Not for publication or presentation

A G E N D A
CIBMTR WORKING COMMITTEE FOR PLASMA CELL DISORDERS
Salt Lake City, UT
Monday, April 25, 2022, 12:15 pm – 1:45 pm

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1. **Introduction**
   a. Minutes and overview plan from February 2021 meeting (Attachment 1)
   b. Instructions for sign-in and voting

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

3. **Presentations, Published or Submitted Papers**
   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** Outcomes after Autologous stem cell transplant outcome for patients with POEMS syndrome (Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal protein, Skin changes). ***Oral presentation, ASH 2021.***

e. **MM20-03** Impact of bortezomib-based vs. lenalidomide maintenance therapy on outcomes of patients with high-risk multiple myeloma. ***Oral presentation, Tandem Meetings 2022.***

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

4. Studies in Progress (Attachment 3)

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) **Manuscript Submitted**

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**

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

a. **PROP 2109-27:** Outcomes of autologous hematopoietic cell transplantation for Light Chain Deposition Disease. (H Hashmi/ B Dhakal) (Attachment 4)

b. **PROP 2110-18:** Utility of urine testing in post-ASCT response assessments in multiple myeloma. (R Banerjee/ N Shah) (Attachment 5)

c. **PROP 2110-238:** Consolidation or Maintenance therapy in AL Amyloidosis Following Autologous Stem Cell Transplantation. (S Cingam/S Sidana) (Attachment 6)

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) (Attachment 7)
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.

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) (Attachment 8)
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.

Future/proposed studies to be presented at the CIBMTR Collaborative Working Committee Study Proposals Session

f. **PROP 2110-241:** Outcomes of second autologous stem cell transplantation vs chimeric antigen receptor T-cell therapy for multiple myeloma patients with prior autologous transplant. (N Bumma) (Attachment 9)

6. Dropped proposed studies

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*.

MINUTES
CIBMTR WORKING COMMITTEE SESSION
Thursday, February 11, 2021, 1:00 - 4:00 pm
Co-Chair: Bronwen Shaw, MD, PhD; CIBMTR Statistical Center, Milwaukee, WI; E-mail: beshaw@mcw.edu
Co-Chair: John Wingard, MD; University of Florida, Gainesville, FL; E-mail: wingajr@ufl.edu

INTRODUCTION:

Dr. Wingard opened the virtual meeting at 1:00 pm by welcoming the working committee members and the presenters. He discussed the proposal selection and voting process. Though the pandemic amended the process for proposal selection, 368 working committee proposals were submitted and evaluated altogether by CIBMTR Working Committee Chairs and Scientific Directors. About 61% were screened out, 30% had less-relative scientific merit, and 3% were combined with overlapping proposals with relevant nature. 21 proposals (about 6%), were considered for advancing of further pro-development. The proposals were pre-recorded 5-minutes presentations of the 15 semi-finalists, which were presented by the principal investigators. Each presentation was followed by a 5-minute question and answer session, in which audience was invited to submit questions via live chat. For those not able to attend the live session, a link was posted with the session recording and voting was closed on Monday, February 15, 2021. Audience was also instructed on where to locate the scoring and voting links for the presentations. It was mentioned that over 1,000 Working Committee members voted on the first screening of these proposals. Dr. Shaw led the second part of the meeting starting with presentation #9.

GENERAL REMINDERS:

The following reminders were mentioned and posted via the chat option:

a. Thank you for participating in the CIBMTR Working Committee Session! Please cast your score here: https://mcwisc.co1.qualtrics.com/jfe/form/SV_7QwO1ZvzfPZV1NY to vote on the proposals that were presented during the session.
b. Several presenters provided their email addresses for any future communication.

PRESENTATIONS:

1. **Risk of subsequent neoplasms in patients with post-transplant cyclophosphamide use for graft-versus-host disease prophylaxis.** This proposal was presented by Dr. Ana Alarcon Tomas. The primary objective of this proposal is to describe the incidence rate, risk factors, characteristics, and outcomes of subsequent neoplasms in patients receiving post-transplant cyclophosphamide (PTCy) and compare it with calcineurin inhibitors-based graft-versus-host disease prophylaxis and the general population. The CIBMTR identified 64,935 patients ≥18 years of age who underwent a first allogeneic for a malignant disease between 2008-2017. 5,771 (9%) of these patients developed a subsequent neoplasm. Currently, there are no published studies on the incidence of subsequent neoplasms in patients who received post-transplant cyclophosphamide. The following questions were answered during the Q&A:
    a. How are we going to prove that these secondary neoplasms are related to post-transplant cyclophosphamide or cyclophosphamide in conditioning and not due to "by chance" itself- as in general population? This is a case-controlled study. For example, for each patient received with a post-transplant cyclophosphamide will be matched with at least three patients who didn't receive post-transplant cyclophosphamide. Characteristics including primary disease, HLA complexity, survival, follow up time etc. would be used for matching and reviewing survival will also allow us to see that this is because of PTCy and not by coincidence.

b. What is the median follow up time from transplant and subsequent malignancy in post-transplant cyclophosphamide group? I assume it is much shorter than other cohort? Information is not available for each median follow up time cohort. What is available is the median follow up for all patients and some numbers related to the type of diseases for each group. Dr. Rachel Phelan included in the chat that the median follow-up for the PT-Cy group is 38.2 months, and for the proposed control population is 60.3 months.
c. How is this in comparison with matched unrelated donor and cord transplants? Cord transplants will be excluded from the analysis because we don't think we can match those patients.
d. Do we have adequate follow up to answer this important question? We have follow-up for mantle hematological diseases but less time for solid tumors. However, when we saw the numbers that we have (around 5,000 - 5,700) subsequent neoplasms, the majority of cases occurred after the 1st - 5th year of post- transplant and have a 5-year median follow up. We think we have enough numbers to address this question now and we should not wait because it hasn't been published before. This is a noble study and if we wait for a longer median follow up, we might lose that opportunity to have it published first.

Additional questions and comments posted via the chat but were unanswered due to limited time can be found in Appendix A.

2. **Outcomes of chimeric antigen receptor-T cell therapy for patients with antecedent chronic lymphocytic leukemia (Richter's Syndrome)**. This proposal was presented by Dr. Farrukh Awan. The objective of this proposal is to assess outcomes in adult patients with chronic lymphocytic leukemia undergoing transformation to diffuse large B-cell lymphoma (Richter's Syndrome) and undergoing CAR-T therapy. The CIBMTR identified 36 patients underwent CAR-T for Richter's Syndrome from 2015-2019. The following questions were answered during the Q&A:
   a. I know that in the Ohio State paper have many patients that used concurrent Bruton Tyrosine Kinase (BTK) inhibitors. Will you be able to collect data on concurrent BTK inhibitors for these patients? Yes, this information is available through the CIBMTR dataset.
   b. Are you looking at diffuse large B-cell lymphoma derived Richter's Syndrome or chronic lymphocytic leukemia derived Richter's Syndrome? Yes, but it is difficult to determine a clonality between related and unrelated Richter's syndrome. Any studies that show similarities versus dissimilarities in the clone would be very helpful but unfortunately, previous studies have shown that this has been consistently difficult.
   c. You mentioned the opportunity of comparing to other treatment groups. Can you talk about that a little more? We can compare to patients with de novo diffuse large B-cell lymphoma. There are multiple approved and ongoing studies within CIBMTR of diffuse large B-cell lymphoma patients, who do undergo CAR-T therapy and look at toxicity outcomes and infectious outcomes, for example. There are efforts in place to look at outcomes of transplantation for patients with Richter's Syndrome, which can improve the impact of this project and be a competitor to those other ongoing studies.
   d. How many pts do we have? 36 patients
   e. How do you plan to deal with the very low patient numbers (n=36) to make meaningful conclusion? I agree that it is a small number, but it is substantial. Despite the small numbers, if the right competitors are used, such as those mentioned previously, this study can still provide an impactful dataset.

Additional questions and comments posted via the chat but were unanswered due to limited time can be found in Appendix B.

3. **Impact of graft versus host disease following allogeneic hematopoietic cell transplantation on leukemia free survival in hematologic malignancies**. This proposal was presented by Dr. Andrea Bauchat. The objectives of this proposal is to determine the impact of development of grade I-II acute graft versus host disease on relapse and leukemia-free survival, to assess the impact of development of grade III-IV acute graft versus host disease on relapse and leukemia-free survival, and to determine whether the impact of graft versus host disease on

relapse and leukemia-free survival is influenced by disease risk prior to HCT. The CIBMTR identified 1,345 children <18 years who received first HCT for acute lymphoblastic leukemia and acute myeloid leukemia receiving first allogeneic transplantation between 2008 - 2017. The following questions were answered during the Q&A:

a. What is the sample size of each sub-group: disease-risk index (DRI)-low, -intermediate, -high? Exact sample size not available but the high-risk group was less in comparison to others.
b. How will you factor in occurrence of chronic graft versus host disease in your analysis? Our main focus is on acute graft versus host disease because it will have more impact on our clinical practice. However, we will collect the data for the interactions of chronic graft versus host disease alone, and if the patient had a history of acute.
c. What is the biological basis for focusing this study on a pediatric population? The interest from our perspective is looking at the pediatric population compared to the adults. The literature on pediatric is severely lacking in comparison to adults and we need to expand on that for the patient population that we care for.
d. Are you going to separate acute myeloid leukemia and acute lymphoblastic leukemia numbers at DRI level? Yes, they are already divided from DRI protocol. Our acute lymphoblastic leukemia patients are about 1,300 and the acute myeloid leukemia are about 1,200.
e. Is the analysis going to be time dependent or landmark? Landmark
f. Do you have the date of this max acute graft versus host disease grade to take into account the time to event aspect of the effect? No
g. Do you have a plan to include/account for the various GVHD prophylaxis regimen "strengths?" We are taking into consideration of what GVHD prophylaxis regimen the patient uses. This data, which is already categorized, will show us the differences between trends.
h. What is the clinical benefit besides prognostic? This will help define a better foundation of which patients will benefit more from a little bit of graft versus host disease. If we can come up with a patient category that we see is beneficial to have exposure to a little bit of graft versus host disease, it can go forward with clinical trials and GVHD prophylaxis adjustment or manipulation to improve their Leukemia-free survival.

Additional questions and comments posted via the chat but were unanswered due to limited time can be found in Appendix C.

4. **Effect of HLA evolutionary divergence on survival and relapse following allogeneic hematopoietic cell transplant**. This proposal was presented by Dr. Christine Camacho-Bydume. The primary objective of this proposal is to determine if HLA evolutionary divergence (HED) of HLA class I alleles of HLA-A, -B, -C and HLA class II alleles of HLA-DR is associated with overall survival and relapse. The objective is to also evaluate association of HED with acute and chronic GVHD and treatment-related mortality (TRM). The CIBMTR identified pediatric and adult patients with acute myeloid leukemia, myelodysplastic syndromes, acute lymphoblastic leukemia, chronic myeloid leukemia, or lymphoma (non-Hodgkin or Hodgkin's lymphoma), who have received initial allogeneic 8/8 HLA-matched (HLA-A, -B, -C, -DR) transplant between 2008 - 2018. The following questions were answered during the Q&A:

   a. Could HLA diversity simply be a surrogate for race? How would you account for race in the study? Great question given there are particular HLA alleles that are more common in certain ethnic groups. We do think that evaluation of HED lows and highs within these different ethnicities can help to tease this out more, with potential to adjust for race more in this analysis. We think some of these differences in peptide binding grooves can help us to understand better the different peptides and how antigens are presented to T-cells.
   b. Extrapolating HLA data from solid tumors and checkpoint inhibitors and their antigen presentation is slightly challenging in context of allo donor T-cell interaction with antigen presented for bone marrow origin cancers. Yes, have to consider there could be some differences. Was a small previous study that

looked at this question, saw some signals there, larger population and different types of cancers, may be able to explore that more.

c. Leukemia (both lymphoblastic and myeloid) have low mutational burden as compared to melanoma and lung. Will the HED algorithm still work? Yes, we do expect to see differences in mutational burdens, and we do plan to look at the cohort at large to look at the disease subgroups to see more or less of this phenomenon in these groups. Do you have preliminary data in leukemias? There was a small study in Germany that looked at AML, to my knowledge only one that looked at leukemias. Mutational burden did see some differences, so we do expect it and also, besides the overall cohort, also plan to look at disease subgroups.
d. Given HED implications for infection surveillance, are you going to look at infectious sequelae differences? No, at the moment we have initially requested information in terms of tumor control, relapse, overall survival, graft versus host disease, and TRM. Not sure of availability of the other information but would be interesting to look at if available.
e. Would you please discuss the confounding effects of HLA mismatching for HLA-DRB3, 4, 5, DQ, and DP? Not known off the top of my head the percentages of mismatching differences in this cohort. For DR at least they will be matched, 8/8 matched, in terms of DP, don't have that info but if available it is something that can be looked at.

Additional questions and comments posted via the chat but were unanswered due to limited time can be found in Appendix D.

5. **Impact of IDH1 and IDH2 mutations on outcomes of acute myeloid leukemia patients undergoing allogeneic hematopoietic cell transplantation**. This proposal was presented by Dr. Evan C. Chen. The primary objective of this proposal is to identify differences in survival outcomes between mutIDH1/2 and wtIDH1/2 acute myeloid leukemia patients and to assess the prognostic significance of disease features in mutIDH1/2 and wtIDH1/2 acute myeloid leukemia patients. The CIBMTR identified patients ≥ 18 years old with a diagnosis of normal karyotype acute myeloid leukemia, receiving first allogeneic HCT during CR1 in 2013 - 2019. The following questions were answered during the Q&A:
   a. Is there any concern that patients with IDH1/2 mutated acute myeloid leukemia would have received more intensive conditioning / therapy than IDH1/2 wild-type? Yes, and it's important to look at how conditioning intensity can be an important covariant, which is a variable captured in CIBMTR.
   b. Will you have registry information on the type and duration of use of IDH inhibitors before/after HCT? It's currently not available with CIBMTR.
   c. IDH mutations are usually seen in older subjects. How will you a priori adjust for this known association? Age will certainly be a covariant in our multi-variant analysis.
   d. How reliable are the wild-type patients as some may just not be tested for IDH mutations? It is double checked. There is a datapoint in the forms that indicate whether or not testing has been done, versus if testing was done and IDH was found to be absent.
   e. Do you have information what the numbers will be like when you divide your patient groups with concomitant mutations such FLT3 or p53 that may have an impact on outcomes? Yes, the numbers are about 20-40 for co-mutated for ITD and NPM1 patients. p53 not provided.
   f. Is there data in CIBMTR forms that collect use of IDH inhibitors pre transplant? Will you be able to study their impact on the transplant? I'm not aware of this data point being available in the forms but it is something that we should follow up on.
   g. How do you analyze its (or ITS?) with multiple mutations? With regards to double-mutated patients, IDH1, and IDH2 patients, which are generally rarely reported, we would look at the CIBMTR forms to ensure accurate data entry. In regard to analyzing IDH with other co-mutations, we would include co-mutations as a co-variant in a multi-variant analysis, should the sample size permit.

h. What about other mutations in Wild type IDH? We focus on NPM1 and FLT3-ITD because they are prevalent in the cytogenetic risk population. We will look at the other mutations to see if they have any relevance at all.
i. Do the data forms reliably collect information on use of IDH inhibitors pretransplant? Data point is not available.

