Myeloma with plasmacytomas and Macrofocal Multiple Myeloma- selected by the Plasma Cell Disorders and Adult Solid Tumors Working Committee leadership for presentation on the annual meeting of the Plasma Cell Disorders Working Committee of the CIBMTR
-Early versus delayed autologous hematopoietic cell transplantation for Multiple Myeloma patients- selected by the Plasma Cell Disorders and Adult Solid Tumors Working Committee leadership for presentation on the annual meeting of the Plasma Cell Disorders Working Committee of the CIBMTR

Q13. PROPOSED WORKING COMMITTEE:

- Plasma Cell Disorders

Q14. Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.

- No

Q15. RESEARCH QUESTION:

Determine the predictors of safety and efficacy of CAR T cell therapy in relapsed refractory multiple myeloma in the real world

Q16. RESEARCH HYPOTHESIS:

Patient-, disease-, CAR T-cell therapy related factors impact safety and efficacy of CAR T cell therapy in relapsed refractory multiple myeloma in the real world

Q17. SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.) *Suggested word limit of 200 words:*

Determine the impact of patient-, disease-, CAR T-cell therapy related factors on the safety (CRS, ICANS, cytopenias, infections) and efficacy (overall response rate, complete response, progression free survival) of CAR T-cell therapy.

Q18. SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.

This study may help identify potentially modifiable patient, disease, CAR T related factors that can improve the efficacy and safety of CAR T-cell therapy, allow for better patient selection and counseling, and explore new strategies to mitigate CAR T related toxicities in high risk patient populations.

Q19. 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.

Based on KarMMa trial, determinants of efficacy [overall response] included R-ISS stage and CAR T-cell dose. Similarly, higher CAR T dose was associated with worse toxicity profile. Patients who achieved deep responses (MRD negative sCR) achieved more durable remissions. Whether that holds true in the real-world settings where CAR T-cell therapy is given at a dose of 300-450 million cells per kilogram remains unknown. This study may help identify modifiable patient, disease, CAR T-cells related factors that can improve the efficacy and safety of CAR T-cell therapy, allow for better patient selection and counseling, and explore new strategies to mitigate CAR T related toxicities in high risk patient populations.

Q19a. SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF)

N/A

Q20. PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.

Patient with relapsed refractory multiple myeloma having received either idecabtagene vicleucel or ciltacabtagene autoleucel

Q21. Does this study include pediatric patients?

- No

Q21a. If this study does not include pediatric patients, please provide justification:

Multiple Myeloma is not seen in pediatric patient population

Q22. DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Data collection forms available at: http://www.cibmtr.org/DataManagement/DataCollectior Outline any supplementary data required. Additional data collection is extremely difficult and will make your proposal less feasible.

Patient related:
• Age at CAR T-cell therapy
• Gender: male vs. female
• Race: Caucasian vs. African American vs. vs. Hispanic
• Ethnicity: Hispanic or Latino vs. Non-Hispanic or non-Latino vs. non-resident of the U.S.
• ECOG Performance status: 0 vs 1-2 vs 3+
• renal function [GFR 30-60, GFR 15-30, GFR less than 15, ESRD on hemodialysis]
Disease-related:
• Myeloma subtype: IgG versus IgA versus IgM versus light chain [kappa versus lambda] vs non- secretory
• Diagnosis of plasma cell leukemia: primary vs secondary
• Secondary involvement with AL amyloidosis
• High risk disease [del 17, t(4; 14), t(14; 16)]
• R-ISS at CAR-T infusion
• Number of prior lines of chemotherapy
• Response to prior therapy [lenalidomide, pomalidomide, bortezomib, carfilzomib, daratumumab]: Exposed versus refractory
• Triple class exposed
• Triple class refractory
• Penta class exposed
• Penta class refractory
• Prior autologous transplant
• Extramedullary disease at referral
• Bone marrow plasma cell percentage prior to infusion
• Disease status at referral
• Disease status prior to infusion
• Baseline markers of inflammation (ferritin, CRP) prior to infusion
• Exposure to BCMA agent (commercial versus trial)
CAR T-cell therapy related:
• Time from diagnosis to infusion
• Time from leukapheresis to infusion
• Use of bridging therapy
• Type of bridging therapy: Chemotherapy versus radiotherapy versus both chemo and radiotherapy
• Bridging chemotherapy regimen
• CAR-T cell dose
• CRS: grade, onset, duration
• ICANS: grade, onset, duration
• Use of tocilizumab
• Use of corticosteroids
• Persistent cytopenias at day +30 and day +90
• Use of G-CSF
• Use of TPO agonists
• Response at 1 month, 3-month, 6 months, 9 months, 12 months
• Time from infusion to progression
• Date of Death
• Cause of death
• Date of last contact

Q23. **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 specific to PROS.**

For additional information on what PRO measures have been collected and timepoints of collection, please reach out to the Late Effects and Quality of Life or Health Services Working Committee leadership: https://www.cibmtr.org/About/WhoWeAre/Com

NA

Q24. **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 experience with the proposed assay systems. PIs should be encouraged to review the inventory details, sample types collected and reach out to research_repos@nmdp.org with any questions.**

More information can be found at: https://www.cibmtr.org/Samples/Inventory/Pages/index

NA

Q25. NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required, i.e., neither database contains all the data required to answer the study question.

N/A

Q26. REFERENCES:

N/A

Q27. CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning:

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

- No, I do not have any conflicts of interest pertinent to this proposal

Q27a. 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.

N/A

BEFORE FINAL SUBMISSION, please review the PI checklist to ensure that you have completed all necessary steps. This will increase the likelihood of submitting a feasible and successful proposal.

Embedded Data:

N/A

Response Summary:

This form is intended to be completed by a physician/researcher for the purpose of proposing a study. Content should not include Personal Identifiable Information (PII) or Protected Health Information (PHI). If you are a patient, do not complete this form. Patients: Contact your healthcare provider immediately for reports of problems with your treatment or problems with products received for your treatment. The CIBMTR uses de-identified data and is unable to associate reported treatment problems, adverse events, or corrections of information with a center, clinical trial, or healthcare provider.

Q1. Study Title

Predictors of early progression after CAR-T cell therapy for relapsed refractory multiple myeloma

Q2. Key Words

Progression, CAR T-cell therapy, relapsed refractory, multiple myeloma

Q3. PRINCIPAL INVESTIGATOR

Provide the following information for each investigator:

Principal Investigator #1:

First and last name, degree(s):	Hamza Hashmi, M.D.
Email address:	hashmih@musc.edu
Institution name:	Medical University of South Carolina
Academic rank:	Assistant Professor

Q4. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- Yes

Q5. Do you identify as an underrepresented/minority?

- Yes

Q6. Principal Investigator #2 (If applicable):

First and last name, degree(s):	Saad Usmani, M.D.
Email address:	usmanis@mskcc.org
Institution name:	Memorial Sloan Kettering
Academic rank:	Professor

Q7. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- No

Q8. Do you identify as an underrepresented/minority?

- Yes

Q9. 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:

N/A

Q10. If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:

N/A

LETTER OF COMMITMENT:

Please note: *A letter of commitment will be signed by Lead and Last authors as it describes the expectations for filling that role. By signing the letter of commitment, the authors accept their responsibilities and will be held accountable for timely completion of all steps in the project. More details regarding author responsibilities can be found here:* *https://www.cibmtr.org/Studies/Observational/StudyManagement/p*

Q12. CURRENT ONGOING WORK WITH CIBMTR: Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.

-CIBMTR Study Proposal: Development of comorbidity scores that could impact the treatment related mortality and overall survival in patients receiving CD19 directed CAR T-cell therapy; proposal selected for full study ASTCT 2020-manuscript in preparation
-CIBMTR Study Proposal: Role of CD19 directed CAR T cell therapy for CNS lymphoma; proposal selected for full study ASTCT 2022-manuscript in preparation
-Outcomes of autologous hematopoietic cell transplantation for Light Chain Deposition Disease- proposal selected by the Plasma Cell Disorders and Adult Solid Tumors Working Committee leadership for full study on the annual meeting of the Plasma Cell Disorders Working Committee of the CIBMTR in 2022
-Outcomes of autologous hematopoietic cell transplantation for Multiple Myeloma with plasmacytomas and Macrofocal Multiple Myeloma- selected by the Plasma Cell Disorders and Adult Solid Tumors Working Committee leadership for presentation on the annual meeting of the Plasma Cell Disorders Working Committee of the CIBMTR
-Early versus delayed autologous hematopoietic cell transplantation for Multiple Myeloma patients- selected by the Plasma Cell Disorders and Adult Solid Tumors Working Committee leadership for presentation on the annual meeting of the Plasma Cell Disorders Working Committee of the CIBMTR

Q13. PROPOSED WORKING COMMITTEE:

- Plasma Cell Disorders

Q14. Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.

- No

Q15. RESEARCH QUESTION:

Determine predictors of early progression after CAR-T cell therapy for relapsed refractory multiple myeloma

Q16. RESEARCH HYPOTHESIS:

Exposure to previous B Cell Maturation Antigen targeting therapy is predictive of early relapse after CAR-T cell therapy

Q17. SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.)

Suggested word limit of 200 words:

Determine predictors of progression within 1, 3 and 6 months after CAR-T cell infusion

Q18. SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.

The study will help identify potentially modifiable risk factors that impact early progression after CAR T-cell therapy and measures can be taken to avoid these risk factors prior to CAR-T infusion.

Q19. 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 has emerged as an option for relapsed/refractory multiple myeloma patients that have failed 4 prior lines of therapy. Median progression free survival after idecabtagene vicleucel (Ide-cel) for relapsed refractory multiple myeloma was 8.9 months. The purpose of our study is to identify factors that may predict failure, particularly early progression, within the first 6 month after infusion. If any modifiable risk factors are identified, measures can be taken to avoid these risk factors prior to CAR-T infusion.

Q19a. SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF)

N/A

Q20. PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.

Patient with relapsed refractory multiple myeloma having received idecabtagene vicleucel

Q21. Does this study include pediatric patients?

- No

Q21a. If this study does not include pediatric patients, please provide justification:

MM is not seen in pediatric patient population

Q22. DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Data collection forms available at: http://www.cibmtr.org/DataManagement/DataCollectior Outline any supplementary data required. Additional data collection is extremely difficult and will make your proposal less feasible.

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

Q23. **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 specific to PROS.**

For additional information on what PRO measures have been collected and timepoints of collection, please reach out to the Late Effects and Quality of Life or Health Services Working Committee leadership: https://www.cibmtr.org/About/WhoWeAre/Com

NA

Q24. **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 experience with the proposed assay systems. PIs should be encouraged to review the inventory details, sample types collected and reach out to research_repos@nmdp.org with any questions.**

More information can be found at: https://www.cibmtr.org/Samples/Inventory/Pages/index

NA

Q25. NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required, i.e., neither database contains all the data required to answer the study question.

