2021 STATUS REPORT
PLASMA CELL DISORDERS AND ADULT SOLID TUMORS WORKING COMMITTEE

Working Committee Leadership	
Co-Chair:	Shaji Kumar; Mayo Clinic Rochester; kumar.shaji@mayo.edu
Co-Chair:	Nina Shah; University of California San Francisco Medical Center; nina.shah@ucsf.edu
Co-Chair:	Muzaffar Qazilbash; M.D. Anderson Cancer Center; mqazilba@mdanderson.org
Scientific Director:	Anita D'Souza; CIBMTR Statistical Center; anitadsouza@mcw.edu
Statistical Director:	Raphael Fraser; CIBMTR Statistical Center; rfraser@mcw.edu
Statistician:	Noel Estrada-Merly; CIBMTR Statistical Center; nestrada@mcw.edu

INTRODUCTION

a. Minutes and overview plan from 2020 TCT meeting (Attachment 1)

PROPOSALS MOVING FORWARD FOR SCORING (click here to cast your score)

a. PROP 2010-132 Characteristics and outcomes of adolescent and young adults with multiple myeloma after autologous hematopoietic stem cell transplant (Christin DeStefano/ Steven Gibson). (Attachment 2)

b. PROP 2010-161 Outcomes of autologous hematopoietic cell transplantation for light chain deposition disease (Hamza Hashmi/ Taiga Nishihori). (Attachment 3)

PROPOSALS DROPPED (PLEASE NOTE: OUT OF 33 NEW PROPOSALS, ONLY A MAXIMUM OF 2 STUDIES WERE ALLOWED TO BE SELECTED FOR SCORING)

a. PROP 2008-03 Do plerixafor mobilized products increase the risk of engraftment syndrome in patients receiving autologous stem cell transplants for multiple myeloma? (John Wagner/ Adam Binder).

b. PROP 2009-14 Outcomes of multiple myeloma patients with +1q abnormalities after high dose therapy and autologous stem cell transplantation (Binod Dhakal).

c. PROP 2010-18 Plerixafor-based stem cell mobilization and incidence of engraftment syndrome in multiple myeloma patients following peripheral blood autologous stem cell transplant (Tara Gregory/ Devin Nelson).

d. PROP 2010-23 Does plasma cell percentage in the bone marrow at last evaluation prior to the start of the preparative regimen influence outcome especially if more than 1 line of induction is given? (John Wagner/ Adam Binder).

e. PROP 2010-25 The effect of coexistent amyloid and multiple myeloma in patients undergoing autologous stem cell transplant (Jeff Schriber).

f. PROP 2010-30 Matched-pair analysis of race to evaluate the impact of optimal vs. suboptimal pre- and post-autologous stem cell transplant (ASCT) therapy for multiple myeloma (Manisha Bhutani/ Saad Usmani/ Peter Voorhees).

g. PROP 2010-31 Survival after myeloma recurrence after HCT. Impact of age, remission duration and post-transplant cellular therapies on loss of life years (Sergio A Giralt/ Gunjun Shah/ Meera Mohan/ Parameswaran Hari).

h. PROP 2010-50 Clinical outcomes and prognostic factors in patients with IgM-associated amyloid light-chain amyloidosis treated with autologous hematopoietic stem-cell transplantation (Yazeed Sawalha).

i. PROP 2010-70 Trends in utilization of a delayed autologous transplant approach (ASCT) in newly diagnosed multiple myeloma (NDMM) (Meera Mohan).

j. PROP 2010-72 Comparing outcomes and maintenance strategies of multiple myeloma patients with R-ISS defined high-risk cytogenetics abnormalities and chromosome 1 abnormalities after autologous hematopoietic stem cell transplant (Sanaz N. Ghafouri/ Sarah M. Larson).

k. PROP 2010-73 Effects of duration of induction therapy and kinetics of disease response on clinical outcomes in newly diagnosed MM (NDMM) (Maurizio Zangari/ Meera Mohan).

l. PROP 2010-84 Correlation of melphalan dose reduction with frailty in multiple myeloma patients undergoing autologous transplant (Maxwell M. Krem/ Charlotte B. Wagner/ Gregory P. Monohan).