Additional questions and comments posted via the chat but were unanswered due to limited time can be found in Appendix E.

6. **Characteristics and outcomes of adolescent and young adults with multiple myeloma treated with autologous hematopoietic cell transplant**. This proposal was presented by Dr. Christin B. DeStefano. The primary objective of this proposal is to describe patient and disease related characteristics of adolescent and young adults (AYAs) with multiple myeloma treated with early high dose melphalan and AutoHCT and to characterize response to AutoHCT, survival outcomes, SPMs, and infections of AYA multiple myeloma patients and AutoHCT. The CIBMTR identified 1,142 AYA multiple myeloma patients who underwent autologous hematopoietic cell transplant) between 2008 -2018. The following questions were answered during the Q&A:
   a. What will differentiate this study from MM18-03 "To compare the outcomes in young patients with multiple myeloma at diagnosis undergoing upfront autologous hematopoietic stem cell transplant with older patients in the US: progression-free and overall survival"? There appears to be substantial population overlap. The Scientific Director clarified via the chat function that MM18-03 included the years 2013-2017 and excluded patients less than 40 years from the outcome analysis owing to small numbers.
   b. How do you plan to control for differences between your AYA group and older control group which would be attributable to age? In total, there are about 1,700 TED and CRF cases. We can adjust the critical variables of these cases, such as stage, treatment rendered, and cytogenetics, for example, to control for differences.
   c. Will results be stratified according to different induction regimens? Yes, we will adjust those critical variables amongst the CRF cases where this information is available.
   d. A cohort going back to 1995 seems too outdated. What was the N for a more recent group (since 2010)? There were 1,142 AYA cases between 2008-2018.
   e. This is a long cohort 1995-2019 with lots of changes in induction treatment, novel agents and time to bone marrow transplant. How will this be controlled for? We are going to study induction regimens, post-transplant treatment, use of tandem transplants in our analysis.
   f. Will you be also studying the effect of post-transplant maintenance therapy? Also, any effect of extramedullary plasmacytomas in this AYA group? We will for cases where this information is available. Extramedullary plasmacytomas are a good focus, as AYA patients may have a more aggressive presentation of myeloma.
   g. Are plasma cell leukemias included in this analysis? No

   Additional questions and comments posted via the chat but were unanswered due to limited time can be found in Appendix F.

7. **Impact of measurable residual disease status on outcomes of AML in patients 18-65 years old in CR1 undergoing Allo-HCT**. This proposal was presented by Dr. Firas El Chaer. The objectives of this proposal is to determine if acute myeloid leukemia measurable residual disease (MRD) analysis as currently performed has prognostic value when measured prior to AlloHCT, to explore factors that may modify the risk associated with detectable acute myeloid leukemia MRD pre-AlloHCT, and identification, using MRD combined with other clinical factors, of patients most at risk of post-AlloHCT relapse. The CIBMTR identified 753 MRD positive and 1986 MRD negative adult patients receiving first AlloHCT for de-novo AML in CR1 in 2007-2018. The following questions were answered during the Q&A:

a. What kind of MRD data is collected? Depending on the individual participating centers, the methodology uses molecular or immunotherapy? MRD
b. What is the rate of missing MRD status and are those patients different from those with MRD data available? The answer is not included in this study.
c. Are you going to also study the effect of post-transplant maintenance in AML FLT3, IHD mutations on relapse and overall survival? One of the aims of this study is to have future studies look at post-transplant maintenance from this study.
d. What do you mean by most "recent" pre-conditioning MRD assessment? Would testing need to be completed within a specific time frame before conditioning? All patients who will be receiving a stem cell transplant are required to get a bone marrow biopsy and peripheral blood aspiration before transplantation. Within a month before the transplant, we would look at data point.
e. What is your working definition of MRD? A combination of molecular testing as well as immunotherapy by NFC.
f. Are all mutations equivalent when thinking about MRD? Absolutely not.
g. How sure are you that the MRD patients are really MRD negative? We can never be absolutely sure.
h. How are you going to account for the different sensitivity of methods used to determine MRD? Are ELN risk available at CIBMTR, since when? The way that CIBMTR reports the acute myeloid leukemia data is by reporting their cytogenetics and mutation analysis so we can calculate the data for this population. The point of this study is to look at the commercial availability of these tests and we can rely on it or if we should standardize one testing at all centers.

Additional questions and comments posted via the chat but were unanswered due to limited time can be found in Appendix G.

8. **Racial, ethnicity and socioeconomic disparity in outcome of patients with chronic graft versus host disease.** This proposal was presented by Dr. Nosha Farhadfar. The objectives of this proposal are to determine whether clinical manifestations and severity of chronic GVHD differ based on racial/ethnic and socioeconomical status (SES) differences, to determine whether treatment patterns of chronic GVHD differ based on racial/ethnic and SES differences, and to evaluate whether chronic GVHD treatment outcomes differ based on racial/ethnic and SES differences. The CIBMTR identified 17,665 patients, age 18 years or older, who have received first allogeneic transplant for hematologic malignancy (acute myeloid leukemia, acute lymphoblastic leukemia, myelodysplastic syndrome) between 2008 - 2019. The following questions were answered during the Q&A:
   a. I like the idea for looking at outcomes based on race/ethnicity/SES but not sure if incidence should be a primary outcome because it will be dependent on donor type which is very different amongst the groups. The primary outcome of this study is to look at the outcome of patients who develop chronic graft versus host disease. We need to look at the whole cohort, report the incidence, and then focus on chronic graft versus host disease cohort as the primary endpoint of this study.
   b. How will you correct for the impact of race on HLA mismatch between recipients and donors due to the lower chance of identifying a fully matched donor in non-Hispanic white patients? For the same reason, should cord blood recipients be excluded? We are going to include both the donor type, graft source and degree of HLA matching as covariables in a multi-variable analysis. Cord blood recipients should not be excluded, as there was near 14% of Non-Hispanic black, 14% Hispanic, and 15% Asian who received cord transplant. Approximately 7-8% of cord transplants were received by Non-Hispanic whites. We do have the number to look into cords but if a statistician reviews and determines we don't have the power, then we can eliminate the cords.
   c. Is it possible to access constitutional DNA to look at ancestry information markers in this population? This information is not available for the population. The analysis will focus on self-reported race/ethnicity.
   d. All patients in your cohort from 2008 were not reported with NIH consensus criteria for chronic GVHD. Since you have large numbers, should you limit this to more recent time period? We do have all of the

information on graft versus host disease and whether it was limited or extensive. There is information on whether graft versus host disease is progressive, de-novo or interrupted. We have organ involvement and maximum grade of chronic graft versus host disease. NIH scoring is available for at least the past 4 years and maybe we can look at that group separately. Within the past 4 years, the population limited to NIH grading only in about 1,500 non-Hispanic white, 270 non-Hispanic black, and 200 Hispanic, who have developed chronic graft versus host disease.

Additional questions and comments posted via the chat but were unanswered due to limited time can be found in Appendix H.

9. **Time from diagnosis to transplant as an important contributor for post allogeneic stem cell transplant infections, immune reconstitution and its associated mortality/morbidity**. This proposal was presented by Dr. Lohith Gowda. The objectives of this proposal are to identify density and types of early and late infections (bacterial, viral and fungal) in patients that went to transplant a) <6 months b) between 6- 12 months and c) > 12 months from diagnosis; to identify T cell lymphocyte absolute numbers at days 100 and 180 and CD4/CD8 ratio for the timeline cohorts examining individual donor types; to evaluate the impact of bacterial, viral or fungal infections by day 100 and day 180 on 1-year post-transplant outcomes (relapse, non-relapse mortality, disease free survival, acute and chronic graft versus host disease); and to evaluate quantitative immunoglobulin levels at D+ 100 and + 180 if available. The CIBMTR identified 6,877 ≥ 18 years old patients who underwent first allogeneic transplants for AML in CR1, ALL in CR1 or MDS in the United States from 2012 to 2019. The following questions were answered during the Q&A:
    a. How many patients in the registry have the immune parameters you wish to assess? >2100
    b. How will you account for the type of treatment used prior to transplant? For example, treatments such as hypomethylating agents may require months of treatment before transplant versus induction chemo that works more quickly. We do have some variables that are available, such as types of therapy, and we can analyze levels of intensity of therapy (low to high) and post-transplantation outcomes. The exact number of how many patients who have had different intensities of therapies is not available.

    Additional questions and comments posted via the chat but were unanswered due to limited time can be found in Appendix I.

10. **Efficacy and safety of CD19 directed CAR T-cell therapy for non-Hodgkin B-cell lymphomas with secondary central nervous system involvement**. This proposal was presented by Dr. Hamza Hashmi. The primary objective of this proposal. The CIBMTR identified 55 adult patients (age ≥ 18) who received CD19 CAR T-cell therapy for B-cell NHL with secondary central nervous system (CNS) involvement. The following questions were answered during the Q&A:
    a. How will you differentiate between immune effector cell-associated neurotoxicity syndrome (ICANS) and CNS relapse? ICANS will be documented as a neurotoxicity and CNS relapse will be when the form is filled out.
    b. Is this active CNS disease or previously treated CNS disease? The data received from CIBMTR looks at CNS disease at the time of diagnosis and the CNS disease that is present at the time of cellular therapy.
    c. Do you have any registry information on concomitant CNS therapy (chemo/radiation) pre, peri and post transplantation? Answer was not available at this time.
    d. How many patients are in your study? How will you define whether the patients have cleared their CNS involvement? There are currently 60 patients in the history of this data. Of the 60, 40 had this disease at the time of diagnosis and 20 had this disease at the time of cellular therapy. Whether the patients have cleared their CNS involvement, this information is not available at the time.
    e. Since this is your primary endpoint, how will you account for the differences of frequency of CRS and ICANS across different products (e.g. high in Yescarta, lower in Kymriah, low in Breyanzi)? If you look at the toxicity profile of CD19 therapy, they seem to be relatively similar.

f. Could you please include other agents such as anakinra, siltuximab, and other agents? Dasatinib for this populations for ICANS? Also, was CNS disease under control at CAR-T therapy? As for Anakinra, siltuximab, and other agents, I'm not sure if CIBMTR is capturing this data. As for dasatinib, I'm not sure if this information is available as well. Per Dr. Pasquini of CIBMTR in the live chat, he commented "we capture treatment of ICANS, like siltuximab, dasatinib has been reported as other treatment."
g. Will you have detail on the nature and extender features of secondary CNS involvement to associate with the toxicity and outcome? I only have the essential data with me but am hopeful that this comprehensive research will have further detail.
h. Will all the patients included have active CNS disease at the time of CAR-T or, are treated CNS disease are also included? They are both included, and we are able to tell who has had active disease with a prior history at the time they got the CAR-T therapy.

Additional questions and comments posted via the chat but were unanswered due to limited time can be found in Appendix J.

11. **Haploidentical donor versus matched donor allogeneic hematopoietic cell transplantation in patients with myelofibrosis**. This proposal was presented by Dr. Tania Jain. The primary objective of this proposal is to explore the impact of donor type on overall survival of patients undergoing HCT for myelofibrosis. The CIBMTR identified 1,640 patients ≥18 years old diagnosed with primary, post-ET or post-PV myelofibrosis and undergoing first HCT between 2013 and 2019. The following questions were answered during the Q&A:
    a. Are you also going to compare the effect of pretransplant Ruxo in haplo vs MUD/MRD? Also, are you going to look for graft failures as well in these patient populations? Yes, this will be included. We also do look at graft failures in these populations.
    b. Is there a difference in time from diagnosis to HCT across the groups? The median time from diagnosis to transplant for haploidentical patients was 38 months, while for HLA- identical sibling and URD 8/8 was 21 and 24 months, respectively.
    c. Are you including all conditioning regimens types: MAC, RIC and NMA? Yes, and they will be looked at for comparison in the univariable and may be taken to the multivariable analysis as well.
    d. For the graft failure or rejection analysis are you going to include spleen size? Ideally it should be included but the spleen size measurement has many variables and it may not be a clean assessment. We don't collect precise spleen size in our forms, but it can be analyzed as spleen size as splenomegaly, no splenomegaly or splenectomy.
    e. Can you comment on the bone marrow vs peripheral blood in the three groups? Peripheral blood is more common in the donor source (about 80%).

    Additional questions and comments posted via the chat but were unanswered due to limited time can be found in Appendix K.

12. **Assessing utilization and clinical outcome differences by sex and race in CAR-T for relapsed/refractory NHL**. This proposal was presented by Dr. Arushi Khurana. The objective of this proposal is to enhance our understanding of sex- and race-based differences in utilization of CAR-T vs AutoHCT and outcomes after CAR-T. The CIBMTR identified 1,133 patients to compare sex and race/ethnicity rates for first cellular infusion (AutoHCT vs. CAR-T) for relapsed/refractory non-hodgkins lymphoma patients from 2017 – 2019 (aim 1a). The CIBMTR identified 619 non-hodgkins lymphoma patients who relapse after first AutoHCT to describe subsequent treatment patterns (e.g. CAR-T, second AutoHCT, AlloHCT, other treatment, no treatment) by sex and race/ethnicity (aim 1b). The CIBMTR identified 1,253 patients to identify sex-and race-based differences in response to CD19 CAR-T in aggressive lymphomas (aim 2). The following questions were answered during the Q&A:
    a. Is there gender and race-based difference in SEER data with or without treatment for diffuse large B-cell lymphoma even before CAR T? Yes, that data does exist.

b. Can this be stratified by center/geography (private/public, large urban/rural)? Yes, it will be shown based on zip code (of patient and of recorded center), which will allow us to differentiate from urban/rural as well.
c. We saw almost no neurotoxicity in women so would you be plotting CRS and ICANS based on gender and race? Yes, and we believe CIBMTR is the best resource for this because of the larger numbers
d. How do you differentiate between larger trial centers vs less resourced centers? The information is reported based on the center type. Basing on academic or zip code, or city versus rural center, that will also be a way to differentiate the centers.
e. Would disease response status prior to cellular therapy be taken into account for analysis? Yes, that is one of the co-variants that will be included.
f. How reliable is the data you will get to study "access", as there are many factors, depending on patient specific factors (education, resource, finances, mobility, support, performance, etc.), center specific (criteria), and also access depends on the hematologist/oncologist who sees these patients in the community? Access to a center is not one of the main issues in this study. It is more about why some of these minorities receiving other treatments when they should be receiving cellular therapy at the time of indication.
g. Is there any way to take into account insurance issues? We do look at the insurance statuses as one of the co-variants.
h. Would it be possible to look at differences in access based on commercial CAR T vs. clinical trials? The majority of the patients from the forms received are from commercial CAR T.

