Not for publication or presentation

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

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1. Introduction

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

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

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

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

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

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

2. Accrual summary

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

3. Publications and Presentations

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

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

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

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

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

4. Studies in progress

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

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

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

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

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

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

5. Future/proposed studies

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

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

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

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

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

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

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

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

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

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

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

Submitted proposals:

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

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

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

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

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

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

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

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

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

Primary:

- *Progression-free survival*

Secondary:

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Dr. Bhutani presented this proposal with the following hypotheses:

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Proposed studies; not accepted for consideration at this time

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

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

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

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

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

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

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

6. Other Business

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

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

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

Proposals:

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

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

Submitted proposals:

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

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

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

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

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

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

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

Not for publication or presentation

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

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

Not for publication or presentation

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