NA

Q26. REFERENCES:

Munshi NC, Anderson LD, Jr., Shah N, et al: Idecabtagene Vicleucel in Relapsed and Refractory Multiple Myeloma. N Engl J Med 384:705-716, 2021

Raje N, Berdeja J, Lin Y, et al: Anti-BCMA CAR T-Cell Therapy bb2121 in Relapsed or Refractory Multiple Myeloma. N Engl J Med 380:1726-17

Lee DW, Santomasso BD, Locke FL, et al: ASTCT Consensus Grading for Cytokine Release Syndrome and Neurologic Toxicity Associated with Immune Effector Cells. Biol Blood Marrow Transplant 25:625-638, 2019

Berdeja JG, Madduri D, Usmani SZ, et al: Ciltacabtagene autoleucel, a B-cell maturation antigen-directed chimeric antigen receptor T-cell therapy in patients with relapsed or refractory multiple myeloma (CARTITUDE-1): a phase 1b/2 open-label study. Lancet 398:314-324, 2021

Martin T, Usmani SZ, Berdeja JG, et al: Ciltacabtagene Autoleucel, an Anti-B-cell Maturation Antigen Chimeric Antigen Receptor T-Cell Therapy, for Relapsed/Refractory Multiple Myeloma: CARTITUDE-1 2-Year Follow-Up. J Clin Oncol:Jco2200842, 2022

Q27. CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning:

1. Employment (such as an independent contractor, consultant or providing expert testimony)?

2. Relationships (such as executive and advisory committee positions, medical consultant, speaker's bureau)?

3. Ownership (such as equity, ownership or financial interests)?

4. Transactions (such as honoraria, patents, royalties and licenses)?

5. Legal (such as pending or current arbitration or legal proceedings)?

- No, I do not have any conflicts of interest pertinent to this proposal

Q27a. 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.

N/A

BEFORE FINAL SUBMISSION, please review the PI checklist to ensure that you have completed all necessary steps. This will increase the likelihood of submitting a feasible and successful proposal.

Embedded Data:

N/A

Response Summary:

This form is intended to be completed by a physician/researcher for the purpose of proposing a study. Content should not include Personal Identifiable Information (PII) or Protected Health Information (PHI). If you are a patient, do not complete this form. Patients: Contact your healthcare provider immediately for reports of problems with your treatment or problems with products received for your treatment. The CIBMTR uses de-identified data and is unable to associate reported treatment problems, adverse events, or corrections of information with a center, clinical trial, or healthcare provider.

Q1. Study Title

Determinants of outcomes after chimeric antigen receptor T-cell therapy for multiple myeloma.

Q2. Key Words

multiple myeloma; chimeric antigen receptor T-cell therapy

Q3. PRINCIPAL INVESTIGATOR

Provide the following information for each investigator:

Principal Investigator #1:

First and last name, degree(s):	Baldeep Wirk, M.D.
Email address:	bmwirk@gmail.com
Institution name:	Penn State Cancer Institute
Academic rank:	Associate Professor

Q4. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- No

Q5. Do you identify as an underrepresented/minority?

- Yes

Q6. Principal Investigator #2 (If applicable):

First and last name, degree(s):	N/A
Email address:	N/A
Institution name:	N/A
Academic rank:	N/A

Q7. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

N/A

Q8. Do you identify as an underrepresented/minority?

N/A

Q9. 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:

N/A

Q10. If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:

N/A

LETTER OF COMMITMENT:

Please note: *A letter of commitment will be signed by Lead and Last authors as it describes the expectations for filling that role. By signing the letter of commitment, the authors accept their responsibilities and will be held accountable for timely completion of all steps in the project. More details regarding author responsibilities can be found here:* *https://www.cibmtr.org/Studies/Observational/StudyManagement/p*

Q12. CURRENT ONGOING WORK WITH CIBMTR: Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.

LK 22-01 approved study: I am one of the principal co-investigators.

Q13. PROPOSED WORKING COMMITTEE:

- Plasma Cell Disorders

Q14. Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.

- No

Q15. RESEARCH QUESTION:

What are the determinants of response, relapse, and survival after chimeric antigen receptor T cells for multiple myeloma?

Q16. RESEARCH HYPOTHESIS:

Analysis of patient, disease, and treatment-related variables will identify factors predicting remission, relapse, and survival after CAR T cell therapy for multiple myeloma.

Q17. SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.)

Suggested word limit of 200 words:

Primary aims:
1. identify the determinants of overall survival in multiple myeloma patient after CAR T-cell therapy
2. determine the factors associated with disease-free survival and risk of relapse in multiple myeloma patients after CAR T cell therapy

Secondary aims:
3. analyze the outcomes of patients receiving CAR T cell therapy after previous hematopoietic cell transplant
4. determine the rate of hematopoietic cell transplant after CAR T-cell therapy

Q18. SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.

This study will improve
-risk stratification of patients so as to offer tailored therapy to patients.
–knowledge on how to integrate CAR T cell therapy into current multiple myeloma management algorithms.
-identification of optimal candidates for CAR T cell therapy
- identification of factors impacting outcomes of CAR T cell therapy that could be modified.
-identification of patients benefiting from consolidation therapy after CAR T cell therapy
-understanding of the long-term outcomes of CAR T cell therapy.

Q19. 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 FDA has approved idecabtagene vicleucel (idecel)for adult multiple myeloma patients with relapsed and refractory multiple myeloma after four or more lines of therapy, including an immunomodulatory agent, proteasome inhibitor, and anti-CD38 antibody or triple refractory multiple myeloma. Ciltacabtagene autoleucel is also FDA approved in relapsed multiple myeloma.

Triple refractory multiple myeloma has a poor prognosis with current standard chemotherapy options offering a 3 to 4-month progression-free survival and 8-month overall survival [1]. However, ide-cel in the KarMMa study for triple refractory multiple myeloma patients had a complete remission rate of 33% [2]. Those patients who achieved complete remission had a median progression-free survival of 8.8 months. However, not all multiple myeloma patients achieve complete remission after CAR t cell therapy, and there was no plateau on the survival curve, in contrast to CD19 CAR T cell therapy in acute lymphoblastic leukemia.

The determinants of response and acquired resistance to CAR T cell therapy in multiple myeloma are unknown. For example, the impact of cytogenetics is unknown due to the small numbers of patients in most studies with limited data on response duration [2]. Also, in some but not other studies, extramedullary disease was associated with poor outcomes after CAR T cell therapy [2, 3]. The optimal CAR T cell therapy ide-cel or ciltacel, for example, is unknown. The larger CIBMTR database with real-world data will clarify the determinants of outcomes after CAR T cell therapy. Results of this study will help clinicians to integrate CAR T cell therapy into current multiple myeloma management algorithms and identify optimal candidates for CAR T cell therapy.

Q19a. SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF)

N/A

Q20. PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.

Participant Selection Criteria:
All patients of any age with multiple myeloma who receive CAR T cell therapy
Data requirements
Patient related:
Age years
Gender: male versus female
Karnofsky performance score: ≥90 or <90
Race: White vs. Black vs. Asian/Pacific Islander vs. Hispanics vs Others
HCT-CI: 0-2 versus 3 or more
Disease related:
Stage: Durie-Salmon stage I, III, III A or B; ISS stage I versus II versus III; R-ISS stage I versus II versus III
Monoclonal antibody: IgG, IgA, IgM, IgD, light chain only kappa or lambda
Cytogenetic abnormalities: +1q, del 1p, t(11;14), del 17p, t(4;14), t(14;16), t(14;20), del 13, complex cytogenetics, trisomy 5,9,15; myc rearrangement, hyperdiploidy, hypodiploidy
Number of lines of previous therapies, 1, 2, 3, 4, 5 or more
Types of prior therapy: immunomodulatory agent lenalidomide pomalidomide, proteasome inhibitor bortezomib carfilzomib, anti-CD38 antibody daratumumab isatuximab, elotuzumab
Previous autologous HCT: yes versus no; if yes then either 1 or 2 prior autologous HCT
Previous allogeneic HCT: yes versus no
Refractory status: yes versus no; refractory to IMiD and proteasome inhibitor; refractory to IMiD, proteasome inhibitor and anti-CD38 antibody; refractory to lenalidomide, pomalidomide, bortezomib, carfilzomib and daratumumab.
Bone marrow percentage plasma cells at CAR T cell infusion:
PET CT showed extramedullary plasmacytomas: yes versus no
CAR T cell therapy related:
Type of CAR T cell:
Bridging therapy: yes versus no: if yes then type—including lenalidomide, pomalidomide
Adverse events: CRS, ICANS, cytopenias
After CAR T cell therapy: subsequent allogeneic HCT yes versus no
CAR T cell cell dose:

Q21. Does this study include pediatric patients?

- Yes

Q22. DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Data collection forms available at: http://www.cibmtr.org/DataManagement/DataCollectior Outline any supplementary data required. Additional data collection is extremely difficult and will make your proposal less feasible.

None

Q23. **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 specific to PROS.**

For additional information on what PRO measures have been collected and timepoints of collection, please reach out to the Late Effects and Quality of Life or Health Services Working Committee leadership: https://www.cibmtr.org/About/WhoWeAre/Com

none

Q24. **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 experience with the proposed assay systems. PIs should be encouraged to review the inventory details, sample types collected and reach out to research_repos@nmdp.org with any questions.**

More information can be found at: https://www.cibmtr.org/Samples/Inventory/Pages/index

none

Q25. NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required, i.e., neither database contains all the data required to answer the study question.

none

Q26. REFERENCES:

1. Gandhi UH, Cornell RF, Lakshman A, et al. Outcomes of patients with multiple myeloma refractory to CD38-targeted monoclonal antibody therapy. Leukemia. 2019; 33: 2266-75.
2. Munshi N, Anderson LD, Shah N, et al. Idecabtagene vicleucel in relapsed and refractory multiple myeloma. New Engl J Med 2021; 384: 705- 716.
3. Xu J, Chen LJ, Yang SS, et al. Exploratory trial of a biepitopic CAR T-targeting B cell maturation antigen in relapsed/refractory multiple myeloma. Proc Natl Acad Sci U S A 2019;116:9543–51.

Q27. CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning:

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

- No, I do not have any conflicts of interest pertinent to this proposal

Q27a. **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.**

N/A

BEFORE FINAL SUBMISSION, please review the PI checklist to ensure that you have completed all necessary steps. This will increase the likelihood of submitting a feasible and successful proposal.