Additional questions and comments posted via the chat but were unanswered due to limited time can be found in Appendix L.

13. **Optimal GVHD prevention strategy in older, robust patients with acute leukemias and myeloid malignancies undergoing myeloablative, matched donor hematopoietic cell transplantation**. This proposal was presented by Dr. Richard J. Lin. The primary objective of this proposal is to compare CRFS among patients ≥ 60 years old undergoing myeloablative conditioned, allogeneic hematopoietic cell transplantation with following graft versus host disease prophylaxis in 2 matched-pair analysis and to compare other transplant outcomes in the above 2 matched-pair analysis. The CIBMTR identified 1,301 patients at ≥ 60 years old at the time of first allo-HCT between 2010 and 2019, with any myeloablative conditioning defined by CIBMTR, 8/8 matched related or unrelated donor only, graft versus host disease prophylaxis (ex-vivo TCD/CD34+ selection versus PTCy-based versus Tac/MTX). The following questions were answered during the Q&A:
    a. What do you mean by "robust?" Is it based on KPS, HCT-CI, or just the fact that someone got MA. regimen? We use the definition of a patient getting a myelo-conditioning as a way of saying that they are robust by their transplant centers.
    b. Are patients with In-vivo T cell depletion (Campath or ATG) excluded from this analysis? T cell depletion and CD34 selection does include ATG and does not include Campath.
    c. Why do you pool post-CY and ex vivoCD34+ selection? Can we still consider ex vivoCD34 selection to be a promising transplant modality in 2021? We wanted to compare a 2-match pair analysis and not a direct comparison between CD34 selection and post-CY. We do know which will be better for an older patient.
    d. Why exclude TBI? For older patients, we don't consider TBI to be a conditioning regimen.
    e. How many patients with Tac/methotrexate prophylaxis had ATG? Answer was not available at the time of Q&A.
    f. Do we know GFR (creatinine) coming into allo in these groups? In this study, we didn't include the GFR (creatinine) as a variable but we have some evidence in older patients that does play a major role. I can discuss with our statistician on whether we can include this as a variable.

    Additional questions and comments posted via the chat but were unanswered due to limited time can be found in Appendix M.

14. **Outcomes of elderly patients receiving CD-19 directed CAR-T therapy for B-cell lymphomas**. This proposal was presented by Dr. Sayeef Mirza. The primary objectives of this proposal to evaluate cumulative incidence grades, duration and median time to onset of CRS and CRES/ICANS in patients > 65 years of age receiving CD-19 directed CAR-T therapy, describe post CAR-T clinical outcomes and resource utilization in elderly, and identify disease biology, comorbidities and other clinical predictive markers of toxicity, response, and survival in elderly patients. The CIBMTR identified 1,036 patients (<65y,n=612; 65-74y, n=348; >75y, n=76) with the diagnosis of any B-cell lymphoid malignancy (indolent or aggressive lymphoma) receiving CAR-T cell product (CD19 target). The following questions were answered during the Q&A:
    a. Would you please also look at Incidence of pancytopenia, hypogammaglobulinemia and HLH in elderly versus younger in 3 cohorts <60, 60-75 ,>75? I think it's very important to look at this as the data becomes available to us. We are primarily looking at different age groups. We have 81 patients over the age of 75 and five patients over the age of 85. Overall, there are 435 (40 %) of the group are over 65 years old.
    b. How does this defer from the data presented by Dr. Pasquini last year in older patients? This data will be more helpful in including both CAR-T products.
    c. In case of CAR T was used for post-alloHCT relapse, would the donor age of the CART source be analyzed? This is something that we should include in our analysis.
    d. Are data on baseline geriatric scores or HCT-CI available for all? The answer was not available at the time of the Q&A.
    e. Do we have registry information on whether CAR-T production succeeded or not, when attempted? The answer was not available at the time of the Q&A but the moderator did state that on behalf of CIBMTR, this information is not captured.

    Additional questions and comments posted via the chat but were unanswered due to limited time can be found in Appendix N.

15. **Determinants of successful discontinuation of immune suppression following allogeneic hematopoietic cell transplantation**. This proposal was presented by Dr. Joseph Pidala. The primary objective of this proposal is to validate prediction models for immune suppression discontinuation (ISD) and ISD failure developed in prior DISCIS-defined population, explore ISD and ISD failure in a new population inclusive of full range of diversity in current HCT practices, construct and validate dynamic prediction models of ISD and ISD failure in the expanded population. The CIBMTR identified 20,031 patients with a hematologic malignancy who received an allogeneic HCT from matched sibling donor, matched or mismatched unrelated donor, umbilical cord blood or haploidentical donor between 2009-2018. The following questions were answered during the Q&A:
    a. Can you explain how the ISD data information was made feasible? We used CIBMTR follow up data in the previous analysis that led to the development of the prediction model for ISD that we intend to validate in this study.
    b. Can you provide more granularity on how the time of discontinuation of immune suppression will be defined? In the CIBMTR data, there is a hard stop date for a complete discontinuation of immune suppression. That granular data is available, and it was the data we used for the prior project. We used that hard stop of all systemic immune suppression because that's an unambiguous measure of success.
    c. Many with PTCY may be discontinuing by days 100 or 60- likely based on center practice rather than patient response, how will this be addressed? Our prior project was successfully addressed this issue, specifically within that study population. The first step in this project is to validate those findings. We will definitely be studying how immune suppression was performed and what are the subsequent outcomes.
    d. Do you plan to use age as one of the variables regarding likelihood to discontinue IST, or will you have a separate pediatric specific model? Yes, we will consider age as a variable and evaluate the need for a pediatric specific model.

Additional questions and comments posted via the chat but were unanswered due to limited time can be found in Appendix O.

CLOSING:

Dr. Shaw, on behalf of herself and co-chair, Dr. John Wingard, did thank presenters, conference organizers, and the CIBMTR staff for having coordinated this virtual session. She did mention that this session was recorded and encouraged attendees to take survey, as access would be available until Monday, February 15, 2021.

APPENDICES:

A. Risk of subsequent neoplasms in patients with post-transplant cyclophosphamide use for graft-versus-host disease prophylaxis.

1. How will authorship work for these studies? The same as usual, there are fewer studies being accepted but the process otherwise is the same
2. What if a higher risk of cancer is related to the almost uniform use of 2GyTBI in these patients rather than PTCY?
3. What is the breakdown of haploidentical versus matched sib/MUD in the post-transplant cyclophosphamide group?
4. How can we r/o genetic predisposition on samples and variables of TBI based conditioning therapies?
5. What is your sample size and follow-up period?
6. How long post BMT you will follow up? From where will you receive the SN data?
7. Will you be adjusting for chronic GVHD when looking at your outcome of SN?
8. Is this study statistically powered to detect a difference between PTCY and above a certain threshold? What is the threshold?
9. Will analysis be conducted separately for TBI/non-TBI and MAC/RIC conditioning? Are you evaluating all malignancies?
10. Since the total CY exposure is likely not that different in PTCY vs. BU/CY or CY/TBI, is your hypothesis that the timing of exposure to CY may lead to a difference in risk? And if so, why?
11. Information on skin cancers - ssc, bcc available?
12. Matching for HLA matching could be a limitation because the PTCY patients are more likely to receive haploidentical grafts.

B. Outcomes of chimeric antigen receptor-T cell (CAR-T) therapy for patients with antecedent chronic lymphocytic leukemia (Richter's Syndrome).

1. If patients had failed an auto or allo, how do you plan to compare to the results of auto? Isn't it a different group?
2. Can you please provide your thoughts if the small n will be able to generate meaningful results at this time?
3. Would you include both transformed lymphoma from other low-grade lymphoma and Richter's transformation?
4. Are there concerns about underreporting Richter's?
5. Since the numbers are small, can we go back to centers to establish clonality?

C. Impact of graft versus host disease following allogeneic hematopoietic cell transplantation on leukemia free survival in hematologic malignancies. *No additional questions*

D. Effect of HLA evolutionary divergence on survival and relapse following allogeneic hematopoietic cell transplant.

1. Does the HED algorithm take into account variations outside the peptide binding groove?

2. What is the size of the cohort you are looking at?

E. Impact of IDH1 and IDH2 mutations on outcomes of acute myeloid leukemia patients undergoing allogeneic hematopoietic cell transplantation. *No additional questions*

F. Characteristics and outcomes of adolescent and young adults with multiple myeloma treated with autologous hematopoietic cell transplant.

1. How do you plan to control for differences between your AYA group and older control group?

G. Impact of MRD status on outcomes of AML in patients 18-65 years old in CR1 undergoing Allo-HCT.

1. How are you going to account for the different sensitivity of methods used to determine MRD? Are ELN risk available at CIBMTR, since when?
2. Hi Firas, How are defining the MRD?
3. The methods for MRD assessment may be quite heterogeneous, including the threshold of detection. How will you deal with the high likelihood of false MRD negative assessments from using inadequately sensitive quantification?
4. MRD test is different from different centers. How can you control for this?
5. How do you account for different MRD- cut-offs?
6. To clarify, if AML-MRD is to become a "precision medicine tool", does that mean is will be used to guide treatment decisions in addition to being prognostic?
7. How will control for the various methods for detecting MRD as different techniques have different sensitivities/accuracy?
8. if both multiparameter flow and NGS are available and are discordant on the same patient, how will that be analyzed?
9. is the MRD before alloSCT is the one to be analyzed?
10. Will this require more data from centers to answer some of the questions above?

H. Racial, ethnicity and socioeconomic disparity in outcome of patients with chronic graft versus host disease.

1. Is age significantly different in your Hispanic cohort? How do you adjust for it?
2. Was the MMUD recipient cohort limited to single antigen mismatch? Or all mismatches (understanding most MMUD will likely be single antigen MM)?
3. Do you have information on health insurance? Why not to study this question in a more homogeneous patient population to avoid the complexity and interactions in different factors?
4. Are there any other sociodemographic variables available that could be used to adjust for socioeconomic status, or is median income in the patient's ZIP code the only one?
5. Baker et al 2009 demonstrated no impact of household income on GVHD (acute or chronic) and only minimal impact of race on Grade III-IV aGVHD (none of cGVHD). Why do you think this null relationship should be pursued again?
6. Is there a plan to study as per continent distribution?
7. Is there a better index to gauge SES or poverty level?
8. Are Native American/Hawaiian/Pacific islanders being grouped elsewhere?

I. Time from diagnosis to transplant as an important contributor for post allogeneic stem cell transplant infections, immune reconstitution and its associated mortality/morbidity.

1. Do you plan to address the confounding influence of different factors leading to delay in transplant timing?
2. How are you going to account for number of cycles of chemotherapy versus no

chemotherapy as a confounder in the time delay?

J. Efficacy and safety of CD19 directed CAR T-cell therapy for non-Hodgkin B-cell lymphomas with secondary central nervous system involvement.

1. Is site-specific response (CNS vs. other lesions) and pattern of relapse/progression (CNS vs. systemic) available?
2. Why not to consider a comparative group?
3. Will you stratify patients according if they received IT chemo vs radiation therapy?

K. Haploidentical donor versus matched donor allogeneic hematopoietic cell transplantation in patients with myelofibrosis.

1. Availability of somatic mutations?
2. Is pretransplant Splenectomy data available? Are you going to factor this in the outcomes?
3. At least look at splenectomies?
4. What risk stratification is being used? DIPSS or DIPSS+?

L. Assessing utilization and clinical outcome differences by sex and race in CAR-T for relapsed/refractory NHL. *No additional questions*

M. Optimal GVHD prevention strategy in older, robust patients with acute leukemias and myeloid malignancies undergoing myeloablative, matched donor hematopoietic cell transplantation. *No additional questions*

N. Outcomes of elderly patients receiving CD-19 directed CAR-T therapy for B-cell lymphomas. *No additional questions*

O. Determinants of successful discontinuation of immune suppression following allogeneic hematopoietic cell transplantation.

1. How is immune suppression stop defined in the CIBMTR database?
2. How long after HCT do you expect data regarding ongoing IST usage to be reliable since many patients leave the transplant center and are managed elsewhere long-term?
3. How long will you deal with restart IST?

Accrual Summary for the Plasma Cell Disorders Working Committee

Recipients of first autologous transplant for **Plasma Cell Disorders** registered to the CIBMTR, 1990-2021

Characteristic	TED N (%)	Research N (%)
No. of patients	106799	16114
No. of centers	493	318
Age at transplant, median (range), years - median (min-max)	60 (18-86)	59 (20-83)
Disease - no. (%)		
Multiple Myeloma	100765 (94)	14176 (88)
Amyloidosis	3295 (3)	1442 (9)
Plasma cell leukemia	927 (1)	201 (1)
Solitary plasmacytoma	435 (0)	51 (0)
Waldenstrom macroglobulinemia	348 (0)	47 (0)
POEMS Syndrome	556 (1)	88 (1)
Multiple Plasmacytomas	53 (0)	4 (0)
LCDD	318 (0)	94 (1)
Others	102 (0)	11 (0)
Graft type - no. (%)		
BM	399 (0)	82 (1)
PB	104977 (98)	15885 (99)
CB	7 (0)	2 (0)
Missing	1416 (1)	145 (1)
Year of transplant - no. (%)		
1990-1991	207 (0)	44 (0)
1992-1993	322 (0)	70 (0)
1994-1995	630 (1)	243 (2)
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 (5)	1489 (9)
2006-2007	5234 (5)	1380 (9)
2008-2009	6332 (6)	1520 (9)
2010-2011	9975 (9)	672 (4)
2012-2013	10864 (10)	1186 (7)
2014-2015	11712 (11)	1911 (12)
2016-2017	14256 (13)	2057 (13)
2018-2019	15032 (14)	2395 (15)
2020-2021	15505 (15)	195 (1)
Follow-up - median (range)	58 (0-347)	72 (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, 1990-2018

Characteristic	TED N (%)	Research N (%)
No. of patients	5164	2119
No. of centers	340	266
Age at transplant, median (range), years - median (min-max)	51 (1-78)	50 (10-79)
Disease - no. (%)		
Multiple Myeloma	4649 (90)	1886 (89)
Amyloidosis	32 (1)	7 (0)
Plasma cell leukemia	258 (5)	131 (6)
Solitary plasmacytoma	41 (1)	6 (0)
Waldenstrom macroglobulinemia	123 (2)	73 (3)
POEMS Syndrome	1 (0)	0 (0)
Multiple Plasmacytomas	2 (0)	1 (0)
Others	58 (1)	15 (1)
Graft type - no. (%)		
BM	1164 (23)	627 (30)
PB	3866 (75)	1448 (68)
CB	41 (1)	40 (2)
Missing	93 (2)	4 (0)
Donor - no. (%)		
HLA-identical sibling	3277 (63)	1322 (62)
Monozygotic twin	162 (3)	135 (6)
Other relative	364 (7)	102 (5)
Unrelated donor	1271 (25)	540 (25)
Missing	90 (2)	20 (1)
Prior Auto transplant - no. (%)		
No	2320 (45)	1194 (56)
Yes	2844 (55)	925 (44)
Year of transplant - no. (%)		
1990-1991	71 (1)	95 (4)
1992-1993	171 (3)	141 (7)
1994-1995	282 (5)	146 (7)
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)

Characteristic	TED N (%)	Research N (%)
2006-2007	350 (7)	203 (10)
2008-2009	407 (8)	134 (6)
2010-2011	432 (8)	59 (3)
2012-2013	388 (8)	49 (2)
2014-2015	357 (7)	90 (4)
2016-2017	303 (6)	93 (4)
2018-2019	135 (3)	107 (5)
2020-2021	134 (3)	19 (1)
Follow-up - median (range)	72 (0-361)	120 (0-288)

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

Unrelated Donor HCT Research Sample Inventory for Plasma Cell Disorders - 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	892	270	159
Source of data			
CRF	437 (49)	120 (44)	70 (44)
TED	455 (51)	150 (56)	89 (56)
Number of centers	122	77	73
Disease at transplant			
Plasma cell disorder/Multiple Myeloma	892 (100)	270 (100)	159 (100)
Recipient age at transplant			
10-19 years	3 (<1)	0	1 (1)
20-29 years	6 (1)	3 (1)	2 (1)
30-39 years	78 (9)	29 (11)	17 (11)
40-49 years	264 (30)	69 (26)	34 (21)
50-59 years	375 (42)	118 (44)	73 (46)
60-69 years	161 (18)	50 (19)	31 (19)
70+ years	5 (1)	1 (<1)	1 (1)
Median (Range)	53 (10-77)	53 (22-72)	54 (18-74)
Recipient race/ethnicity			
Caucasian, non-Hispanic	760 (85)	234 (87)	124 (78)
African-American, non-Hispanic	55 (6)	19 (7)	4 (3)
Asian, non-Hispanic	15 (2)	5 (2)	2 (1)
Pacific islander, non-Hispanic	1 (<1)	1 (<1)	0
Native American, non-Hispanic	2 (<1)	1 (<1)	0
Hispanic	42 (5)	7 (3)	6 (4)
Missing	17 (2)	3 (1)	23 (14)
Recipient sex			
Male	556 (62)	174 (64)	103 (65)
Female	336 (38)	96 (36)	56 (35)
Karnofsky score			
10-80	358 (40)	124 (46)	70 (44)
90-100	500 (56)	139 (51)	86 (54)
Missing	34 (4)	7 (3)	3 (2)
HLA-A B DRB1 groups - low resolution			
4/6	4 (<1)	0	0
5/6	105 (12)	26 (11)	13 (9)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
6/6	767 (88)	216 (89)	138 (91)
Unknown	16 (N/A)	28 (N/A)	8 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	11 (1)	0	0
6/8	32 (4)	1 (1)	3 (3)
7/8	134 (17)	25 (13)	20 (18)
8/8	634 (78)	163 (86)	86 (79)
Unknown	81 (N/A)	81 (N/A)	50 (N/A)
HLA-DPB1 Match			
Double allele mismatch	137 (30)	15 (20)	8 (27)
Single allele mismatch	250 (55)	40 (53)	19 (63)
Full allele matched	65 (14)	20 (27)	3 (10)
Unknown	440 (N/A)	195 (N/A)	129 (N/A)
High resolution release score			
No	516 (58)	270 (100)	157 (99)
Yes	376 (42)	0	2 (1)
KIR typing available			
No	824 (92)	270 (100)	159 (100)
Yes	68 (8)	0	0
Graft type			
Marrow	159 (18)	35 (13)	23 (14)
PBSC	730 (82)	235 (87)	136 (86)
BM+PBSC	2 (<1)	0	0
PBSC+UCB	1 (<1)	0	0
Conditioning regimen			
Myeloablative	317 (36)	99 (37)	63 (40)
RIC/Nonmyeloablative	564 (63)	167 (62)	89 (56)
TBD	11 (1)	4 (1)	7 (4)
Donor age at donation			
To Be Determined/NA	6 (1)	28 (10)	4 (3)
10-19 years	20 (2)	13 (5)	2 (1)
20-29 years	374 (42)	111 (41)	64 (40)
30-39 years	246 (28)	69 (26)	46 (29)
40-49 years	170 (19)	33 (12)	33 (21)
50+ years	76 (9)	16 (6)	10 (6)
Median (Range)	32 (18-61)	30 (18-58)	33 (19-58)
Donor/Recipient CMV serostatus			
+/+	209 (23)	67 (25)	34 (21)
+/-	94 (11)	38 (14)	18 (11)
-/+	271 (30)	77 (29)	43 (27)
-/-	309 (35)	81 (30)	58 (36)
Missing	9 (1)	7 (3)	6 (4)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
GvHD Prophylaxis			
No GvHD Prophylaxis	6 (1)	2 (1)	3 (2)
TDEPLETION alone	2 (<1)	2 (1)	1 (1)
TDEPLETION +- other	13 (1)	5 (2)	1 (1)
CD34 select alone	40 (4)	15 (6)	8 (5)
CD34 select +- other	19 (2)	6 (2)	3 (2)
Cyclophosphamide alone	5 (1)	2 (1)	2 (1)
Cyclophosphamide +- others	30 (3)	9 (3)	4 (3)
FK506 + MMF +- others	153 (17)	27 (10)	22 (14)
FK506 + MTX +- others(not MMF)	297 (33)	115 (43)	30 (19)
FK506 +- others(not MMF,MTX)	44 (5)	12 (4)	7 (4)
FK506 alone	21 (2)	5 (2)	4 (3)
CSA + MMF +- others(not FK506)	146 (16)	27 (10)	35 (22)
CSA + MTX +- others(not MMF,FK506)	50 (6)	18 (7)	20 (13)
CSA +- others(not FK506,MMF,MTX)	13 (1)	6 (2)	5 (3)
CSA alone	11 (1)	4 (1)	2 (1)
Other GVHD Prophylaxis	30 (3)	10 (4)	7 (4)
Missing	12 (1)	5 (2)	5 (3)
Donor/Recipient sex match			
Male-Male	391 (44)	106 (39)	67 (42)
Male-Female	204 (23)	54 (20)	33 (21)
Female-Male	161 (18)	64 (24)	35 (22)
Female-Female	130 (15)	40 (15)	20 (13)
CB - recipient M	1 (<1)	0	0
Missing	5 (1)	6 (2)	4 (3)
Year of transplant			
1986-1990	1 (<1)	0	0
1991-1995	20 (2)	4 (1)	5 (3)
1996-2000	59 (7)	19 (7)	10 (6)
2001-2005	139 (16)	20 (7)	31 (19)
2006-2010	267 (30)	45 (17)	39 (25)
2011-2015	270 (30)	80 (30)	46 (29)
2016-2020	125 (14)	99 (37)	28 (18)
2021	11 (1)	3 (1)	0
Follow-up among survivors, Months			
N Eval	193	93	47
Median (Range)	61 (0-288)	47 (0-194)	49 (3-216)

Unrelated Cord Blood Transplant Research Sample Inventory for Plasma Cell Disorders - 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	37	12	11
Source of data			
CRF	29 (78)	6 (50)	4 (36)
TED	8 (22)	6 (50)	7 (64)
Number of centers	19	8	6
Disease at transplant			
Plasma cell disorder/Multiple Myeloma	37 (100)	12 (100)	11 (100)
Recipient age at transplant			
10-19 years	0	0	1 (9)
20-29 years	1 (3)	0	0
30-39 years	2 (5)	0	0
40-49 years	9 (24)	1 (8)	3 (27)
50-59 years	23 (62)	7 (58)	3 (27)
60-69 years	2 (5)	4 (33)	4 (36)
Median (Range)	52 (22-64)	58 (48-67)	53 (19-70)
Recipient race/ethnicity			
Caucasian, non-Hispanic	20 (54)	6 (50)	4 (36)
African-American, non-Hispanic	9 (24)	3 (25)	1 (9)
Asian, non-Hispanic	1 (3)	0	1 (9)
Hispanic	4 (11)	1 (8)	0
Missing	3 (8)	2 (17)	5 (45)
Recipient sex			
Male	20 (54)	7 (58)	7 (64)
Female	17 (46)	5 (42)	4 (36)
Karnofsky score			
10-80	13 (35)	3 (25)	5 (45)
90-100	24 (65)	7 (58)	6 (55)
Missing	0	2 (17)	0
HLA-A B DRB1 groups - low resolution			
4/6	21 (60)	4 (44)	10 (91)
5/6	13 (37)	4 (44)	1 (9)
6/6	1 (3)	1 (11)	0
Unknown	2 (N/A)	3 (N/A)	0 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	21 (78)	4 (80)	5 (63)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
6/8	4 (15)	1 (20)	3 (38)
7/8	2 (7)	0	0
Unknown	10 (N/A)	7 (N/A)	3 (N/A)
HLA-DPB1 Match			
Double allele mismatch	1 (13)	0	2 (67)
Single allele mismatch	6 (75)	0	1 (33)
Full allele matched	1 (13)	0	0
Unknown	29 (N/A)	12 (N/A)	8 (N/A)
High resolution release score			
No	34 (92)	12 (100)	11 (100)
Yes	3 (8)	0	0
KIR typing available			
No	34 (92)	12 (100)	11 (100)
Yes	3 (8)	0	0
Graft type			
UCB	35 (95)	12 (100)	9 (82)
PBSC+UCB	2 (5)	0	2 (18)
Number of cord units			
1	29 (78)	0	7 (64)
2	8 (22)	0	4 (36)
Unknown	0 (N/A)	12 (N/A)	0 (N/A)
Conditioning regimen			
Myeloablative	12 (32)	4 (33)	4 (36)
RIC/Nonmyeloablative	23 (62)	7 (58)	7 (64)
TBD	2 (5)	1 (8)	0
Donor age at donation			
To Be Determined/NA	1 (3)	2 (17)	0
0-9 years	35 (95)	9 (75)	9 (82)
10-19 years	0	1 (8)	1 (9)
50+ years	1 (3)	0	1 (9)
Median (Range)	2 (1-53)	4 (1-11)	3 (1-63)
Donor/Recipient CMV serostatus			
+/+	8 (22)	4 (33)	2 (18)
+/-	4 (11)	3 (25)	3 (27)
-/+	5 (14)	1 (8)	2 (18)
-/-	3 (8)	2 (17)	1 (9)
CB - recipient +	11 (30)	0	2 (18)
CB - recipient -	6 (16)	0	1 (9)
CB - recipient CMV unknown	0	2 (17)	0
GvHD Prophylaxis			
CD34 select +- other	1 (3)	0	1 (9)
Cyclophosphamide +- others	0	1 (8)	0

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
FK506 + MMF +- others	11 (30)	3 (25)	3 (27)
FK506 + MTX +- others(not MMF)	1 (3)	0	2 (18)
FK506 +- others(not MMF,MTX)	1 (3)	0	0
FK506 alone	0	2 (17)	0
CSA + MMF +- others(not FK506)	16 (43)	5 (42)	2 (18)
CSA + MTX +- others(not MMF,FK506)	0	1 (8)	0
CSA +- others(not FK506,MMF,MTX)	0	0	1 (9)
CSA alone	0	0	2 (18)
Other GVHD Prophylaxis	6 (16)	0	0
Missing	1 (3)	0	0
Donor/Recipient sex match			
CB - recipient M	20 (54)	7 (58)	7 (64)
CB - recipient F	17 (46)	5 (42)	4 (36)
Year of transplant			
2006-2010	8 (22)	4 (33)	4 (36)
2011-2015	25 (68)	4 (33)	3 (27)
2016-2020	4 (11)	3 (25)	3 (27)
2021	0	1 (8)	1 (9)
Follow-up among survivors, Months			
N Eval	4	2	2
Median (Range)	59 (48-72)	68 (64-72)	26 (15-37)

Related Donor HCT Research Sample Inventory for Plasma Cell Disorders - 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	254	40	18
Source of data			
CRF	90 (35)	7 (18)	7 (39)
TED	164 (65)	33 (83)	11 (61)
Number of centers	31	13	6
Disease at transplant			
Plasma cell disorder/Multiple Myeloma	254 (100)	40 (100)	18 (100)
Recipient age at transplant			
20-29 years	3 (1)	0	0
30-39 years	13 (5)	2 (5)	0
40-49 years	64 (25)	10 (25)	2 (11)
50-59 years	105 (41)	18 (45)	9 (50)
60-69 years	63 (25)	10 (25)	7 (39)
70+ years	6 (2)	0	0
Median (Range)	55 (26-75)	55 (35-69)	57 (49-69)
Recipient race/ethnicity			
Caucasian, non-Hispanic	164 (65)	26 (65)	13 (72)
African-American, non-Hispanic	24 (9)	7 (18)	2 (11)
Asian, non-Hispanic	13 (5)	1 (3)	1 (6)
Pacific islander, non-Hispanic	1 (<1)	0	0
Native American, non-Hispanic	1 (<1)	0	0
Hispanic	44 (17)	6 (15)	2 (11)
Missing	7 (3)	0	0
Recipient sex			
Male	146 (57)	30 (75)	11 (61)
Female	108 (43)	10 (25)	7 (39)
Karnofsky score			
10-80	102 (40)	13 (33)	7 (39)
90-100	148 (58)	27 (68)	10 (56)
Missing	4 (2)	0	1 (6)
Graft type			
Marrow	22 (9)	1 (3)	2 (11)
PBSC	232 (91)	39 (98)	14 (78)
PBSC+UCB	0	0	2 (11)
Conditioning regimen			