Embedded Data:

N/A

Table. Patients who received first CAR-T infusion between 2016 - 2022 for Multiple Myeloma, with follow-up reported to CIBMTR

Characteristic	N (%)
No. of patients[1]	786
No. of centers	73
Age at infusion, yrs - median (min-max)	64 (29-86)
Age at infusion, by category #1 - no. (%)	
20 - 29 years	2 (0)
30 - 39 years	13 (2)
40 - 49 years	58 (7)
50 - 59 years	200 (25)
60 - 69 years	330 (42)
70+ years	183 (23)
Age at infusion, by category #2 - no. (%)	
18 - 39	15 (2)
40 - 65	407 (52)
65+	364 (46)
Age at Infusion, by category #3 - no. (%)	
>=18 years	786 (100)
Age at infusion, by category #4 - no. (%)	
0 - 64	422 (54)
65+	364 (46)
Gender - no. (%)	
Male	468 (60)
Female	314 (40)
Not reported	4 (1)
Recipient race - no. (%)	
White	624 (79)
Black or African American	102 (13)
Asian	20 (3)
Native Hawaiian or other Pacific Islander	1 (0)
American Indian or Alaska Native	3 (0)
Other	5 (1)
More than one race	11 (1)
Not reported	20 (3)
Recipient ethnicity - no. (%)	
Hispanic or Latino	51 (6)
Not Hispanic or Latino	710 (90)

Characteristic	N (%)
Non-resident of the U.S.	12 (2)
Unknown	13 (2)
Country - no. (%)	
US	765 (97)
Other	21 (3)
Karnofsky performance score prior to CT - no. (%)	
90-100	291 (37)
80	268 (34)
< 80	147 (19)
Not reported	80 (10)
ECOG performance status prior to CT - no. (%)	
0 - Asymptomatic	291 (37)
1 - Symptomatic but completely ambulatory	382 (49)
2 - Symptomatic, < 50% in bed during the day	29 (4)
3 - Symptomatic, > 50% in bed, but not bedbound	3 (0)
4 - Bedbound	1 (0)
Not reported	80 (10)
Body mass index (BMI) category at infusion - no. (%)	
< 18.5 - Underweight	14 (2)
>= 18.5 to < 25 - Normal	224 (28)
>= 25 to < 30 - Overweight	288 (37)
>= 30 - Obese	238 (30)
Not reported	22 (3)
Sub-disease for CT - no. (%)	
Multiple myeloma, NOS	501 (64)
Plasma cell leukemia	11 (1)
Multiple myeloma - IgG	54 (7)
Multiple myeloma - IgA	23 (3)
Multiple myeloma - light chain only	180 (23)
Multiple myeloma - non-secretory	17 (2)
Diagnosis	
Age at initial diagnosis - median (min-max)	57 (25-85)
ISS stage at diagnosis - no. (%)	
1 (beta2-mic < 3.5, albumin >= 3.5)	202 (26)
2 (Not fitting stage 1 or 3)	170 (22)
3 (beta2-mic >= 5.5, regardless of albumin)	160 (20)
Not reported	254 (32)
R-ISS stage at diagnosis - no. (%)	

Characteristic	N (%)
1 (ISS stage I and standard-risk abnormalities by iFISH and normal LDH)	62 (8)
2 (Not R-ISS stage I or III)	188 (24)
3 (ISS stage III and either high-risk chromosomal abnormalities by iFISH or high LDH)	78 (10)
Not reported	458 (58)
Serum creatinine at diagnosis, value - median (min-max)	1 (0-1493)
Time from initial diagnosis to CT - no. (%)	
Median (min-max)	66 (0-324)
>= 0 to < 12 months	39 (5)
>= 12 to < 36 months	131 (17)
>= 36 to < 60 months	185 (24)
>= 60 months	431 (55)
Lymphodepleting regimen - no. (%)	
Yes	779 (99)
Lymphodepleting chemotherapy: bendamustine	3 (0)
Lymphodepleting chemotherapy: cyclophosphamide	3 (0)
Lymphodepleting chemotherapy: cyclophosphamide + Lymphodepleting chemotherapy: cytarabine + Lymphodepleting chemotherapy: fludarabine	1 (0)
Lymphodepleting chemotherapy: cyclophosphamide + Lymphodepleting chemotherapy: fludarabine	761 (97)
Lymphodepleting chemotherapy: cyclophosphamide + Lymphodepleting chemotherapy: fludarabine + Lymphodepleting chemotherapy: other	4 (1)
Lymphodepleting chemotherapy: cyclophosphamide + Lymphodepleting chemotherapy: thiotepa	1 (0)
Lymphodepleting chemotherapy: fludarabine	3 (0)
Lymphodepleting chemotherapy: other	1 (0)
None specified	2 (0)
No	7 (1)
Commercial vs. noncommercial CAR-T product - no. (%)	

Characteristic	N (%)
Commercial	501 (64)
Noncommercial	285 (36)
Clinical trial - no. (%)	
No	499 (63)
Yes	287 (37)
CAR-T Product type (Other - specify) - no. (%)	
Abecma	468 (60)
Carvykti	33 (4)
Other	285 (36)
Non-commercial Idecabtagene vicleucel	84 (11)
Non-commercial Ciltacabtagene autoleucel	14 (2)
Non-commercial Orvacabtagene autoleucel	1 (0)
Non-commercial - No product name	9 (1)
Non-commercial - Other product	94 (12)
Non-commercial - Product name not reported	83 (11)
Prior transplants and therapies	
Types of prior HCTs - no. (%)	
No	78 (10)
Yes	707 (90)
Prior allo-HCT	8 (1)
Prior auto-HCT	668 (85)
Prior auto and allo-HCT	23 (3)
Not reported	8 (1)
Unknown	1 (0)
Total number of prior HCTs - no. (%)	
0	78 (10)
1	508 (65)
2	139 (18)
3	17 (2)
4	1 (0)
Not reported	43 (5)
Prior CT - no. (%)	
No	766 (97)
Yes	20 (3)
CT infusion counting number - no. (%)	
1	777 (99)
2	8 (1)
3	1 (0)

Characteristic	N (%)
Time from prior HCT to CT, months - median (min-max)	
No prior HCT	NE
Prior allo-HCT	36 (9-176)
Prior auto-HCT	46 (0-250)
Prior auto and allo-HCT	51 (5-159)
Time from the latest prior HCT to current CT, days - median (min-max)	1407 (14-7601)
Clinically significant co-existing diseases or organ impairment	
Clinically significant comorbidity prior to CT - no. (%)	
No	256 (33)
Yes	526 (67)
Comorbidity: Arrhythmia, any history	83 (11)
Comorbidity: Cardiac, any history	94 (12)
Comorbidity: Cerebrovascular disease, any history	23 (3)
Comorbidity: Diabetes requiring non-diet treatment, in the last 4 week	93 (12)
Comorbidity: Heart valve disease	19 (2)
Comorbidity: Hepatic disease (mild), any history or at the time of infusion	38 (5)
Comorbidity: Hepatic disease (moderate/severe), any history or at the time of infusion	12 (2)
Comorbidity: Infection requiring antimicrobial treatment, continuation after day 0	36 (5)
Comorbidity: Inflammatory bowel disease, any history	2 (0)
Comorbidity: Obesity, during pre-infusion work-up period	86 (11)
Comorbidity: Peptic ulcer, any history	11 (1)
Comorbidity: Psychiatric disturbance requiring consult/treatment, in the last 4 weeks	124 (16)
Comorbidity: Pulmonary disease (moderate), at the time of infusion	127 (16)
Comorbidity: Pulmonary disease (severe), at the time of infusion	80 (10)

Characteristic	N (%)
Comorbidity: Renal disease (moderate/severe), at the time of infusion or prior renal transplant	31 (4)
Comorbidity: Rheumatologic disease, any history	10 (1)
Comorbidity: Prior malignancy, treated at any time in the past	116 (15)
Comorbidity: Breast cancer	22 (3)
Comorbidity: Central nervous system malignancy	1 (0)
Comorbidity: Genitourinary malignancy	36 (5)
Comorbidity: Leukemia (including acute or chronic leukemia)	4 (1)
Comorbidity: Lung cancer	1 (0)
Comorbidity: Lymphoma (including Hodgkin & non-Hodgkin lymphoma)	1 (0)
Comorbidity: MDS/MPN	1 (0)
Comorbidity: Melanoma	11 (1)
Comorbidity: Multiple myeloma/plasma cell disorder (PCD)	4 (1)
Comorbidity: Oropharyngeal cancer	1 (0)
Comorbidity: Sarcoma	2 (0)
Comorbidity: Thyroid cancer	6 (1)
Comorbidity: Other skin malignancy (basal cell, squamous)	38 (5)
Comorbidity: Other solid tumor	1 (0)
Not reported	4 (1)
Disease/indication - no. (%)	
Malignant hematologic disorder	786 (100)
Disease status prior to infusion - no. (%)	
Stringent complete response	3 (0)
Complete response (CR)	8 (1)
Very good partial response (VGPR)	53 (7)
Partial response (PR)	84 (11)
No response (NR) / stable disease (SD)	124 (16)
Progressive disease (PD)	493 (63)
Relapse from CR (Rel) (untreated)	14 (2)
Not reported	7 (1)
Year of CT - no. (%)	

Characteristic	N (%)
2016	1 (0)
2017	3 (0)
2018	59 (8)
2019	72 (9)
2020	91 (12)
2021	331 (42)
2022	229 (29)
Serum creatinine at the time of best response since infusion, value - median (min-max)	1 (0-8)
Time from receiving H4000 baseline form to infusion, days - median (min-max)	29 (-5-1116)
No. of patients with follow-up	786
Follow-up - median (range)	9 (1-53)

[1] Note: Excluded cases with Amyloidosis, Solitary plasmacytoma, Light chain deposition disease, Smoldering myeloma, Plasma cell myeloma, Plasma cell proliferative disorder, and missing sub-disease data (n=22)

Response Summary:

This form is intended to be completed by a physician/researcher for the purpose of proposing a study. Content should not include Personal Identifiable Information (PII) or Protected Health Information (PHI). If you are a patient, do not complete this form. Patients: Contact your healthcare provider immediately for reports of problems with your treatment or problems with products received for your treatment. The CIBMTR uses de-identified data and is unable to associate reported treatment problems, adverse events, or corrections of information with a center, clinical trial, or healthcare provider.