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Myeloablative	90 (35)	19 (48)	8 (44)
RIC/Nonmyeloablative	164 (65)	21 (53)	10 (56)
Donor age at donation			
To Be Determined/NA	0	0	1 (6)
0-9 years	1 (<1)	0	0
10-19 years	5 (2)	0	0
20-29 years	23 (9)	3 (8)	1 (6)
30-39 years	25 (10)	4 (10)	4 (22)
40-49 years	61 (24)	9 (23)	0
50+ years	139 (55)	24 (60)	12 (67)
Median (Range)	51 (0-76)	54 (27-69)	58 (29-69)
Donor/Recipient CMV serostatus			
+/+	103 (41)	18 (45)	5 (28)
+/-	28 (11)	5 (13)	2 (11)
-/+	51 (20)	7 (18)	4 (22)
-/-	70 (28)	10 (25)	7 (39)
Missing	2 (1)	0	0
GvHD Prophylaxis			
No GvHD Prophylaxis	5 (2)	1 (3)	1 (6)
TDEPLETION +- other	2 (1)	0	0
CD34 select alone	0	1 (3)	0
CD34 select +- other	1 (<1)	0	0
Cyclophosphamide alone	2 (1)	0	0
Cyclophosphamide +- others	43 (17)	6 (15)	3 (17)
FK506 + MMF +- others	25 (10)	2 (5)	0
FK506 + MTX +- others(not MMF)	106 (42)	21 (53)	9 (50)
FK506 +- others(not MMF,MTX)	9 (4)	3 (8)	1 (6)
FK506 alone	2 (1)	1 (3)	0
CSA + MMF +- others(not FK506)	6 (2)	0	0
CSA + MTX +- others(not MMF,FK506)	5 (2)	0	0
CSA +- others(not FK506,MMF,MTX)	1 (<1)	1 (3)	0
CSA alone	1 (<1)	0	0
Other GVHD Prophylaxis	15 (6)	0	1 (6)
Missing	31 (12)	4 (10)	3 (17)
Donor/Recipient sex match			
Male-Male	89 (35)	20 (50)	8 (44)
Male-Female	47 (19)	4 (10)	3 (17)
Female-Male	57 (22)	10 (25)	2 (11)
Female-Female	61 (24)	6 (15)	3 (17)
CB - recipient M	0	0	1 (6)
CB - recipient F	0	0	1 (6)
Year of transplant			

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
2006-2010	28 (11)	7 (18)	5 (28)
2011-2015	116 (46)	20 (50)	7 (39)
2016-2020	105 (41)	11 (28)	5 (28)
2021	5 (2)	2 (5)	1 (6)
Follow-up among survivors, Months			
N Eval	116	15	9
Median (Range)	49 (4-146)	61 (6-122)	37 (3-95)

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TO: Plasma Cell Disorders Working Committee Members

FROM: Anita D'Souza, MD; Scientific Director for the Plasma Cell Disorders Working Committee

RE: 2020-2021 Studies in Progress Summary

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). The study looks to evaluate AHCT use in POEMS and determine pre-transplant disease status, mortality rates, day-100 post-transplant disease status, TRM, relapse/progression PFS and OS.
Status: Manuscript submitted, Jan 2022.

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 Preparation, submitted ASCO abstract and goal to submit manuscript by July 2022.

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 submitted, results to be presented at Tandem Meetings 2022, goal to submit manuscript by July 2022.

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: Analysis is ongoing.

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 Light Chain Deposition Disease

Q2. Key Words

Autologous, hematopoietic cell transplantation, Light Chain Deposition Disease

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):	Binod Dhakal, M.D.
Email address:	bdhakal@mcw.edu
Institution name:	Medical College of Wisconsin
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?

- 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:

Hamza Hashmi, M.D.

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.

Protocol # CT20-03: Comorbidities, Toxicities and Efficacy Outcomes after Chimeric Antigen Receptor T-cell Therapy in B cell Lymphoma

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 Hematopoietic cell transplantation (HCT) have a role for Light Chain Deposition Disease (LCDD)

Q16. RESEARCH HYPOTHESIS:

Hematopoietic cell transplantation (HCT) results in long-term disease control for Light Chain Deposition Disease (LCDD)

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 HCT for LCDD
2. To determine disease response [hematological, clinical], progression-free survival (PFS), transplant-related mortality (TRM), cumulative incidence of relapse after HCT for LCDD

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 HCT for LCDD. This retrospective study will evaluate the outcomes of autologous HCT for LCDD to understand the optimal application of HCT as a treatment modality. This study could identify patient- or disease- related factors that may impact the clinical management of LCDD, 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.

LCDD is a plasma cell dyscrasia in which monoclonal immunoglobin and light chains are deposited in organs, primarily kidneys (1). LCDD may exist as pure LCDD versus LCDD as part of multiple myeloma/ Monoclonal neuropathy of uncertain significance (MGUS)/AL amyloidosis (2). Autologous HCT can produce durable hematological and organ responses in patients with LCDD (3-5). Although association between hematological response and organ recovery is not entirely clear, it is hypothesized that hematological response is associated with successful kidney transplantation and improved graft viability post HCT (4).

Higher level evidence based therapeutic recommendations are lacking in LCDD largely due to its relative rarity, lack of large-sized retrospective data and advanced stage renal disease making patient ineligible for any intensive treatment including HCT. Using the CIBMTR data, we can not only determine long-term survival in a large number of patients undergoing Autologous HCT at multiple centers but also evaluate for clinically meaningful outcomes including recovery of renal function, association between hematological and renal responses, and outcomes of post transplant renal allografts. This study will also help determine patient and disease related variables that predict treatment-related complications (including TRM) in patients undergoing Autologous HCT with advanced age renal disease and allow for better patient selection for transplant.

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 Autologous HCT for LCDD from 2000 to 2018
Exclusion criteria:
Patients with known diagnosis of AL amyloidosis

Q21. Does this study include pediatric patients?

- No

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

AL amyloidosis is a disease of the adult population and 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 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
• Presence of chronic kidney disease: Yes vs no
• Chronic kidney disease stage: 3 vs 4 vs 5
• 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
• Presence of Multiple myeloma vs MGUS vs AL amylodosis
• 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 M protein: yes vs no
• Abnormal free light chain ratio: 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 vs both
• Time from diagnosis to transplant: continuous (months)
• 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
• Recovery of renal function: yes vs no
• Renal transplantation: 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

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. Kanzaki G, Okabayashi Y, Nagahama K, Ohashi R, Tsuboi N, Yokoo T, et al. Monoclonal Immunoglobulin Deposition Disease and Related Diseases. J Nippon Med Sch. 2019. 86 (1):2-9
2. McKenna RW, Kyle RA, Kuehl WM, Grogan TM, Harris NL, Coupland RW. Plasma Cell Neoplasms in WHO Classification of Tumours of Haematolpoietic and Lymphoid Tissues. Lyon: International Agency for Research on Cancer; 2008
3. Lorenz EC, Gertz MA, Fervenza FC, Dispenzieri A, Lacy MQ, Hayman SR, et al. Long–term outcome of autologous stem cell transplantation in light chain deposition disease. Nephrology, Dialysis, Transplantation. 2008. 23:2051-57.
4. Jimenez Zepeda VFN, Winter A, Reece D, Trudel S, Chen C, Rabea A, et al. Light chain deposition disease: impact of stem cell transplant on Hematological response achievement. 2010. 116:2302.
5. Telio D, Shepherd J, Forrest D, Zypchen L, Barnett M, Nevill T. High-dose melphalan followed by auto-SCT has favorable safety and efficacy in selected patients with light chain deposition disease and light and heavy chain deposition disease. Bone Marrow Transplant. 2012 Mar. 47(3):453-5

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.**

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 adult patients who underwent first HCT for LCDD from 2000-2019 and registered with CIBMTR (TED level)

Characteristic	TED	CRF
No. of patients	186	74
No. of centers	81	32
Age at HCT - median (min-max)	59 (24-78)	56 (36-76)
Age at transplant, years - no. (%)		
18-39	13 (7)	2 (3)
40-49	31 (17)	22 (30)
50-59	59 (32)	17 (23)
60-69	70 (38)	24 (32)
70+	13 (7)	9 (12)
Gender - no. (%)		
Male	103 (55)	39 (53)
Female	83 (45)	35 (47)
Region - no. (%)		
US	168 (90)	71 (96)
Canada	13 (7)	0 (0)
Mideast/Africa	1 (1)	0 (0)
Central/South America	4 (2)	3 (4)
Race - no. (%)		
White	133 (72)	50 (68)
Black or African American	24 (13)	20 (27)
Asian	6 (3)	2 (3)
Native Hawaiian or other Pacific islander	1 (1)	0 (0)
American Indian or Alaska Native	2 (1)	0 (0)
Missing	20 (11)	2 (3)
Karnofsky score prior to HCT - no. (%)		
90-100	100 (54)	31 (42)
< 90	82 (44)	41 (55)
Missing	4 (2)	2 (3)
HCT-CI - no. (%)		
0	36 (19)	14 (19)
1	13 (7)	8 (11)
2	37 (20)	13 (18)
3+	100 (54)	39 (53)
Adjusted HCT-CI scores (Renal Comorbidity excluded) - no. (%)		
0	51 (27)	20 (27)

Characteristic	TED	CRF
1	19 (10)	12 (16)
2	34 (18)	8 (11)
3+	82 (44)	34 (46)
Conditioning regimen - no. (%)		
Melphalan only	181 (97)	73 (99)
Melphalan based regimen	5 (3)	1 (1)
Melphalan dose(mg/m) - no. (%)		
MEL 140	92 (49)	29 (39)
MEL 200	94 (51)	44 (59)
Missing	0 (0)	1 (1)
Disease status prior to transplant - no. (%)		
sCR/CR	34 (18)	9 (12)
VGPR	68 (37)	32 (43)
PR	49 (26)	22 (30)
SD	25 (13)	7 (9)
PD/Relapse	4 (2)	2 (3)
Missing	6 (3)	2 (3)
Time from diagnosis to HCT - median (min-max)	8 (0-835)	7 (3-83)
Time from diagnosis to transplant - no. (%)		
<6 months	67 (36)	26 (35)
6-12 months	67 (36)	35 (47)
12-18 months	26 (14)	4 (5)
18-24 months	12 (6)	1 (1)
>24 months	14 (8)	8 (11)
Year of transplant - no. (%)		
2011	1 (1)	1 (1)
2013	5 (3)	2 (3)
2014	21 (11)	2 (3)
2015	26 (14)	5 (7)
2016	51 (27)	7 (9)
2017	36 (19)	12 (16)
2018	20 (11)	29 (39)
2019	26 (14)	16 (22)
Follow-up - median (range)	41 (2-119)	25 (3-81)
CRF-only variables		
Lines of chemotherapy - no. (%)		
1	-	53 (72)
>=2	-	13 (18)

Characteristic	TED	CRF
Missing	-	8 (11)
Chemotherapy - no. (%)		
VTD	-	1 (1)
VRD	-	18 (24)
VCD	-	25 (34)
VD	-	9 (12)
RD	-	4 (5)
TD	-	2 (3)
KRD	-	1 (1)
Daratumumab	-	4 (5)
Others	-	2 (2)
Missing	-	8 (11)
Serum creatinine prior to transplant, mg/dl - no. (%)		
< 2 mg/dl	-	50 (68)
>= 2 mg/dl	-	24 (32)
post-HCT therapy (for current transplant) - no. (%)		
VR +/- other	-	3 (4)
V +/- other	-	7 (9)
R +/- other	-	27 (36)
KR +/- other	-	2 (3)
Dara+Pom +/- other	-	1 (1)
Dara +/- other	-	1 (1)
Thalidomide+/-other	-	1 (1)
Ixazomib+/- other	-	3 (4)
None	-	22 (30)
Missing	-	7 (9)

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
Email address:	rahul.banerjee@ucsf.edu
Institution name:	University of California San Francisco
Academic rank:	Advanced Fellow, BMT/CAR-T Therapy

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:	University of California San Francisco
Academic rank:	Professor, Department of Medicine

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:

Rahul Banerjee, 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.

Dr. Banerjee: Member, Plasma Cell Disorders Working Committee
Dr. Shah: Co-Chair, 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

Q15. RESEARCH QUESTION:

Do 24-hour urine measurements, either as part of pre-ASCT or post-ASCT response assessments, affect the prognostic value of CIBMTR response assessments?

Q16. RESEARCH HYPOTHESIS:

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 with regard to progression-free survival (PFS) will fall no greater than 0.1 points of each other. We additionally hypothesize that fewer than 5% of patients will have divergent response assessments using urine-free CIBMTR versus traditional CIBMTR response criteria.

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

Suggested word limit of 200 words:

1. PRIMARY: Harrell's concordance index for PFS using current CIBMTR response criteria (measured both pre-ASCT and post-ASCT)
2. PRIMARY: Harrell's concordance index for PFS using urine-free CIBMTR response criteria (measured both pre-ASCT and post-ASCT)
3. SECONDARY: Real-world rates of omission of 24-hour urine testing from CIBMTR response criteria
4. SECONDARY: Concordance between urine-free and traditional CIBMTR response criteria

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 are a component of CIBMTR response assessments for patients with multiple myeloma (as with IMWG response criteria). From a practical perspective, these assessments are awkward for patients to collect and to store in a refrigerated environment. If this study 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 European groups have specifically investigated the impact of urine testing on peri-ASCT outcomes in multiple myeloma. Dejoie et al (Blood 2016, PMID 27729323) analyzed outcomes from the French IFM2009 trial among patients with light-chain-only disease (n = 113). The authors found that serum free light chains (which are also included in current CIBMTR response criteria) provided more discriminatory power than did the results of urine assessments. Lahuerta et al (Blood 2019, PMID 31010846) analyzed outcomes from the Spanish GEM2012MENOS65 trial (n = 384) excluding patients with light-chain-only disease. The authors found no difference in outcomes between patients who achieved a standard complete response (CR) and those who achieved an 'uncertain' CR (meeting criteria for CR but missing urine assessments).

These studies, while helpful, have two key limitations. Firstly, only patients on specific clinical trials were enrolled; this may have introduced selection bias given that not all patients with myeloma enroll on clinical trials. Secondly, the two studies focused on specific components of response criteria: serum free light chains versus urine testing and CR versus 'uncertain' CR, respectively. This CIBMTR analysis will overcome both limitations using a larger comprehensive registry of patients to focus on comparing two response criteria systems in their entirety. Specifically, we will use Harrell's concordance indices to compare traditional CIBMTR response criteria and urine-free CIBMTR response criteria. This approach has been used to compare prognostic assessments in myeloma previously (Schavgoulidze et al, ASH 2020 poster) and is well-suited for comparisons of assessment systems.

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 applicable for multiple myeloma.

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 variables: Age, gender, race/ethnicity
• 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.

Not applicable.

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	Unknown	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)
>=10%	2200 (80)	3013 (72)	5213 (75)

Characteristic	Known	Unknown	Total
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)
Serum creatinine prior to transplant, mg/dl - no. (%)			
< 2 mg/dl	2593 (94)	3878 (93)	6471 (93)

Characteristic	Known	Unknown	Total
>= 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)
Urinary original mono bands pr - no. (%)			
No	71 (3)	0 (0)	71 (1)
Yes	1032 (38)	0 (0)	1032 (15)

Characteristic	Known	Unknown	Total
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)
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. (%)			

Characteristic	Known	Unknown	Total
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

Consolidation or Maintenance therapy in AL Amyloidosis Following Autologous Stem Cell Transplantation

Q2. Key Words

Light Chain (AL) Amyloid, Autologous Stem Cell Transplant, Maintenance, or consolidation therapy, Progression Free Survival (PFS), Overall Survival (OS), Very good partial response (VGPR)

Q3. PRINCIPAL INVESTIGATOR

Provide the following information for each investigator:

Principal Investigator #1:

First and last name, degree(s):	Shashank Cingam
Email address:	scingam@stanford.edu
Institution name:	Stanford University
Academic rank:	Fellow

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):	Surbhi Sidana
Email address:	ssidana@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?

- 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:

scingam@stanford.edu

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:

Does maintenance therapy following Autologous Hematopoietic Stem Cell transplant improve outcomes in patients with light chain Amyloidosis?

Q16. RESEARCH HYPOTHESIS:

Our hypothesis is that patients with AL amyloidosis who receive consolidation/ maintenance therapy after autologous stem cell transplant have longer PFS.

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

Suggested word limit of 200 words:

The primary objective of the study is to evaluate the outcomes in patients with AL amyloidosis receiving maintenance/consolidation therapy vs observation after an autologous stem cell transplant (Auto-SCT).
Sub-group analysis will be done and patients will be stratified by day 90 post-transplant response (i) atleast VGPR without evidence of organ related disease progression, (ii)less than VGPR (or) with organ related disease progression
Primary Outcome:
(i) To evaluate progression free survival (progression defined as hematologic or organ progression requiring change in therapy) following autologous stem cell transplant in patients receiving maintenance/consolidation therapy vs observation in the (a) overall population and (b) sub-groups of patients achieving VGPR vs not
Secondary Outcome(s):
(i) Percentage of patients with disease progression (including hematological and organ specific) at 24 months receiving maintenance/consolidation therapy vs observation after an Autologous Stem Cell Transplant (Auto-SCT) grouped by Day + 60- 90 post-transplant response (i) atleast VGPR without evidence of organ related disease progression, (ii)less than VGPR (or) with organ related disease progression)
(ii) Percentage of patients alive at 3 years receiving maintenance/consolidation therapy vs observation after an Autologous Stem Cell Transplant (Auto-SCT) grouped by Day + 60- 90 post-transplant response (i) atleast VGPR without evidence of organ related disease progression, (ii)less than VGPR (or) with organ related disease progression)
(iii)To evaluate PFS and OS in subgroup of patients with > 10% plasma cells at diagnosis with or without maintenance/consolidation therapy post SCT

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 about the use of post HSCT maintenance agents in AL amyloidosis. The currently published data is from single institution retrospective studies. It is difficult to perform a randomized study to answer this question as AL amyloidosis is a rare disease and only ~20% of the patients undergo/ eligible for Auto-HSCT. The data from this study will evaluate the role of maintenance strategies after Auto-HCT in AL amyloidosis. Upon successful completion of the study, it will help guide treatment decisions and instruct further clinical trials on maintenance strategies.

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 continues to be an important strategy to improve outcomes in carefully selected patients with AL Amyloidosis.(1) Although maintenance strategies have been studied extensively in multiple myeloma and maintenance treatment is the current standard of care in myeloma, its role in AL Amyloidosis is not well defined. (2, 3) The current evidence on the use of maintenance treatment after Auto-HCT is from a handful of retrospective studies. Retrospective pooled data of 143 AL amyloid patients from 2 clinical trials who underwent risk adapted melphalan and HSCT with or without consolidation showed an improvement in event-free survival (EFS) and OS compared to historical outcomes. The median event-free survival (EFS) with SCT was 4.04 years and median OS was 10.4 years which was better than the historical outcomes. (4). Similarly, in a large single institution retrospective study showed patients less than very good partial response (VGPR) at Day+100 after Auto- SCT who received consolidation treatment had better PFS and OS compared to who did not. (5). Another single institution study with 50 patients, 28 patients received maintenance and 22 did not. No significant difference in PFS ($p = 0.66$) and OS ($p = 0.32$) between the two groups. (6)

Given the lack of consensus from the retrospective studies, it is unclear whether maintenance/ consolidation therapy is beneficial after Auto-HSCT in AL amyloidosis. It was clear in these retrospective studies that there was no uniform approach on a maintenance vs observation strategy. It is important to define groups that may benefit from consolidation/maintenance strategies as AL Amyloid is a heterogenous disease with variable organ involvement. These groups include patients who achieved less than VGPR after transplant or patients with >10% baseline bone marrow plasma cells.

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.

All patients with AL Amyloid who underwent Auto-HSCT from 2015-2020 within 1 year of diagnosis.

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.**

- Demographics
- Age at diagnosis
- Organ involvement data
- Mayo stage at diagnosis
- Bone marrow plasma cell percentage, NT-pro BNP/ BNP, Troponin I/T, SPEP/IFE, K/L ratio
- Induction chemotherapy details: drugs with start and stop dates, pre-SCT response
- Date of transplant
- Best response (hematologic and organ specific data- Liver, Kidney and Heart) Day + 90 post-transplant.
- Treatment after transplant: consolidation or maintenance, with start and stop dates if available
- Relapse and survival data

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.as

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. Sidiqi MH, Aljama MA, Buadi FK, Warsame RM, Lacy MQ, Dispenzieri A, et al. Stem Cell Transplantation for Light Chain Amyloidosis: Decreased Early Mortality Over Time. Journal of Clinical Oncology. 2018;36(13):1323-9.
2. Attal M, Lauwers-Cances V, Marit G, Caillot D, Moreau P, Facon T, et al. Lenalidomide maintenance after stem-cell transplantation for multiple myeloma. New England Journal of Medicine. 2012;366(19):1782-91.
3. McCarthy PL, Owzar K, Hofmeister CC, Hurd DD, Hassoun H, Richardson PG, et al. Lenalidomide after stem-cell transplantation for multiple myeloma. N Engl J Med. 2012;366(19):1770-81.
4. Landau H, Smith M, Landry C, Chou JF, Devlin SM, Hassoun H, et al. Long-term event-free and overall survival after risk-adapted melphalan and SCT for systemic light chain amyloidosis. Leukemia. 2017;31(1):136-42.
5. Al Saleh AS, Sidiqi MH, Sidana S, Muchtar E, Dispenzieri A, Dingli D, et al. Impact of consolidation therapy post autologous stem cell transplant in patients with light chain amyloidosis. Am J Hematol. 2019;94(10):1066-71.
6. Ozga M, Zhao Q, Benson D, Elder P, Williams N, Bumma N, et al. AL Amyloidosis: The Effect of Maintenance Therapy on Autologous Stem Cell Transplantation Outcomes. J Clin Med. 2020;9(11).

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.

Shashank Cingam : None
Surbhi Sidana: Janssen, BMS and Magenta: Research funding to institution and personal consultancy (consultancy < $5000/yr), Allogene: Research funding to institution

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 US adult patients (>=18 years) who underwent melphalan base first auto PB Amyloidosis transplant from 2015-2019 and reported with CIBMTR, CRF

Characteristic	No	Yes
No. of patients	356	160
No. of centers	68	58
median age (range) - median (min-max)	62 (24-78)	60 (28-76)
Age at transplant, years - no. (%)		
18-39	9 (3)	4 (3)
40-49	28 (8)	22 (14)
50-59	108 (30)	54 (34)
60-69	169 (47)	68 (43)
70+	42 (12)	12 (8)
Gender - no. (%)		
Male	190 (53)	100 (63)
Female	166 (47)	60 (38)
Race - no. (%)		
White	292 (82)	132 (83)
Black or African-American	48 (13)	16 (10)
Other	9 (3)	6 (4)
Missing	7 (2)	6 (4)
Karnofsky score - no. (%)		
>= 90	158 (44)	72 (45)
< 90	190 (53)	83 (52)
Missing	8 (2)	5 (3)
HCT-CI - no. (%)		
0	73 (21)	31 (19)
1	34 (10)	24 (15)
2	52 (15)	24 (15)
3+	197 (55)	79 (49)
TBD, inconsistencies between parent and sub-questions	0 (0)	2 (1)
Time from diagnosis to transplant - median (min-max)	6 (1-12)	6 (2-12)
Serum light chain - no. (%)		
Kappa	62 (17)	34 (21)
Lambda	207 (58)	80 (50)
Missing	87 (24)	46 (29)
Serum creatinine at diagnosis, mg/dl - no. (%)		
< 2 mg/dl	279 (78)	123 (77)
>= 2 mg/dl	36 (10)	21 (13)
Missing	41 (12)	16 (10)
Serum creatinine prior to transplant, mg/dl - no. (%)		
< 2 mg/dl	298 (84)	134 (84)

Characteristic	No	Yes
>= 2 mg/dl	55 (15)	24 (15)
Missing	3 (1)	2 (1)
Serum albumin at diagnosis, g/dL - no. (%)		
< 3.5 g/dl	206 (58)	81 (51)
>= 3.5 g/dl	98 (28)	57 (36)
Missing	52 (15)	22 (14)
Serum albumin prior to transplant, g/dl - no. (%)		
< 3.5 g/dl	236 (66)	91 (57)
>= 3.5 g/dl	101 (28)	64 (40)
Missing	19 (5)	5 (3)
Bone marrow plasma cells at diagnosis - no. (%)		
<10%	209 (59)	83 (52)
>=10%	96 (27)	59 (37)
Missing	51 (14)	18 (11)
Cytogenetic score for MM - no. (%)		
High risk	42 (12)	24 (15)
Standard risk	259 (73)	121 (76)
Test not done / unknown / no metaphases	55 (15)	15 (9)
Lines of chemotherapy - no. (%)		
0	116 (32)	34 (22)
1	214 (60)	107 (67)
>=2	26 (7)	19 (12)
Chemotherapy - no. (%)		
Chemo not given	119 (33)	34 (21)
VTD	2 (1)	0 (0)
VRD	12 (3)	22 (14)
VCD	192 (54)	85 (53)
VD	15 (4)	10 (6)
RD	1 (0)	2 (1)
KRD	0 (0)	1 (1)
Daratumumab	9 (3)	5 (3)
Others	6 (2)	1 (1)
Conditioning regimen - no. (%)		
Melphalan only	350 (98)	159 (99)
Other Melphalan based regimen	6 (2)	1 (1)
Melphalan dose in conditioning regimen, mg/m - no. (%)		
MEL 100	37 (10)	16 (10)
MEL 140	101 (28)	56 (35)
MEL 180	46 (13)	22 (14)
MEL 200	172 (48)	66 (41)

Characteristic	No	Yes
Renal involvement - no. (%)		
Yes	247 (69)	86 (54)
No	36 (10)	13 (8)
Test not done	53 (15)	58 (36)
Missing	20 (6)	3 (2)
Cardiac involvement - no. (%)		
Yes	156 (44)	71 (44)
No	128 (36)	56 (35)
Test not done	46 (13)	29 (18)
Missing	26 (7)	4 (3)
Liver involvement - no. (%)		
Yes	38 (11)	18 (11)
No	271 (76)	128 (80)
Test not done	22 (6)	10 (6)
Missing	25 (7)	4 (3)
Autonomic Nervous system involvement - no. (%)		
Yes	26 (7)	11 (7)
No	305 (86)	145 (91)
Missing	25 (7)	4 (3)
post-HCT therapy (for current transplant) - no. (%)		
VR +/- other	0 (0)	7 (4)
VC +/- other	0 (0)	14 (9)
V +/- other	0 (0)	50 (31)
R +/- other	0 (0)	66 (41)
Other	0 (0)	23 (15)
None	356 (100)	0 (0)
Year of transplant - no. (%)		
2015	81 (23)	41 (26)
2016	100 (28)	46 (29)
2017	70 (20)	42 (26)
2018	76 (21)	24 (15)
2019	29 (8)	7 (4)
Follow-up - median (range)	37 (4-75)	37 (4-74)

Other: Doxycycline (n=1), Dara+Pom +/-other (n=1), Dara +/-other (n=7), Pom +/-other (n=2), Ixazomib +/- other (n=9)

CIBMTR Study Proposal

Study Title:
Trends in utilization of a delayed autologous transplant approach (ASCT) in Newly Diagnosed Multiple Myeloma (NDMM)

PI Information:
Hamza Hashmi, MD
Email Address: hashmih@musc.edu
Institution Name: Medical University of South Carolina, Charleston, SC
Meera Mohan MD, MS
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Institution Name: Medical College of Wisconsin
Saad Z. Usmani, MD
Email Address: usmanis@mskcc.org
Institution Name: Memorial Sloan Kettering Cancer Center, New York, NY

Hypothesis:
Autologous hematopoietic cell transplantation (AHCT) within 12 months of diagnosis of multiple myeloma (early) leads to deeper durable remission

Specific Aims:
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.