Q1. Study Title

Outcomes of autologous hematopoietic cell transplantation for Macrofocal Multiple Myeloma

Q2. Key Words

autologous, hematopoietic cell transplantation, Macrofocal, Multiple Myeloma

Q3. PRINCIPAL INVESTIGATOR

Provide the following information for each investigator:

Principal Investigator #1:

First and last name, degree(s):	Hamza Hashmi
Email address:	hashmih@musc.edu
Institution name:	Medical University of South Carolina
Academic rank:	Assistant Professor

Q4. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- Yes

Q5. Do you identify as an underrepresented/minority?

- Yes

Q6. Principal Investigator #2 (If applicable):

First and last name, degree(s):	N/A
Email address:	N/A
Institution name:	N/A
Academic rank:	N/A

Q7. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

N/A

Q8. Do you identify as an underrepresented/minority?

N/A

Q9. 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:

N/A

Q10. If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:

- Yes, I am a junior investigator and would like assistance identifying a senior mentor for my project

LETTER OF COMMITMENT:

Please note: *A letter of commitment will be signed by Lead and Last authors as it describes the expectations for filling that role. By signing the letter of commitment, the authors accept their responsibilities and will be held accountable for timely completion of all steps in the project. More details regarding author responsibilities can be found here:* *https://www.cibmtr.org/Studies/Observational/StudyManagement/p*

Q12. CURRENT ONGOING WORK WITH CIBMTR: Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.

-CIBMTR Study Proposal: Development of comorbidity scores that could impact the treatment related mortality and overall survival in patients receiving CD19 directed CAR T-cell therapy; proposal selected for full study ASTCT 2020-manuscript in preparation
-CIBMTR Study Proposal: Role of CD19 directed CAR T cell therapy for CNS lymphoma; proposal selected for full study ASTCT 2022-manuscript in preparation
-Outcomes of autologous hematopoietic cell transplantation for Light Chain Deposition Disease- proposal selected by the Plasma Cell Disorders and Adult Solid Tumors Working Committee leadership for full study on the annual meeting of the Plasma Cell Disorders Working Committee of the CIBMTR in 2022
-Outcomes of autologous hematopoietic cell transplantation for Multiple Myeloma with plasmacytomas and Macrofocal Multiple Myeloma- selected by the Plasma Cell Disorders and Adult Solid Tumors Working Committee leadership for presentation on the annual meeting of the Plasma Cell Disorders Working Committee of the CIBMTR
-Early versus delayed autologous hematopoietic cell transplantation for Multiple Myeloma patients- selected by the Plasma Cell Disorders and Adult Solid Tumors Working Committee leadership for presentation on the annual meeting of the Plasma Cell Disorders Working Committee of the CIBMTR

Q13. PROPOSED WORKING COMMITTEE:

- Plasma Cell Disorders

Q14. Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.

- No

Q15. RESEARCH QUESTION:

Does autologous stem cell transplantation (ASCT) results in long-term disease control for macrofocal multiple myeloma?

Q16. RESEARCH HYPOTHESIS:

Autologous stem cell transplantation (ASCT) results in long-term disease control for macrofocal multiple myeloma

Q17. SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.)

Suggested word limit of 200 words:

1. To determine overall survival (OS) after autologous ASCT for macrofocal multiple myeloma
2. To determine disease response [hematological], progression-free survival (PFS), transplant-related mortality (TRM), cumulative incidence of relapse after ASCT for macrofocal multiple myeloma

Q18. SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.

There is limited data available on the outcomes of ASCT for macrofocal multiple myeloma. This retrospective study will evaluate the outcomes of ASCT for macrofocal multiple myeloma
to understand the optimal application of ASCT as a treatment modality. This study could identify patient- or disease-related factors that may impact the clinical management of macrofocal multiple myeloma, outcomes of ASCT for this patient population, and could lead to future novel research on improving the transplant outcomes.

Q19. 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.

Macrofocal multiple myeloma is described as a distinct entity of multiple myeloma which is characterized by young age, multiple lytic lesions, limited bone marrow involvement, absence of anemia, renal insufficiency or hypercalcemia (1-4). Retrospective studies has shown that macrofocal multiple myeloma when compared with typical symptomatic multiple myeloma tends to have lower tumor burden, higher frequency of extra medullary plasmacytomas, and better long-term survival (3-4).
Higher level evidence based therapeutic recommendations are lacking in largely due to its relative rarity, lack of large-sized retrospective data and excellent outcomes associated with frontline therapy. Using the CIBMTR data; we can describe incidence, characteristics, and outcomes of ASCT in a large cohort of patients from multiple centers, and compare these outcomes with typical multiple myeloma undergoing ASCT [historical cohort]. This will have meaningful impact on disease prognostication, patient counseling, patient selection prior to ASCT, and long-term outcomes

Q19a. SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF)

N/A

Q20. PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.

Inclusion Criteria:
Adult patients (age>18 years) who received ASCT for macrofocal multiple myeloma from 2000 to 2018
Exclusion criteria:
None

Q21. Does this study include pediatric patients?

- No

Q21a. If this study does not include pediatric patients, please provide justification:

MM is not seen in pediatric patient population

Q22. DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Data collection forms available at: http://www.cibmtr.org/DataManagement/DataCollectior Outline any supplementary data required. Additional data collection is extremely difficult and will make your proposal less feasible.

Variables to be described: (variables to be included in the multivariate analysis are bolded)
• Age at diagnosis: continuous and separated by decades
• Age at transplant: continuous and separated by decades
• Gender: male vs. female
• Race: Caucasian vs. African American vs. Asian/Pacific Islander vs. Hispanic vs. Others vs. missing
• Ethnicity: Hispanic or Latino vs. Non-Hispanic or non-Latino vs. non-resident of the U.S.
• Karnofsky performance status at transplant: <90% vs. ≥90%
• Comorbidity index 0 vs. 1-2 vs. ≥3
• CD34 cell dose (/recipient body weight)
Disease-related:
• Ig heavy chain: IgG vs IgA vs IgM vs no heavy chain
• Ig light chain: Lambda vs kappa
• International Staging System (ISS) stages: 1 vs 2 vs 3
• Durie-Salmon (DS) Staging System; 1 vs 2 vs 3
• Bone marrow involvement at time of diagnosis: yes vs. no
• Bone marrow involvement by monoclonal plasma cell %:>10% vs 5-10% vs <5%
• Presence of solitary plasamcytoma: yes vs no
• Presence of extramedullary disease: yes vs no
• Disease status (hematological) prior to transplant: Complete response [CR], very good partial response [VGPR], partial response [PR], stable disease [SD] vs progressive disease [PD]
• Number of prior chemotherapy lines: continuous
• Prior treatment: bortezomib-based vs immunomodulatory drugs-based vs both
• Time from diagnosis to transplant: continuous (months)
• Prior radiotherapy: yes vs. no
• Mobilization: G-CSF vs Plerixafor vs chemo-based
• Conditioning regimen: Melphalan 200 mg/m^2 vs melphalan 140 mg/m^2 vs other
• Peri engraftment syndrome: yes vs no
• Secondary myelodysplastic syndrome/leukemia: yes vs no

Q23. **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 specific to PROS.**

For additional information on what PRO measures have been collected and timepoints of collection, please reach out to the Late Effects and Quality of Life or Health Services Working Committee leadership: https://www.cibmtr.org/About/WhoWeAre/Com

NA

Q24. **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 experience with the proposed assay systems. PIs should be encouraged to review the inventory details, sample types collected and reach out to research_repos@nmdp.org with any questions.**

More information can be found at: https://www.cibmtr.org/Samples/Inventory/Pages/index

NA

Q25. **NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required, i.e., neither database contains all the data required to answer the study question.**

NA

Q26. **REFERENCES:**

N/A

Q27. **CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning:**

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

- No, I do not have any conflicts of interest pertinent to this proposal

Q27a. **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.**

N/A

BEFORE FINAL SUBMISSION, please review the PI checklist to ensure that you have completed all necessary steps. This will increase the likelihood of submitting a feasible and successful proposal.

Embedded Data:

N/A

Response Summary:

This form is intended to be completed by a physician/researcher for the purpose of proposing a study. Content should not include Personal Identifiable Information (PII) or Protected Health Information (PHI). If you are a patient, do not complete this form. Patients: Contact your healthcare provider immediately for reports of problems with your treatment or problems with products received for your treatment. The CIBMTR uses de-identified data and is unable to associate reported treatment problems, adverse events, or corrections of information with a center, clinical trial, or healthcare provider.

Q1. Study Title

Outcomes of autologous hematopoietic cell transplantation for Multiple Myeloma with plasmacytoma(s)

Q2. Key Words

autologous, hematopoietic cell transplantation, Multiple Myeloma, plasmacytomas

Q3. PRINCIPAL INVESTIGATOR

Provide the following information for each investigator:

Principal Investigator #1:

First and last name, degree(s):	Hamza Hashmi, M.D.
Email address:	hashmih@musc.edu
Institution name:	Medical University of South Carolina
Academic rank:	Assistant Professor

Q4. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- Yes

Q5. Do you identify as an underrepresented/minority?

- Yes

Q6. Principal Investigator #2 (If applicable):

First and last name, degree(s):	N/A
Email address:	N/A
Institution name:	N/A
Academic rank:	N/A

Q7. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

N/A

Q8. Do you identify as an underrepresented/minority?

N/A

Q9. 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:

N/A

Q10. If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:

- Yes, I am a junior investigator and would like assistance identifying a senior mentor for my project

LETTER OF COMMITMENT:

Please note: *A letter of commitment will be signed by Lead and Last authors as it describes the expectations for filling that role. By signing the letter of commitment, the authors accept their responsibilities and will be held accountable for timely completion of all steps in the project. More details regarding author responsibilities can be found here:* https://www.cibmtr.org/Studies/Observational/StudyManagement/p

Q12. CURRENT ONGOING WORK WITH CIBMTR: Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.

N/A

Q13. PROPOSED WORKING COMMITTEE:

- Plasma Cell Disorders

Q14. Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.

- No

Q15. RESEARCH QUESTION:

Does Autologous Hematopoietic cell transplantation (AHCT) results in long-term disease control for patients with multiple myeloma with current or previous plasmacytoma(s)?

Q16. RESEARCH HYPOTHESIS:

Autologous Hematopoietic cell transplantation (AHCT) results in long-term disease control for patients with multiple myeloma with current or previous plasmacytoma(s).

Q17. SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.)

Suggested word limit of 200 words:

1. To determine overall survival (OS) after AHCT for multiple myeloma with plasmacytoma(s)
2. To determine disease response [hematological, radiological], progression-free survival (PFS), transplant-related mortality (TRM), cumulative incidence of relapse after AHCT for multiple myeloma with plasmacytoma(s)

Q18. SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.