Analyse the clinical parameters in this group of patients including age, gender, race/ethnicity, ISS stage, cytogenetic risk at diagnosis, type of induction therapy and duration of treatment, timing of stem cell collection and dose, myeloma disease response pre-ASCT, duration of pre-ASCT remission, HCT CI , use of post-ASCT therapy, time of next progression and overall survival .

To compare overall survival (OS) of multiple myeloma patients receiving early (less than 12 months from diagnosis) versus late (more than 12 months from diagnosis) AHCT. To compare disease response, progression-free survival (PFS), transplant-related mortality (TRM) and cumulative incidence of relapse in patients receiving early versus late AHCT for multiple myeloma

Compare clinical characteristics and outcomes of the group that received delayed ASCT and compare with previously published data from an upfront ASCT approach (as in BMT CTN Protocol 0702).

Scientific impact:
There is limited data available on the role of early versus late AHCT for patients with newly diagnosed multiple myeloma in the era of novel agents. This retrospective study will evaluate the outcomes of early (within 12 months from diagnosis) versus late (greater than 12 months from diagnosis) AHCT in a large cohort of patients from multiple centers across the U.S. over a period of 2 decades. This study could identify patient-, disease- or transplant- related factors that may impact choice and timing of AHCT for patients with multiple myeloma, and could lead to future novel research on improving the transplant outcomes.

Scientific Justification:

The optimal timing of AHCT in multiple myeloma has been a topic of debate, given the IFM 2009 trial showed similar OS between upfront and delayed transplant, along with the deep and durable responses seen with novel chemotherapeutic agents including anti-CD38 monoclonal antibody, proteasome inhibitors and immunomodulatory agents. Upfront AHCT, done within 12 months of diagnosis and in non-relapsing patients, has several advantages, both related to the patient and disease. Upfront AHCT is the best initial intervention in the management of newly diagnosed multiple myeloma, as it can lead to deep and durable responses, likely due to the chemo-sensitive nature of the disease early in the course. Incorporation of transplant early in the management of multiple myeloma will shorten the duration of multi drug chemotherapy, thereby avoiding the physical and financial toxicity associated with chemotherapy. Transplant is a very safe procedure with the transplant related mortality of less than 1% at experienced centers. Sub-analysis of IFM2009 trial showed improvement in health-related quality of life for patients with upfront transplant. On the other hand, delayed transplant does not negatively affect survival. However, 25 to 50% of the patients may not be eligible for transplant later in the disease course due to age, comorbidities with refractory disease status.

Using the CIBMTR data; we can determine and compare the incidence, characteristics, and outcomes of early versus delayed AHCT in a large cohort of patients with newly diagnosed multiple myeloma from multiple centers in the U.S. during different time periods, allowing us to study the impact of incorporation of novel chemotherapeutic agents. This will have meaningful impact on disease prognostication, duration of induction chemotherapy, patient counseling, and patient selection prior to AHCT. This study will allow for evaluation of role of early versus delayed AHCT in patients with standard-risk versus high-risk disease (based on ISS, revised ISS, cytogenetic abnormalities on FISH).

Patient Eligibility Population:

Inclusion Criteria:
Adult patients (age>18 years) who underwent first AHCT for newly diagnosed multiple myeloma from 2000 to 2018
Exclusion criteria:
Patients with relapsed refractory multiple myeloma

Variables to be described:
Patient related:

- 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:

- Time from diagnosis to transplant: continuous (months)
- Time for initiation of induction chemotherapy to transplant: continuous (months)
- Time from stem cell mobilization to transplant: continuous (months)
- 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)
- Presence of high-risk cytogenetic abnormalities [Del 17p, t(4;14), t(14;16)]: yes vs no
- Ig heavy chain: IgG vs IgA vs IgM vs no heavy chain
- Ig light chain: Lambda vs kappa
- 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: Proteasome inhibitor-based vs immunomodulatory drugs-based vs anti-CD38 monoclonal antibody-based vs both/all
- Prior radiotherapy: yes vs. no
- Mobilization: G-CSF vs Plerixafor vs chemo-based vs both/all
- Conditioning regimen: Melphalan 200 mg/m² vs melphalan 140 mg/m² vs other
- Peri engraftment syndrome: yes vs no
- Secondary myelodysplastic syndrome/leukemia: yes vs no
- Post-transplant maintenance: yes vs no
- Post-transplant maintenance: immunomodulatory agents-based vs proteasome inhibitor-based vs both

Data Requirements:
No additional data collection requested.

Sample Requirements:
No samples requested.

Study Design:

Outcomes:

- Overall survival: Time from AHCT to death from any cause. Patients will be censored at the time of last follow up.
- Progression-free survival: Time from AHCT to death or relapse. Patients will be censored at the time of last follow up.
- Transplant-related mortality: Death due to any cause in the first 28 days or death due to conditions other than disease relapse or progression beyond 28 days. Events will be summarized by the cumulative incidence estimate with relapse as a competing risk.
- Relapse: Development of hematological relapse as defined by the CIBMTR. The event will be summarized by the cumulative incidence estimate and patients analyzed at last follow-up. TRM will be a competing risk for this outcome.
- Hematologic response: CR: negative bone marrow, PETCT/ MRI/ Low dose CT imaging,

and negative immunofixation of the serum and urine; VGPR: 90% reduction in M-protein or immunofixation positive only as long as M-protein was at least 0.5 g/dL at baseline; PR: 50% reduction in M-protein or immunofixation positive as long as baseline M-protein was at least 1.0 g/dL; no response: no response.

The goal of this study is to evaluate the clinical outcomes early versus late AHCT for patients with multiple myeloma between 2000 and 2018 while adjusting for significant patient-, disease-, and transplant-related variables. The probabilities of OS and PFS will be calculated using the Kaplan-Meier estimator. Probabilities of TRM, relapse/progression and response endpoints will be generated using cumulative incidence estimates to account for competing risks. Cox proportional hazards regression will be performed. The potential variables to be considered in the multivariate models are listed in the previous section. The assumption of proportional hazards for each factor in the Cox model will be tested using time-dependent covariates. The proportionality assumptions will be further tested. A backward stepwise model selection approach will be used to identify all significant risk factors. Each step of model building may contain the main effect. Factors that are significant at 5% level will be kept in the final model. The potential interactions between the main effect and all significant risk factors will be tested. Adjusted probability of PFS and OS and adjusted cumulative incidence curves for competing risks endpoints will be generated from the final regression models. We will also compare the outcomes based on the year of AHCT to understand the impact of induction chemotherapy and supportive care measures for multiple myeloma.

Non-CIBMTR Data Source:
May be needed from individual institution

BMT CTN Protocol 0702 (Specifically patients randomized to lenalidomide maintenance after planned upfront ASCT -arm B of the study)

References:

Perrot A, Lauwers-Cances V, Cazaubiel T, et al: Early versus late autologous stem cell transplant in newly diagnosed multiple myeloma: Long-term follow-up analysis of the IFM 2009 trial. 2020 ASH Annual Meeting & Exposition. Abstract 143.

Nishimura, K.K.; Barlogie, B.; Van Rhee, et al. Long-term outcomes after autologous stem cell transplantation for multiple myeloma. Blood Adv. 2020, 4,422–431.

Gertz, M.A.; Ansell, S.M.; Dingli, D.; et al. Autologous stem cell transplantation in 716 patients with multiple myeloma: Low treatment-related mortality,feasibility of outpatient transplant, and impact of a multidisciplinary quality initiative. Mayo Clin. Proc. 2008, 83, 1131–1135.

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Table 1. Characteristics of Multiple Myeloma cases undergoing first autologous stem cell transplants from 2008 to 2019

Characteristic	Upfront	Delayed
No. of patients	5055	1477
No. of centers	155	131
median age (range) - median (min-max)	60 (20-83)	61 (31-80)
Age at transplant, years - no. (%)		
18-39	165 (3)	16 (1)
40-49	647 (13)	153 (10)
50-59	1649 (33)	498 (34)
60-69	2146 (42)	665 (45)
70+	448 (9)	145 (10)
Gender - no. (%)		
Male	2819 (56)	785 (53)
Female	2236 (44)	692 (47)
Race - no. (%)		
White	3163 (63)	812 (55)
Black or African-American	1445 (29)	562 (38)
Asian	222 (4)	49 (3)
Native Hawaiian or other Pacific islander	13 (0)	3 (0)
American Indian or Alaska Native	50 (1)	5 (0)
More than one race	22 (0)	8 (1)
Missing	140 (3)	38 (3)
Karnofsky score - no. (%)		
>= 90	2658 (53)	741 (50)
< 90	2269 (45)	696 (47)
Missing	128 (3)	40 (3)
HCT-CI - no. (%)		
0	1499 (30)	404 (27)
1	738 (15)	212 (14)
2	845 (17)	238 (16)
3+	1924 (38)	614 (42)
Missing	49 (1)	9 (1)
ISS stage at diagnosis - no. (%)		
ISS/DS stage I	1509 (30)	460 (31)
ISS/DS stage II	1475 (29)	336 (23)
ISS/DS stage III	1085 (21)	216 (15)
Missing	986 (20)	465 (31)

Characteristic	Upfront	Delayed
Lines of chemotherapy - no. (%)		
1	3830 (76)	619 (42)
>=2	1027 (20)	788 (53)
Missing	198 (4)	69 (4)
Immunochemical subtype - no. (%)		
IgG	2896 (57)	947 (64)
IgA	1012 (20)	252 (17)
IgD	31 (1)	5 (0)
IgE	3 (0)	0 (0)
IgM	14 (0)	10 (1)
Light chain	1034 (20)	244 (17)
Non-secretory	62 (1)	17 (1)
Unknown Type	3 (0)	2 (0)
Hemoglobin prior to transplant - no. (%)		
< 10 g/dl	1068 (21)	380 (26)
>= 10 g/dl	3934 (78)	1077 (73)
Missing	53 (1)	20 (1)
Serum creatinine prior to transplant, mg/dl - no. (%)		
< 2 mg/dl	4718 (93)	1368 (93)
>= 2 mg/dl	274 (5)	85 (6)
Missing	63 (1)	24 (2)
Conditioning regimen - no. (%)		
Melphalan only	4928 (97)	1418 (96)
TBI + Melphalan	13 (0)	5 (0)
Other Melphalan based regimen	108 (2)	51 (3)
Others	5 (0)	3 (0)
Missing	1 (0)	0 (0)
Melphalan dose in conditioning regimen, mg/m - no. (%)		
MEL 140	1436 (28)	522 (35)
MEL 200	3613 (71)	952 (64)
Unknown dose	6 (0)	3 (0)
Disease status prior to transplant - no. (%)		
sCR/CR	835 (17)	172 (12)
VGPR	1916 (38)	372 (25)
PR	1978 (39)	661 (45)
SD	232 (5)	149 (10)
PD/Relapse	71 (1)	117 (8)
Missing	23 (0)	6 (0)

Characteristic	Upfront	Delayed
Chemotherapy - no. (%)		
VTD	149 (3)	42 (3)
VRD	2578 (51)	523 (35)
VCD	806 (16)	198 (13)
VD	462 (9)	251 (17)
RD	460 (9)	159 (11)
TD	148 (3)	76 (5)
Carfilzomib	9 (0)	4 (0)
Pomalidomide	0 (0)	1 (0)
KRD	51 (1)	39 (3)
Daratumumab	68 (1)	41 (3)
Others	126 (2)	73 (5)
Missing	198 (4)	70 (5)
Time from diagnosis to transplant - median (min-max)	7 (0-12)	20 (12-321)
Time from diagnosis to transplant - no. (%)		
< 6 months	1984 (39)	0 (0)
6 - 12 months	3071 (61)	0 (0)
12 - 24 months	0 (0)	896 (61)
>= 24 months	0 (0)	581 (39)
Type of transplant - no. (%)		
Single Auto	5055 (100)	1477 (100)
Year of transplant - no. (%)		
2008	556 (11)	275 (19)
2009	198 (4)	97 (7)
2010	164 (3)	62 (4)
2011	233 (5)	59 (4)
2012	243 (5)	51 (3)
2013	470 (9)	115 (8)
2014	402 (8)	142 (10)
2015	518 (10)	186 (13)
2016	587 (12)	185 (13)
2017	557 (11)	144 (10)
2018	1127 (22)	161 (11)
Post-HCT therapy - no. (%)		
No	1120 (22)	511 (35)
Yes	3863 (76)	945 (64)
Missing	72 (1)	21 (1)
post-HCT therapy (for current transplant) - no. (%)		

Characteristic	Upfront	Delayed
VR +/- other	388 (8)	47 (3)
VC +/- other	23 (0)	6 (0)
V +/- other	372 (7)	105 (7)
R +/- other	2700 (53)	588 (40)
KR +/- other	48 (1)	20 (1)
K +/- other	70 (1)	28 (2)
Other	262 (5)	151 (10)
None	1120 (22)	511 (35)
Missing	72 (1)	21 (1)
Follow-up - median (range)	58 (3-155)	61 (3-157)

CIBMTR Study Proposal

Study Title:
Outcomes of autologous hematopoietic cell transplantation for Multiple Myeloma with plasmacytoma(s)

PI Information:
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Hypothesis:
Autologous Hematopoietic cell transplantation (AHCT) results in long-term disease control for patients with multiple myeloma with current or prior plasmacytoma(s).

Specific Aims:
1. 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.

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) and compare these outcomes with patients with multiple myeloma without prior or current plasmacytomas.

Scientific impact:
There is limited data available on the outcomes of AHCT for patients with multiple myeloma and current or prior 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, current or prior), compare the outcomes with patients without plasmacytoma and, understand the optimal application of AHCT as a treatment modality for this patient population. 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.

Scientific Justification:
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 prior plasmacytomas undergoing AHCT [historical cohort]. This will have meaningful impact on disease prognostication, patient counseling and, patient selection prior to AHCT.

Patient Eligibility Population:

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

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/m² vs melphalan 140 mg/m² vs other
- Peri engraftment syndrome: yes vs no
- Secondary myelodysplastic syndrome/leukemia: yes vs no
- Post-transplant maintenance: yes vs no

Data Requirements:
No additional data collection requested.

Sample Requirements:
No samples requested.

Study Design:

Outcomes:

- Overall survival: Time from AHCT to death from any cause. Patients will be censored at the time of last follow up.