There is limited data available on the outcomes of AHCT for patients with multiple myeloma and current or previous history of plasmacytoma(s). This retrospective study will evaluate the outcomes of AHCT for patients with multiple myeloma and solitary/multiple plasmacytomas (bony and extramedullary), to understand the optimal application of AHCT as a treatment modality. This study could identify patient- or disease- related factors that may impact the clinical management of multiple myeloma with plasmacytomas, outcomes of AHCT for this patient population, and could lead to future novel research on improving the transplant outcomes.

Q19. 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.

Solitary plasmacytoma is a localized tumor comprised of a single clone of plasma cells in the absence of other features of multiple myeloma (anemia, hypercalcemia, renal insufficiency, or multiple lytic bone lesions) [1, 2]. The primary treatment for patients with solitary plasmacytoma is localized radiation therapy with local response rate of 80 to 90% [3]. However, some patients with solitary plasmacytoma may demonstrate up to 10% clonal plasma cells, and are considered to have a solitary plasmacytoma with minimal marrow involvement [4]. These patients can be treated in a similar manner with radiation therapy but have a higher risk of progression to symptomatic myeloma with a 60% chance of recurrence or progression within three years [5]. Patients may also develop multiple plasmacytomas [2 or more, concurrently or sequentially] without bone marrow involvement [6] and treatment strategies for these patients remain unclear. For patients with recurrent or multiple plasmacytomas or progression to symptomatic multiple myeloma, induction chemotherapy followed by autologous stem cell transplant is well-established treatment strategy.
Outcomes of patients with history of current or prior history of single/multiple or bony/extramedullary plasmacytomas undergoing AHCT has not been studied previously. Using the CIBMTR data; we can describe incidence, characteristics, and outcomes of AHCT in a large cohort of patients from multiple centers, and compare these outcomes with multiple myeloma without current or previous plasmacytomas undergoing AHCT [historical cohort]. This will have meaningful impact on disease prognostication, patient counseling and, patient selection prior to AHCT.

Q19a. SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF)

N/A

Q20. PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.

Inclusion Criteria:
Adult patients (age>18 years) who received AHCT for multiple myeloma with current or previous plasmacytomas (solitary plasmacytoma, solitary plasmacytoma with minimal bone marrow involvement, multiple plasmacytomas without bone marrow involvement) from 2000 to 2018
Exclusion criteria:
None

Q21. Does this study include pediatric patients?

- No

Q21a. If this study does not include pediatric patients, please provide justification:

MM is not seen in pediatric patient population

Q22. DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Data collection forms available at: http://www.cibmtr.org/DataManagement/DataCollectior Outline any supplementary data required. Additional data collection is extremely difficult and will make your proposal less feasible.

Variables to be described:
- Age at diagnosis: continuous and separated by decades
- Age at transplant: continuous and separated by decades
- Gender: male vs. female
- Race: Caucasian vs. African American vs. Asian/Pacific Islander vs. Hispanic vs. Others vs. missing
- Ethnicity: Hispanic or Latino vs. Non-Hispanic or non-Latino vs. non-resident of the U.S.
- Karnofsky performance status at transplant: <90% vs. ≥90%
- Comorbidity index 0 vs. 1-2 vs. ≥3
- CD34 cell dose (/recipient body weight)

Disease-related:
- Presence of solitary plasmacytoma: yes vs no
- Presence of multiple plasmacytomas: 2 vs more than 2
- Presence of extramedullary plasmacytoma: yes vs no
- Bone marrow involvement at time of diagnosis: yes vs. no
- Bone marrow involvement by monoclonal plasma cell %:>10% vs 5-10% vs <5%
- Ig heavy chain: IgG vs IgA vs IgM vs no heavy chain
- Ig light chain: Lambda vs kappa
- Presence of M protein: yes vs no
- Abnormal free light chain ratio: yes vs no
- International Staging System (ISS) stages: 1 vs 2 vs 3
- Revised International Staging System (RISS) stages: 1 vs 2 vs 3
- Durie-Salmon (DS) Staging System; 1 vs 2 vs 3 (A or B)
- Disease status (hematological / radiological) prior to transplant: Complete response [CR], Very good partial response [VGPR], partial response [PR], stable disease [SD] vs progressive disease [PD]
- Number of prior chemotherapy lines: continuous
- Prior treatment: bortezomib-based vs immunomodulatory drugs-based vs both
- Time from diagnosis of plasmacytoma(s) to transplant: continuous (months)
- Time for diagnosis of multiple myeloma to transplant: continuous (months)
- Prior radiotherapy: yes vs. no
- Mobilization: G-CSF vs Plerixafor vs chemo-based
- Conditioning regimen: Melphalan 200 mg/m^2 vs melphalan 140 mg/m^2 vs other
- Peri engraftment syndrome: yes vs no
- Secondary myelodysplastic syndrome/leukemia: yes vs no
- Post-transplant maintenance: yes vs no

Q23. **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 specific to PROS.**

For additional information on what PRO measures have been collected and timepoints of collection, please reach out to the Late Effects and Quality of Life or Health Services Working Committee leadership: https://www.cibmtr.org/About/WhoWeAre/Com

NA

Q24. **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 experience with the proposed assay systems. PIs should be encouraged to review the inventory details, sample types collected and reach out to research_repos@nmdp.org with any questions.**

More information can be found at: https://www.cibmtr.org/Samples/Inventory/Pages/index

NA

Q25. **NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required, i.e., neither database contains all the data required to answer the study question.**

NA

Q26. **REFERENCES:**

N/A

Q27. **CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning:**

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

- No, I do not have any conflicts of interest pertinent to this proposal

Q27a. **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.**

N/A

BEFORE FINAL SUBMISSION, please review the PI checklist to ensure that you have completed all necessary steps. This will increase the likelihood of submitting a feasible and successful proposal.

Embedded Data:

N/A

Table 1. Characteristics of multiple Myeloma with current or previous plasmacytomas undergoing first autologous stem cell transplant in the US from 2000 to 2019, CRF

Characteristic	N (%)
No. of patients	270
No. of centers	84
Chronological number of this HSCT - no. (%)	
1	270 (100)
Median age (range) - median (min-max)	58 (27-76)
Age at transplant, years - no. (%)	
18-39	16 (6)
40-49	38 (14)
50-59	91 (34)
60-69	99 (37)
70+	26 (10)
Gender - no. (%)	
Male	165 (61)
Female	105 (39)
Region - no. (%)	
US	270 (100)
Race - no. (%)	
White	192 (71)
Black or African American	62 (23)
Asian	4 (1)
American Indian or Alaska Native	2 (1)
Other	5 (2)
Missing	5 (2)
Karnofsky score - no. (%)	
>= 90	156 (58)
< 90	104 (39)
NA, not collected before 2007	10 (4)
HCT-CI - no. (%)	
0	24 (9)
1	16 (6)
2	19 (7)
3	61 (23)
Missing	150 (56)
Bone marrow plasma cells at diagnosis - no. (%)	
<10%	117 (43)

Characteristic	N (%)
>=10%	153 (57)
Bone marrow plasma cells at transplant - no. (%)	
<10%	179 (66)
>=10%	30 (11)
Missing	61 (23)
ISS stage at diagnosis - no. (%)	
ISS stage I	112 (41)
ISS stage II	46 (17)
ISS stage III	17 (6)
Missing	95 (35)
Lines of chemotherapy - no. (%)	
0	2 (1)
1	189 (70)
>=2	76 (28)
Missing	3 (1)
Chemotherapy - no. (%)	
VTD	4 (1)
VRD	69 (26)
VCD	14 (5)
VD	29 (11)
RD	13 (5)
TD	54 (20)
Carfilzomib	1 (0)
VAD/similar	72 (27)
Others	4 (1)
KRD	2 (1)
Daratumumab	3 (1)
Missing	5 (2)
Immunochemical subtype - no. (%)	
IgG	141 (52)
IgA	38 (14)
IgD	2 (1)
IgE	1 (0)
IgM	2 (1)
Light chain	63 (23)
Non-secretory	20 (7)
Unknown Type	3 (1)
Hemoglobin prior to transplant - no. (%)	

Characteristic	N (%)
< 10 g/dl	52 (19)
>= 10 g/dl	215 (80)
Missing	3 (1)
Serum creatinine prior to transplant, mg/dl - no. (%)	
< 2 mg/dl	261 (97)
>= 2 mg/dl	7 (3)
Missing	2 (1)
Conditioning regimen - no. (%)	
Melphalan only	251 (93)
TBI + Melphalan	6 (2)
Other Melphalan based regimen	8 (3)
Others	5 (2)
Melphalan dose in conditioning regimen, mg/m - no. (%)	
MEL 140	63 (23)
MEL 200	199 (74)
Unknown dose	8 (3)
Disease status prior to transplant - no. (%)	
sCR/CR	49 (18)
VGPR	48 (18)
PR	127 (47)
SD	25 (9)
PD/Relapse	13 (5)
Missing	8 (3)
Time from diagnosis to transplant - median (min-max)	8 (3-146)
Time from diagnosis to transplant - no. (%)	
< 6 months	62 (23)
6 - 12 months	148 (55)
12 - 24 months	31 (11)
>= 24 months	29 (11)
Year of transplant - no. (%)	
2000	14 (5)
2001	15 (6)
2002	10 (4)
2003	14 (5)
2004	28 (10)
2005	36 (13)
2006	27 (10)
2007	5 (2)

Characteristic	N (%)
2009	1 (0)
2010	3 (1)
2012	2 (1)
2013	13 (5)
2014	12 (4)
2015	9 (3)
2016	21 (8)
2017	9 (3)
2018	37 (14)
2019	14 (5)
Post-HCT therapy - no. (%)	
No	111 (41)
Yes	107 (40)
Missing	52 (19)
Post-HCT therapy (for current transplant) - no. (%)	
VR +/- other	4 (1)
V +/- other	9 (3)
R +/- other	77 (29)
KR +/- other	3 (1)
Other	14 (5)
No Maintenance	111 (41)
Missing	52 (19)
Follow-up - median (range)	72 (2-207)

Table 2. Characteristics of multiple Myeloma with current or previous plasmacytomas undergoing first autologous stem cell transplant in the US from 2000 to 2019, CRF (stratified by Bone marrow plasma cells at diagnosis)

	Bone marrow plasma cells at diagnosis	
Characteristic	**<10%**	**>=10%**
No. of patients	117	153
No. of centers	57	61
Chronological number of this HSCT - no. (%)		
1	117 (100)	153 (100)
median age (range) - median (min-max)	57 (27-75)	59 (34-76)
Age at transplant, years - no. (%)		
18-39	7 (6)	9 (6)
40-49	18 (15)	20 (13)
50-59	42 (36)	49 (32)
60-69	39 (33)	60 (39)
70+	11 (9)	15 (10)
Gender - no. (%)		
Male	75 (64)	90 (59)
Female	42 (36)	63 (41)
Region - no. (%)		
US	117 (100)	153 (100)
Race - no. (%)		
White	85 (73)	107 (70)
Black or African American	25 (21)	37 (24)
Asian	3 (3)	1 (1)
American Indian or Alaska Native	0 (0)	2 (1)
Other	2 (2)	3 (2)
Missing	2 (2)	3 (2)
Karnofsky score - no. (%)		
>= 90	67 (57)	89 (58)
< 90	46 (39)	58 (38)
NA, not collected before 2007	4 (3)	6 (4)
HCT-CI - no. (%)		
0	10 (9)	14 (9)
1	7 (6)	9 (6)
2	7 (6)	12 (8)
3	24 (21)	37 (24)
Missing	69 (59)	81 (53)

Characteristic	Bone marrow plasma cells at diagnosis <10%	Bone marrow plasma cells at diagnosis >=10%
Bone marrow plasma cells at transplant - no. (%)		
<10%	79 (68)	100 (65)
>=10%	4 (3)	26 (17)
Missing	34 (29)	27 (18)
ISS stage at diagnosis - no. (%)		
ISS stage I	54 (46)	58 (38)
ISS stage II	17 (15)	29 (19)
ISS stage III	5 (4)	12 (8)
Missing	41 (35)	54 (35)
Lines of chemotherapy - no. (%)		
0	2 (2)	0 (0)
1	87 (74)	102 (67)
>=2	28 (24)	48 (31)
Missing	0 (0)	3 (2)
Chemotherapy - no. (%)		
VTD	1 (1)	3 (2)
VRD	30 (26)	39 (25)
VCD	4 (3)	10 (7)
VD	11 (9)	18 (12)
RD	6 (5)	7 (5)
TD	30 (26)	24 (16)
Carfilzomib	1 (1)	0 (0)
VAD/similar	31 (26)	41 (27)
Others	1 (1)	3 (2)
KRD	0 (0)	2 (1)
Daratumumab	0 (0)	3 (2)
Missing	2 (2)	3 (2)
Immunochemical subtype - no. (%)		
IgG	60 (51)	81 (53)
IgA	13 (11)	25 (16)
IgD	1 (1)	1 (1)
IgE	1 (1)	0 (0)
IgM	1 (1)	1 (1)
Light chain	24 (21)	39 (25)
Non-secretory	15 (13)	5 (3)
Unknown Type	2 (2)	1 (1)

Characteristic	Bone marrow plasma cells at diagnosis <10%	>=10%
Hemoglobin prior to transplant - no. (%)		
< 10 g/dl	17 (15)	35 (23)
>= 10 g/dl	98 (84)	117 (76)
Missing	2 (2)	1 (1)
Serum creatinine prior to transplant, mg/dl - no. (%)		
< 2 mg/dl	113 (97)	148 (97)
>= 2 mg/dl	3 (3)	4 (3)
Missing	1 (1)	1 (1)
Conditioning regimen - no. (%)		
Melphalan only	107 (91)	144 (94)
TBI + Melphalan	4 (3)	2 (1)
Other Melphalan based regimen	5 (4)	3 (2)
Others	1 (1)	4 (3)
Melphalan dose in conditioning regimen, mg/m - no. (%)		
MEL 140	29 (25)	34 (22)
MEL 200	87 (74)	112 (73)
Unknown dose	1 (1)	7 (5)
Disease status prior to transplant - no. (%)		
sCR/CR	19 (16)	30 (20)
VGPR	15 (13)	33 (22)
PR	64 (55)	63 (41)
SD	13 (11)	12 (8)
PD/Relapse	3 (3)	10 (7)
Missing	3 (3)	5 (3)
Time from diagnosis to transplant - median (min-max)	9 (3-100)	8 (3-146)
Time from diagnosis to transplant - no. (%)		
< 6 months	22 (19)	40 (26)
6 - 12 months	65 (56)	83 (54)
12 - 24 months	16 (14)	15 (10)
>= 24 months	14 (12)	15 (10)
Year of transplant - no. (%)		
2000	10 (9)	4 (3)
2001	6 (5)	9 (6)
2002	2 (2)	8 (5)
2003	5 (4)	9 (6)
2004	12 (10)	16 (10)

Characteristic	Bone marrow plasma cells at diagnosis <10%	>=10%
2005	18 (15)	18 (12)
2006	11 (9)	16 (10)
2007	4 (3)	1 (1)
2009	0 (0)	1 (1)
2010	2 (2)	1 (1)
2012	2 (2)	0 (0)
2013	6 (5)	7 (5)
2014	7 (6)	5 (3)
2015	4 (3)	5 (3)
2016	8 (7)	13 (8)
2017	5 (4)	4 (3)
2018	12 (10)	25 (16)
2019	3 (3)	11 (7)
Post-HCT therapy - no. (%)		
No	49 (42)	62 (41)
Yes	46 (39)	61 (40)
Missing	22 (19)	30 (20)
Post-HCT therapy (for current transplant) - no. (%)		
VR +/- other	1 (1)	3 (2)
V +/- other	4 (3)	5 (3)
R +/- other	34 (29)	43 (28)
KR +/- other	2 (2)	1 (1)
Other	5 (4)	9 (6)
No Maintenance	49 (42)	62 (41)
Missing	22 (19)	30 (20)
Follow-up - median (range)	73 (2-207)	64 (4-202)

Response Summary:

This form is intended to be completed by a physician/researcher for the purpose of proposing a study. Content should not include Personal Identifiable Information (PII) or Protected Health Information (PHI). If you are a patient, do not complete this form. Patients: Contact your healthcare provider immediately for reports of problems with your treatment or problems with products received for your treatment. The CIBMTR uses de-identified data and is unable to associate reported treatment problems, adverse events, or corrections of information with a center, clinical trial, or healthcare provider.

Q1. Study Title

Machine learning in predicting the factors associated with early relapse after autologous stem cell transplant in Multiple myeloma patients

Q2. Key Words

Autologous stem cell transplant, multiple myeloma, melphalan, Machine learning

Q3. PRINCIPAL INVESTIGATOR

Provide the following information for each investigator:

Principal Investigator #1:

First and last name, degree(s):	Sowjanya Vuyyala
Email address:	svuyyal1@hfhs.org
Institution name:	henry ford cancer institute
Academic rank:	fellow interested in SCT

Q4. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- Yes

Q5. Do you identify as an underrepresented/minority?

- Yes

Q6. Principal Investigator #2 (If applicable):

First and last name, degree(s):	shatha farhan
Email address:	sfarhan1@hfhs.org
Institution name:	henry ford cancer institute
Academic rank:	clinical assistant professor

Q7. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- No

Q8. Do you identify as an underrepresented/minority?

- Yes

Q9. 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:

N/A

Q10. If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:

N/A

LETTER OF COMMITMENT:

Please note: *A letter of commitment will be signed by Lead and Last authors as it describes the expectations for filling that role. By signing the letter of commitment, the authors accept their responsibilities and will be held accountable for timely completion of all steps in the project. More details regarding author responsibilities can be found here:* *https://www.cibmtr.org/Studies/Observational/StudyManagement/p*

Q12. CURRENT ONGOING WORK WITH CIBMTR: Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.

CT22-2 PI
CK20-01 participated in reviewing concept, data analysis and manuscript prep
CK17-02 participated in reviewing concept, data analysis and manuscript prep

Q13. PROPOSED WORKING COMMITTEE:

- Plasma Cell Disorders

Q14. Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.

- No

Q15. RESEARCH QUESTION:

To assess if machine learning can help predict factors that are associated with early relapse in multiple myeloma patients undergoing autologous stem cell transplant.

Q16. RESEARCH HYPOTHESIS:

We hypothesize that the data routinely collected for patients with multiple myeloma who undergo autologous stem cell transplant as part of the CIBMTR reporting contain predictive information which can be used to build predictive machine learning models that can provide physician and providers with more precise information regarding the risk of early relapse after autologous transplant for multiple myeloma.

Q17. SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.)

Suggested word limit of 200 words:

Primary outcomes – Early relapse within 2 years after autologous transplant
Secondary outcomes – PFS, OS after autologous transplant, identify which patients benefit the most from SCT especially high risk

Q18. SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.

Given the highly heterogenous and multiple factors involved including better induction regimen, post-transplant maintenance, prognosticating and predicting response to treatment is highly complex.
Machine learning is a field of artificial intelligence that performs outcome prediction based on complex interactions between multiple variables. ML makes no assumption about the relationship between the dependent and independent variables, and models are created with examples. ML can help analyze the multiple patient data collected with autologous SCT and help in predicting the risk of early relapse. The patient and disease related data collected for autologous SCT therapy patients can be used to build statistical and machine learning models which can help predict the risk of early relapse and also assist in developing a prototype clinical decision support tool to help guide the physician and patient

Q19. 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.

Autologous stem cell transplant has the been standard of care for patients with newly diagnosed multiple myeloma who are fit and eligible(1). Use of the triplet regimen has improved the rate and depth of response in myeloma and use of autologous stem cell transplant significantly prolonged the progression free survival(2). Early relapse after autologous stem cell transplant was associated with worse progression free survival and overall survival. Studies have evaluated the risk factors associated with early relapse and have demonstrated that factors contributing to early relapse are mostly disease specific. Anemia, thrombocytopenia, high plasma cell infiltration, high risk cytogenetics, advanced ISS stage was identified as some of the prognostic markers for early relapse(3). A study by Kumar et al from CIBMTR database showed post relapse OS was associated early relapse, thus highlighting the poorer prognosis even in the era of novel drugs(4). Given the highly heterogenous and multiple factors involved including better induction regimen, post-transplant maintenance, prognosticating and predicting response to treatment is highly complex.
Machine learning is a field of artificial intelligence that performs outcome prediction based on complex interactions between multiple variables. ML makes no assumption about the relationship between the dependent and independent variables, and models are created with examples(5, 6). ML can help analyze the multiple patient data collected with autologous SCT and help in predicting the risk of early relapse. The patient and disease related data collected for autologous SCT therapy patients can be used to build statistical and machine learning models which can help predict the risk of early relapse and also assist in developing a prototype clinical decision support tool to help guide the physician and patient.

Q19a. SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF)

N/A

Q20. PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.