- Progression-free survival: Time from AHCT to death or relapse. Patients will be censored at the time of last follow up.
- Transplant-related mortality: Death due to any cause in the first 28 days or death due to conditions other than disease relapse or progression beyond 28 days. Events will be summarized by the cumulative incidence estimate with relapse as a competing risk.
- Relapse: Development of hematological relapse as defined by the CIBMTR. The event will be summarized by the cumulative incidence estimate and patients analyzed at last follow-up. TRM will be a competing risk for this outcome.
- Hematologic response: CR: negative bone marrow, PETCT/ MRI/ Low dose CT imaging, and negative immunofixation of the serum and urine; VGPR: 90% reduction in M-protein or immunofixation positive only as long as M-protein was at least 0.5 g/dL at baseline; PR: 50% reduction in M-protein or immunofixation positive as long as baseline M-protein was at least 1.0 g/dL; no response: no response.

The goal of this study is to evaluate the clinical outcomes AHCT for patients with multiple myeloma and current/previous history of plasmacytomas between 2000 and 2018 while adjusting for significant patient-, disease-, and transplant-related variables. The probabilities of OS and PFS will be calculated using the Kaplan-Meier estimator. Probabilities of TRM, relapse/progression and response endpoints will be generated using cumulative incidence estimates to account for competing risks. Cox proportional hazards regression will be performed. The potential variables to be considered in the multivariate models are listed in the previous section. The assumption of proportional hazards for each factor in the Cox model will be tested using time-dependent covariates. The proportionality assumptions will be further tested. A backward stepwise model selection approach will be used to identify all significant risk factors. Each step of model building may contain the main effect. Factors that are significant at 5% level will be kept in the final model. The potential interactions between the main effect and all significant risk factors will be tested. Adjusted probability of PFS and OS and adjusted cumulative incidence curves for competing risks endpoints will be generated from the final regression models. We will also consider comparing the outcomes based on the year of AHCT if there is sufficient number of cases for such evaluation to understand the impact of year of AHCT for multiple myeloma with plasmacytomas. Outcomes after AHCT in patients with multiple myeloma and current or prior plasmacytomas will then be compared with historical cohort [multiple myeloma without plasmacytoma].

Non-CIBMTR Data Source:
May be needed from individual institution

References:

1. Dimopoulos MA, Moulopoulos LA, Maniatis A, Alexanian R. Solitary plasmacytoma of bone and asymptomatic multiple myeloma. Blood 2000; 96:2037.

2. World Health Organization Classification of Tumours of Haematopoietic and Lymphoid Tissues, Swerdlow SH, Campo E, Harris NL, et al. (Eds), IARC Press, Lyon 2008

3. Mayr NA, Wen BC, Hussey DH, et al. The role of radiation therapy in the treatment of solitary plasmacytomas. Radiother Oncol 1990; 17:293.

4. Rajkumar SV, Dimopoulos MA, Palumbo A, et al. International Myeloma Working Group updated criteria for the diagnosis of multiple myeloma. Lancet Oncol 2014; 15:e538.

5. Hill QA, Rawstron AC, de Tute RM, Owen RG. Outcome prediction in plasmacytoma of bone: a risk model utilizing bone marrow flow cytometry and light-chain analysis. Blood 2014; 124:1296.

6. Frassica DA, Frassica FJ, Schray MF, et al. Solitary plasmacytoma of bone: Mayo Clinic experience. Int J Radiat Oncol Biol Phys 1989; 16:43.

Table 1. Characteristics of Multiple Myeloma current or previous plasmacytomas undergoing first autologous stem cell transplants from 2000 to 2019 in US, CRF

Characteristic	N (%)
No. of patients	277
No. of centers	81
Median age (range) - median (min-max)	57 (26-76)
Age at transplant, years - no. (%)	
18-39	20 (7)
40-49	40 (14)
50-59	100 (36)
60-69	93 (34)
70+	24 (9)
Gender - no. (%)	
Male	177 (64)
Female	100 (36)
Region - no. (%)	
US	277 (100)
Race - no. (%)	
White	195 (70)
Black or African-American	69 (25)
Asian	3 (1)
American Indian or Alaska Native	2 (1)
Missing	8 (3)
Karnofsky score - no. (%)	
>= 90	157 (57)
< 90	112 (40)
NA, not collected before 2007	8 (3)
HCT-CI - no. (%)	
0	23 (8)
1	18 (6)
2	17 (6)
3+	66 (24)
Missing	153 (55)
Bone marrow plasma cells at diagnosis - no. (%)	
<10%	83 (30)
>=10%	128 (46)
Missing	66 (24)
Bone marrow plasma cells at transplant - no. (%)	

Characteristic	N (%)
<10%	239 (86)
>=10%	38 (14)
ISS stage at diagnosis - no. (%)	
ISS stage I	100 (36)
ISS stage II	45 (16)
ISS stage III	14 (5)
Missing	118 (43)
Lines of chemotherapy - no. (%)	
0	3 (1)
1	193 (70)
>=2	79 (29)
Missing	2 (1)
Chemotherapy - no. (%)	
VTD	8 (3)
VRD	69 (25)
VCD	18 (6)
VDD/DVD	2 (1)
VD	26 (9)
RD	13 (5)
TD	59 (21)
Carfilzomib	1 (0)
VAD/similar	67 (24)
KRD	3 (1)
Daratumumab	3 (1)
Others	3 (1)
Missing	5 (1)
Immunochemical subtype - no. (%)	
IgG	148 (53)
IgA	42 (15)
IgD	1 (0)
IgM	1 (0)
Light chain	63 (23)
Non-secretory	16 (6)
Unknown Type	6 (2)
Hemoglobin prior to transplant - no. (%)	
< 10 g/dl	53 (19)
>= 10 g/dl	221 (80)
Missing	3 (1)

Characteristic	N (%)
Serum creatinine prior to transplant, mg/dl - no. (%)	
< 2 mg/dl	268 (97)
>= 2 mg/dl	7 (3)
Missing	2 (1)
Conditioning regimen - no. (%)	
Melphalan only	255 (92)
TBI + Melphalan	8 (3)
Other Melphalan based regimen	8 (3)
Others	6 (2)
Melphalan dose in conditioning regimen, mg/m - no. (%)	
MEL 140	73 (26)
MEL 200	196 (71)
Unknown dose	8 (3)
Disease status prior to transplant - no. (%)	
Never treated	1 (0)
sCR/CR	58 (21)
VGPR	46 (17)
PR	129 (47)
SD	21 (8)
PD/Relapse	15 (5)
Missing	7 (3)
Time from diagnosis to transplant - median (min-max)	9 (3-146)
Time from diagnosis to transplant - no. (%)	
< 6 months	62 (22)
6 - 12 months	138 (50)
12 - 24 months	40 (14)
>= 24 months	37 (13)
Year of transplant - no. (%)	
2000	16 (6)
2001	11 (4)
2002	13 (5)
2003	11 (4)
2004	27 (10)
2005	36 (13)
2006	34 (12)
2007	5 (2)
2009	2 (1)
2010	3 (1)

Characteristic	N (%)
2012	3 (1)
2013	12 (4)
2014	15 (5)
2015	14 (5)
2016	16 (6)
2017	12 (4)
2018	34 (12)
2019	13 (5)
Post-HCT therapy - no. (%)	
No	117 (42)
Yes	114 (41)
Missing	46 (17)
Post-HCT therapy (for current transplant) - no. (%)	
VR +/- other	6 (2)
V +/- other	10 (4)
R +/- other	78 (28)
KR +/- other	3 (1)
Other	17 (6)
None	117 (42)
Missing	46 (17)
Follow-up - median (range)	73 (3-207)

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 second autologous stem cell transplantation vs chimeric antigen receptor T-cell therapy for multiple myeloma patients with prior autologous transplant.

Q2. Key Words

second autologous transplant, CAR-T cell

Q3. PRINCIPAL INVESTIGATOR

Provide the following information for each investigator:

Principal Investigator #1:

First and last name, degree(s):	Naresh Bumma MD
Email address:	naresh.bumma@osumc.edu
Institution name:	The Ohio State 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?

- 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.

MM20-03

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.

N/A

Q15. RESEARCH QUESTION:

To compare outcomes of patients with relapsed refractory MM having undergone an autologous stem cell transplant with a second transplant versus chimeric antigen receptor T-cell (CAR-T cell) therapy

Q16. RESEARCH HYPOTHESIS:

CAR-T therapy is not inferior to a salvage/2nd autologous SCT for patients with MM with relapsed disease who underwent autologous stem cell transplantation (ASCT) after induction.

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

Suggested word limit of 200 words:

1. To evaluate outcomes in patients with MM with relapsed disease who underwent autologous stem cell transplantation (ASCT) after induction undergoing CAR-T therapy or salvage/2nd autologous SCT
2. To evaluate progression free survival (PFS) in patients with MM with relapsed disease who underwent autologous stem cell transplantation (ASCT) after induction undergoing CAR-T therapy versus salvage/2nd autologous SCT
3. To evaluate overall survival (OS) in patients with MM with relapsed disease who underwent autologous stem cell transplantation (ASCT) after induction undergoing CAR-T therapy versus salvage/2nd autologous SCT

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 treatment landscape of relapsed MM had changed drastically with the recent approval of CAR-T therapy. It is unclear whether this modality should be favored over a second transplant or not. As a result, practice patterns and institutional guidelines vary significantly. We believe exploration of the CIBMTR database will provider real life data and help answer this question

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.

Most patients with MM have disease progression at some point following AHCT1. Many factors influence the appropriate next line of therapy, including previous lines of therapy, response to these treatments, time to relapse and performance status1. For eligible patients, one of the therapeutic options is a second autologous transplant. 2 Chimeric antigen receptor (CAR)–modified T cells are a promising new treatment in many hematological malignancies. The B-cell maturation antigen (BCMA)–directed CAR T cell idecabtagene vicleucel (ide-cel, also called bb2121) showed promising efficacy in a phase 1 study involving patients with relapsed or refractory myeloma.3 The phase 2 KarMMa4 study further confirmed these results, with impressive response rates in heavily pretreated patients. Efficacy after a single infusion was encouraging, with a median response duration of 10.7 months, progression-free survival of 8.8 months, and overall survival of 19.4 months across treated patients. However, this is not a therapy devoid of side effects with 84% of the patients experiencing cytokine release syndrome.
While CAR-T provides a new therapy in our armamentarium, it should not supersede stem cell transplantation just based on novelty.

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.

Adult patients MM with relapsed disease who underwent autologous stem cell transplantation (ASCT) after induction undergoing CAR-T therapy versus salvage/2nd autologous SCT from January 2013 to December 2020 after receiving induction and within 12 months of diagnosis.

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.

aseline demographics and diagnosis data
• Data for risk stratification: Baseline labs (hemoglobin, creatinine, calcium, albumin, beta-2-microglobulin, LDH, bone marrow plasma cell percentage, FISH (fluorescence in-situ hybridization) data
• First line chemotherapy details: drugs with start and stop dates
• Date of transplant
• Best hematologic response before transplant
• Treatment after transplant: consolidation or maintenance, with start and stop dates if available
• Relapse and survival data
• Date of 2nd transplant
• Date of CAR-T

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. Rajkumar SVJAjoh. Multiple myeloma: 2020 update on diagnosis, risk-stratification and management. 2020;95:548-67.
2. Chim C, Kumar S, Orlowski R, et al. Management of relapsed and refractory multiple myeloma: novel agents, antibodies, immunotherapies and beyond. 2018;32:252-62.
3. Raje N, Berdeja J, Lin Y, et al. Anti-BCMA CAR T-cell therapy bb2121 in relapsed or refractory multiple myeloma. 2019;380:1726-37.
4. Munshi NC, Anderson LD, Shah N, et al. Idecabtagene Vicleucel in Relapsed and Refractory Multiple Myeloma. 2021;384:705-16.

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 adult patients who underwent salvage auto-HCT or CART[1] for relapsed MM from 2019-2021 and registered with CIBMTR

Characteristic	N(%)
No. of patients	504
No. of centers	97
Track - no. (%)	
TED	443 (88)
CRF	61 (12)
Age at CART or salvage HCT - median (min-max)	64 (35-86)
Age at CART or salvage HCT - no. (%)	
18-39	7 (1)
40-49	31 (6)
50-59	127 (25)
60-69	229 (45)
70+	110 (22)
Recipient Gender - no. (%)	
Male	294 (58)
Female	210 (42)
Region - no. (%)	
US	504 (100)
Race - no. (%)	
White	393 (78)
Black or African American	82 (16)
Asian	14 (3)
American Indian or Alaska Native	2 (0)
More than one race	4 (1)
Missing	9 (2)
Karnofsky score - no. (%)	
90-100	229 (45)
< 90	255 (51)
Missing	20 (4)
HCT-CI - no. (%)	
0	97 (19)
1	54 (11)
2	82 (16)
3+	267 (53)

Characteristic	N(%)
TBD, review needed for history of malignancies	1 (0)
Missing	3 (1)
Disease status prior to CART or salvage HCT - no. (%)	
SCR / CR	67 (13)
VGPR	127 (25)
PR	121 (24)
SD	51 (10)
PD / Relapse	133 (26)
Missing	5 (1)
CART or HCT after 1st relapse (Main effect) - no. (%)	
Salvage HCT	395 (78)
CART	104 (21)
CART after salvage HCT	5 (1)
Time from diagnosis to HCT1 - median (min-max)	7 (1-174)
Time from diagnosis to HCT1 - no. (%)	
<6 months	215 (43)
6-12 months	187 (37)
>12 months	100 (20)
Missing	2 (0)
Time from diagnosis to salvage HCT/ CART - median (min-max)	76 (5-272)
Time from diagnosis to salvage HCT/ CART - no. (%)	
<24 months	3 (1)
24-60 months	152 (30)
>60 months	348 (69)
Missing	1 (0)
Time from HCT1 to HCT2/ CART - median (min-max)	64 (2-265)
Time from HCT1 to salvage HCT/ CART - no. (%)	
<24 months	22 (4)
24-60 months	203 (40)
>60 months	278 (55)
Missing	1 (0)
Year of CART or salvage HCT after 1st relapse - no. (%)	
2019	277 (55)
2020	120 (24)
2021	107 (21)
Follow-up - median (range)[2]	13 (1-27)

Characteristic	**N(%)**

[1] B-cell maturation antigen (BCMA)–directed CAR T cell (idecabtagene vicleucel) considered standard of care.

[2] Median follow up for Salvage HCT. CART cases do not contain enough follow up reported as when accrual table was prepared.