Inclusion criteria - Adults patients age more than 18yrs, who underwent autologous peripheral stem cell transplant with high dose melphalan for multiple myeloma last 10 years

Q21. Does this study include pediatric patients?

- No

Q21a. If this study does not include pediatric patients, please provide justification:

myeloma rare <18 y old

Q22. DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Data collection forms available at: http://www.cibmtr.org/DataManagement/DataCollectior Outline any supplementary data required. Additional data collection is extremely difficult and will make your proposal less feasible.

Patient related characteristics:
• Age of recipient
• Gender (male or female)
• Ethnicity
• Karnofsky performance status
• HCT-CI Disease related characteristics:
• WBC, hemoglobin, platelet, absolute monocyte at diagnosis
• LDH , creatinine, albumin
• Percentage of blast count in peripheral blood and bone marrow at diagnosis
• R-ISS stage,
serum B2-microglobulin,
first-line treatment,
• MM-specific cytogenetic risk levels at diagnosis
• Molecular genetic abnormality (if available)
• Time from diagnosis to AHCT
• Number of cycles of induction treatment
• Disease response before AHCT according to the CIBMTR response criteria
Transplant related characteristics:
• Year of AHCT
• Transplant center
• Conditioning regimen , melphalan dose
For this purpose, RWE data from patients treated with MM treated with SCT in the CIBMTR will be used to create ML models of survival. Machine learning algorithms will be applied in order to select the optimal variables and create predictive personalized models. Models will be validated in a geographically independent test set within the CIBMTR registry. Cross-validation will be used to compare model results within the training set, and concordance indexes (c-index) will be calculated to assess model's predictability in the test set. we will use baseline data before SCT in order to: 1) predict patients who will relapse with in 2 years post SCT 2)overall and progression free survival, 3) identify which patients benefit the most from SCT especially high risk

Q23. 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 specific to PROS.

For additional information on what PRO measures have been collected and timepoints of collection, please reach out to the Late Effects and Quality of Life or Health Services Working Committee leadership: https://www.cibmtr.org/About/WhoWeAre/Com

na

Q24. 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 experience with the proposed assay systems. PIs should be encouraged to review the inventory details, sample types collected and reach out to research_repos@nmdp.org with any questions.

More information can be found at: https://www.cibmtr.org/Samples/Inventory/Pages/index

na

Q25. NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required, i.e., neither database contains all the data required to answer the study question.

na

Q26. REFERENCES:

Devarakonda S, Efebera Y, Sharma N. Role of Stem Cell Transplantation in Multiple Myeloma. Cancers (Basel). 2021;13(4).
2. Richardson PG, Jacobus SJ, Weller EA, Hassoun H, Lonial S, Raje NS, et al. Triplet Therapy, Transplantation, and Maintenance until Progression in Myeloma. New England Journal of Medicine. 2022;387(2):132-47.
3. Bygrave C, Pawlyn C, Davies F, Craig Z, Cairns D, Hockaday A, et al. Early relapse after high-dose melphalan autologous stem cell transplant predicts inferior survival and is associated with high disease burden and genetically high-risk disease in multiple myeloma. British Journal of Haematology. 2021;193(3):551-5.
4. Kumar SK, Dispenzieri A, Fraser R, Mingwei F, Akpek G, Cornell R, et al. Early relapse after autologous hematopoietic cell transplantation remains a poor prognostic factor in multiple myeloma but outcomes have improved over time. Leukemia. 2018;32(4):986-95.
5. Rajkomar A, Dean J, Kohane I. Machine Learning in Medicine. N Engl J Med. 2019;380(14):1347-58.
6. Bender R. Introduction to the use of regression models in epidemiology. Methods Mol Biol. 2009;471:179-95.

Q27. CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning:

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

- No, I do not have any conflicts of interest pertinent to this proposal

Q27a. 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.

N/A

BEFORE FINAL SUBMISSION, please review the PI checklist to ensure that you have completed all necessary steps. This will increase the likelihood of submitting a feasible and successful proposal.

Embedded Data:

N/A

Table. Characteristics of Multiple Myeloma patients, transplanted from 2008 to 2020, CRF

Characteristic	N (%)
No. of patients	7600
No. of centers	169
Chronological number of this HSCT - no. (%)	
1	7600 (100)
Median age (range) - median (min-max)	60 (20-83)
Age at transplant, years - no. (%)	
18-39	215 (3)
40-49	956 (13)
50-59	2485 (33)
60-69	3231 (43)
70+	713 (9)
Gender - no. (%)	
Male	4208 (55)
Female	3392 (45)
Region - no. (%)	
US	7290 (96)
Canada	82 (1)
Europe	22 (0)
Asia	66 (1)
Australia/New Zealand	9 (0)
Mideast/Africa	13 (0)
Central/South America	118 (2)
Race - no. (%)	
White	4496 (59)
Black or African American	2455 (32)
Asian	319 (4)
Native Hawaiian or other Pacific Islander	18 (0)
American Indian or Alaska Native	67 (1)
More than one race	40 (1)
Missing	205 (3)
Karnofsky score - no. (%)	
>= 90	3965 (52)
< 90	3427 (45)
Missing	208 (3)
HCT-CI - no. (%)	
0	2211 (29)
1	1109 (15)
2	1242 (16)
3	2977 (39)

Characteristic	N (%)
Missing	61 (1)
Bone marrow plasma cells at diagnosis - no. (%)	
<10%	756 (10)
>=10%	5662 (75)
Missing	1182 (16)
ISS stage at diagnosis - no. (%)	
ISS stage I	2323 (31)
ISS stage II	2079 (27)
ISS stage III	1512 (20)
Missing	1686 (22)
Lines of chemotherapy - no. (%)	
0	8 (0)
1	5093 (67)
>=2	2068 (27)
Missing	431 (6)
Chemotherapy - no. (%)	
VTD	219 (3)
VRD	3595 (47)
VCD	1108 (15)
VD	756 (10)
RD	702 (9)
TD	244 (3)
Carfilzomib	18 (0)
Pomalidomide	1 (0)
VAD/similar	71 (1)
Others	158 (2)
KRD	110 (1)
Daratumumab	179 (2)
Missing	439 (6)
Immunochemical subtype - no. (%)	
IgG	4393 (58)
IgA	1441 (19)
IgD	42 (1)
IgE	5 (0)
IgM	28 (0)
Light chain	1508 (20)
Non-secretory	87 (1)
Unknown Type	96 (1)
Hemoglobin prior to transplant - no. (%)	
< 10 g/dl	1672 (22)

Characteristic	N (%)
>= 10 g/dl	5824 (77)
Missing	104 (1)
Serum creatinine prior to transplant, mg/dl - no. (%)	
< 2 mg/dl	7073 (93)
>= 2 mg/dl	408 (5)
Missing	119 (2)
Conditioning regimen - no. (%)	
Melphalan only	7362 (97)
TBI + Melphalan	18 (0)
Other Melphalan based regimen	208 (3)
Mel +Flud	1 (0)
Others	10 (0)
Missing	1 (0)
Melphalan dose in conditioning regimen, mg/m - no. (%)	
MEL 140	2262 (30)
MEL 200	5327 (70)
Unknown dose	11 (0)
Disease status prior to transplant - no. (%)	
sCR/CR	1171 (15)
VGPR	2712 (36)
PR	3029 (40)
SD	445 (6)
PD/Relapse	205 (3)
Missing	38 (1)
Time from diagnosis to transplant - median (min-max)	7 (0-321)
Time from diagnosis to transplant - no. (%)	
< 6 months	2356 (31)
6 - 12 months	3568 (47)
12 - 24 months	1029 (14)
>= 24 months	645 (8)
Missing	2 (0)
Year of transplant - no. (%)	
2008	904 (12)
2009	317 (4)
2010	250 (3)
2011	341 (4)
2012	345 (5)
2013	653 (9)
2014	553 (7)
2015	724 (10)

Characteristic	**N (%)**
2016	780 (10)
2017	709 (9)
2018	1329 (17)
2019	576 (8)
2020	119 (2)
Post-HCT therapy - no. (%)	
No	2070 (27)
Yes	5029 (66)
Missing	501 (7)
Follow-up - median (range)	52 (3-162)

Response Summary:

This form is intended to be completed by a physician/researcher for the purpose of proposing a study. Content should not include Personal Identifiable Information (PII) or Protected Health Information (PHI). If you are a patient, do not complete this form. Patients: Contact your healthcare provider immediately for reports of problems with your treatment or problems with products received for your treatment. The CIBMTR uses de-identified data and is unable to associate reported treatment problems, adverse events, or corrections of information with a center, clinical trial, or healthcare provider.

Q1. Study Title

Comparison of survival outcomes for patients with relapsed multiple myeloma with salvage autologous SCT versus novel therapies

Q2. Key Words

relapsed myeloma, salvage transplant, novel drugs

Q3. PRINCIPAL INVESTIGATOR

Provide the following information for each investigator:

Principal Investigator #1:

First and last name, degree(s):	Srinivas Devarakonda
Email address:	Srinivas.devarakonda@osumc.edu
Institution name:	The Ohio State University Comprehensive Cancer Center
Academic rank:	Associate professor

Q4. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- No

Q5. Do you identify as an underrepresented/minority?

- No

Q6. Principal Investigator #2 (If applicable):

First and last name, degree(s):	Yvonne Efebera
Email address:	yvonne.efebera@ohiohealth.com
Institution name:	Ohio Health
Academic rank:	Professor

Q7. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- No

Q8. Do you identify as an underrepresented/minority?

- Yes

Q9. 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:

Srinivas Devarakonda

Q10. If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:

N/A

LETTER OF COMMITMENT:

Please note: *A letter of commitment will be signed by Lead and Last authors as it describes the expectations for filling that role. By signing the letter of commitment, the authors accept their responsibilities and will be held accountable for timely completion of all steps in the project. More details regarding author responsibilities can be found here:* *https://www.cibmtr.org/Studies/Observational/StudyManagement/p*

Q12. CURRENT ONGOING WORK WITH CIBMTR: Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.

N/A

Q13. PROPOSED WORKING COMMITTEE:

- Plasma Cell Disorders

Q14. Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.

- No

Q15. RESEARCH QUESTION:

Is salvage autologous stem cell transplantation (ASCT) inferior to novel agents for multiple myeloma at relapse?

Q16. RESEARCH HYPOTHESIS:

Salvage ASCT is feasible and effective in the treatment of relapsed multiple myeloma. However, with the introduction of several novel agents from different classes and varied mechanisms of action, treatment landscape has changed. Given the deep and durable responses, including remission in some cases, seen with the novel agents, the role of ASCT is questioned. Our hypothesis is that the outcomes of salvage ASCT are non-inferior to novel therapies for the management of relapsed multiple myeloma.

Q17. SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.)

Suggested word limit of 200 words:

Outcomes:
Primary:
1. PFS and OS of patients with relapsed MM who received salvage ASCT as 2nd or 3rd line of therapy.
2. PFS and OS of patients with relapsed MM who received novel drugs as 2nd or 3rd line of therapy.
Secondary:
1. Proportion of patients with relapsed MM receiving salvage ASCT as part of 2nd or 3rd line of therapy.
2. Proportion of patients with relapsed MM receiving novel drugs as 2nd or 3rd line of therapy.
3. Response rates (Overall response rate, complete response, very good partial response, partial response, progression, and stable disease).

Q18. 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 is the second most common hematological malignancy1. It is incurable and relapse is inevitable in most patients2. Relapsed myeloma is treated with chemotherapy to induce response and/or resolve end-organ damage. This is followed by autologous stem cell transplantation (ASCT) as salvage therapy in eligible patients. ASCT is an important component of therapy for MM patients. It yields significantly improved progression free survival (PFS) when used early in the course of relapsed disease3. It has the advantage of being impactful with just a one-time treatment as opposed to indefinite treatment with chemotherapy along with significant difference in the healthcare costs associated with the treatment. A scientific analysis of the trends in the usage and patient survival outcomes could provide useful information to design better clinical trials. This study will utilize CIBMTR data to assess the true trend in survival outcomes in salvage ASCT roughly corresponding to when novel treatments were introduced (2010- 2014, 2015-2020). The survival outcomes of patients treated with salvage ASCT will be compared to those for non-ASCT patients treated with novel drugs (daratumumab, carfilzomib, pomalidomide, isatuximab-based regimens) during the same period as second- or third-line therapy using data obtained from the SEER database.

Q19. 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.

ASCT in MM is feasible and effective even when used for the treatment of relapsed disease. In fact, it has been demonstrated to be more effective than salvage chemotherapy with improved PFS and even OS3. Salvage ASCT is often done at the time of first relapse, in whom it was not performed in the frontline setting or a second time in patients who had a progression-free interval of at least 18 months from the time of first transplant4. There have been several novel agents developed for the management of relapsed myeloma in the last five years and there have been limited studies comparing them with salvage ASCT. ASCT, while being a one-time treatment, offers a PFS benefit of over 2 years in selected patients5 with relapsed myeloma as opposed to the continued use of novel agents with the risk of both physical and financial toxicities. It has the added advantage of creating a bone marrow reset. The use of ASCT as a treatment option as compared to various immunotherapies and targeted therapies is not clear. This study aims to study the trends of utilization of salvage ASCT for the management of relapsed myeloma and compare outcomes to non-ASCT approaches utilizing novel drugs.

Q19a. SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF)

N/A

Q20. PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.

Inclusion criteria:
1. Patients aged 18-80 years old with relapsed disease diagnosed between the years 2010-2020.
2. All patients who received ASCT as part of frontline therapy.
3. Salvage autologous transplant as 2nd or 3rd line therapy.
4. Melphalan conditioning regimen (200 mg/m2 or 140 mg/m2) only for salvage ASCT.
5. For SEER database, patients with relapsed MM who received ASCT as frontline therapy and treated with novel agents as 2nd or 3rd line therapy without ASCT.

Q21. Does this study include pediatric patients?

- No

Q21a. If this study does not include pediatric patients, please provide justification:

Multiple myeloma is a disease of the elderly and rare in pediatric population.

Q22. DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Data collection forms available at: http://www.cibmtr.org/DataManagement/DataCollectior Outline any supplementary data required. Additional data collection is extremely difficult and will make your proposal less feasible.

Data points:
A. Patient related
• Age, gender, race, performance status, medical comorbidities
B. Disease related
• Stage, conventional myeloma versus light chain disease, cytogenetic/FISH risk features, end organ damage, PFS and OS from salvage ASCT
C. Treatment related
• Relapse-free interval after first ASCT
• Induction therapy used at initial diagnosis
• Response to first transplant- sCR, CR, VGPR, PR, progression
• Maintenance used after first transplant
• Time from first transplant to second transplant
• Salvage induction regimen at relapse
• Dose of Melphalan used for conditioning for second ASCT 200 mg/m2 versus 140 mg/m2
• Maintenance used after salvage auto

Q23. **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 specific to PROS.**

For additional information on what PRO measures have been collected and timepoints of collection, please reach out to the Late Effects and Quality of Life or Health Services Working Committee leadership: https://www.cibmtr.org/About/WhoWeAre/Com

N/A

Q24. **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 experience with the proposed assay systems. PIs should be encouraged to review the inventory details, sample types collected and reach out to research_repos@nmdp.org with any questions.**

More information can be found at: https://www.cibmtr.org/Samples/Inventory/Pages/index

N/A

Q25. NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required, i.e., neither database contains all the data required to answer the study question.

Surveillance, Epidemiology, and End Results (SEER) Program database will be used to collect information about the treatment and survival outcomes of non-ASCT patients treated with novel drugs (daratumumab, carfilzomib, pomalidomide, isatuximab-based regimens) during the same period as salvage ASCT as second- or third-line therapy for relapsed MM since neither database contains all the data required to answer the study question.

Q26. REFERENCES:

1. National Cancer Institute: Surveillance, Epidemiology, and End Results Program. Cancer Stat Facts: Myeloma. https://seer.cancer.gov/statfacts/html/mulmy.html.
2. Sundar Jagannath, Robert M. Rifkin, Cristina J. Gasparetto, Kathleen Toomey, Brian G.M. Durie, James W. Hardin, Howard R. Terebelo, Lynne Wagner, Mohit Narang, Sikander Ailawadhi, James L. Omel, Shankar Srinivasan, Mia He, Brian Ung, Amani Kitali, E. Dawn Flick, Amit Agarwal, Rafat Abonour. Treatment Journeys of Patients With Newly Diagnosed Multiple Myeloma (NDMM): Results From The Connect MM Registry. Clinical Lymphoma Myeloma and Leukemia,Volume 20, Issue 5,2020. 272-276. ISSN 2152-2650. https://doi.org/10.1016/j.clml.2019.10.002
3. Holstein, Sarah A., et al. "Management of relapsed multiple myeloma after autologous stem cell transplant." Biology of Blood and Marrow Transplantation 21.5 (2015): 793-798.
4. Jimenez-Zepeda VH, Mikhael J, Winter A et al. Second autologous stem cell transplantation as salvage therapy for multiple myeloma: impact on progression-free and overall survival. Biol Blood Marrow Transplant. 2012 May;18(5):773-9. doi: 10.1016/j.bbmt.2011.10.044. Epub 2011 Nov 4. PMID: 22062804
5. Garderet L, Iacobelli S, Koster L, et al. Outcome of a Salvage Third Autologous Stem Cell Transplantation in Multiple Myeloma. Biol Blood Marrow Transplant. 2018;24(7):1372-1378.

Q27. **CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning:**

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

- No, I do not have any conflicts of interest pertinent to this proposal

Q27a. **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.**

N/A

BEFORE FINAL SUBMISSION, please review the PI checklist to ensure that you have completed all necessary steps. This will increase the likelihood of submitting a feasible and successful proposal.

Embedded Data:

N/A

Table. Characteristics of adult patients who underwent salvage auto-HCT for relapsed MM from 2016-2022 in the US, registered in CIBMTR (TED-level information)

Characteristic	TED	CRF
No. of patients	1513	212
No. of centers	135	76
Median age (range) - median (min-max)	63 (29-81)	63 (35-81)
Age at transplant, years - no. (%)		
18-39	6 (0)	5 (2)
40-49	95 (6)	20 (9)
50-59	419 (28)	60 (28)
60-69	719 (48)	100 (47)
70+	274 (18)	27 (13)
Gender - no. (%)		
Male	842 (56)	123 (58)
Female	671 (44)	89 (42)
Region - no. (%)		
US	1513 (100)	212 (100)
Race - no. (%)		
White	1155 (76)	140 (66)
Black or African American	262 (17)	59 (28)
Asian	45 (3)	4 (2)
American Indian or Alaska Native	8 (1)	3 (1)
More than one race	9 (1)	2 (1)
Not reported	34 (2)	4 (2)
Immunochemical subtype - no. (%)		
IgG	508 (34)	62 (29)
IgA	215 (14)	30 (14)
Light chain	307 (20)	56 (26)
Non-secretory	36 (2)	0 (0)
Others	14 (1)	2 (1)
Unknown Type	433 (29)	62 (29)
Creatinine at diagnosis, mg/dL - no. (%)		
<2mg/dL	718 (47)	93 (44)
>2mg/dL	57 (4)	7 (3)
Missing	738 (49)	112 (53)
Stage at diagnosis (ISS) - no. (%)		
stage III	249 (16)	36 (17)
stage I-II	778 (51)	110 (52)

Characteristic	TED	CRF
Missing	486 (32)	66 (31)
Karnofsky score - no. (%)		
>= 90	725 (48)	103 (49)
< 90	756 (50)	100 (47)
Missing	32 (2)	9 (4)
HCT-CI - no. (%)		
0	309 (20)	38 (18)
1	177 (12)	22 (10)
2	243 (16)	40 (19)
3+	777 (51)	110 (52)
TBD, review needed for history of malignancies	1 (0)	0 (0)
TBD, inconsistencies between parent and sub-questions	6 (0)	2 (1)
Conditioning regimen - no. (%)		
Melphalan only	1358 (90)	192 (91)
Other Melphalan based regimen	155 (10)	20 (9)
Melphalan dose(mg/m) - no. (%)		
MEL 140	450 (30)	46 (22)
MEL 200	1052 (70)	165 (78)
Missing	11 (1)	1 (0)
Disease status prior to transplant - no. (%)		
sCR/CR	226 (15)	38 (18)
VGPR	522 (35)	71 (33)
PR	419 (28)	64 (30)
SD	121 (8)	17 (8)
PD/Relapse	218 (14)	21 (10)
Missing	7 (0)	1 (0)
Time from diagnosis to first transplant - median (min-max)	7 (0-690)	7 (0-158)
Time from diagnosis to second transplant - median (min-max)	70 (2-772)	73 (4-272)
Interval from first to second transplant - median (min-max)	60 (2-162)	59 (11-147)
Year of transplant - no. (%)		
2016	222 (15)	29 (14)
2017	230 (15)	37 (17)
2018	274 (18)	36 (17)
2019	265 (18)	27 (13)
2020	198 (13)	33 (16)
2021	198 (13)	31 (15)
2022	126 (8)	19 (9)
Follow-up - median (range)		