m. PROP 2010-85 Early versus late allogeneic hematopoietic cell transplant in multiple myeloma patients (Maxwell M. Krem/ Sergio Giralt/ Gerhard C. Hildebrandt).

n. PROP 2010-106 New cancers after autologous hematopoietic cell transplantation for systemic light-chain amyloidosis (Rajshekhar Chakraborty/ Suzanne Lentzsch/ Navneet S. Majhail/ Divaya Bhutani).

o. PROP 2010-130 Persistent bone pains in patients with multiple myeloma after successful autologous hematopoietic stem cell transplantation: Risk factors and relation with cancer survivor syndrome (Safaa A A Khaled).

p. PROP 2010-131 Outcomes of hematopoietic cell transplantation for multiple myeloma with extramedullary plasmacytomas (Baldeep Wirk).

q. PROP 2010-140 Survival in multiple myeloma patients undergoing autologous SCT over the years: A time trend analysis (Nidhi Sharma/ Yvonne Efebera).

r. PROP 2010-160 Outcomes of autologous hematopoietic cell transplantation for macrofocal multiple myeloma and multiple plasmacytomas (Hamza Hashmi/ Taiga Nishihori).

s. PROP 2010-170 Impact of day + 100 lymphocyte subset recovery on outcomes in patients with multiple myeloma undergoing autologous hematopoietic cell transplantation (Omotayo Fasan/ Joseph Vadakara).

t. PROP 2010-178 Role of autologous stem cell transplant for patients with newly diagnosed systemic AL amyloidosis achieving hematological CR/light chain remission (Naresh Bumma).

u. PROP 2010-179 Role of upfront versus delayed autologous stem cell transplant for patients with newly diagnosed multiple myeloma in the era of novel regimen (Naresh Bumma).

v. PROP 2010-184 Comparison of outcomes with second salvage autologous transplant in patients with relapsed multiple myeloma treated with induction using daratumumab versus non-daratumumab based regimens (Sowjanya Vuyyala/ Shatha Farhan).

w. PROP 2010-202 Inductions and consolidations number around auto SCT for MM and outcomes (Shatha Farhan).

x. PROP 2020-211 Assessing impact of concomitant cytogenetic abnormalities on outcome of multiple myeloma patient who undergo autologous hematopoietic stem cell transplantation (Ehsan Malek/ Marcos de Lima/ Amin Firoozmand).

y. PROP 2010-216 Post autologous stem cell transplantation maintenance treatment in multiple myeloma with high-risk cytogenetics: Proteasome inhibitor in combination with lenalidomide versus lenalidomide alone (Aimaz Afrough/ Muzaffar H. Qazilbash).

z. PROP 2010-222 Assessment of feasibility, safety, and efficacy of anti-BCMA CAR T-cell therapy in the standard-of-care setting for patients with relapsed or refractory multiple myeloma (Christopher Ferreri/ Melody Becnel/ Krina Patel).

aa. PROP 2010-240 KRD vs. VRD induction in transplant eligible multiple myeloma patients undergoing autologous stem cell transplantation (Binod Dhakal/ Abid Muhammad).

ab. PROP 2010-255 Timing of second (tandem) autologous hematopoietic stem cell transplantation for newly diagnosed multiple myeloma patients (MM) – a CIBMTR analysis (Pashna N. Munshi/ David H. Vesole).

ac. PROP 2010-290 Comparative efficacy of conditioning regimens for multiple myeloma (Asya Varshavsky-Yanovsky/ Yuliya Shestovska/ Henry Fung).

ad. PROP 2010-308 Impact of daratumumab and carfilzomib-based induction therapy in newly diagnosed multiple myeloma patients undergoing autologous transplant (Sayeef Mirza/ Taiga Nishihori/ Lohith Gowda).

ae. PROP 2010-320 Third stem cell transplant (SCT) for multiple myeloma: An analysis from the CIBMTR database (Murali Kodali/ Rajneesh Nath/ Zheng Zhou).

STUDIES IN PROGRESS

a. **MM18-03b** Transplant outcomes of elderly (>=75 years) multiple myeloma patients. Status: Manuscript Preparation. The manuscript was drafted by the PI, it will be circulated to the writing committee. Goal: Manuscript Submission by June 2021.

b. **MM19-01** Impact of induction therapy with bortezomib, lenalidomide and dexamethasone vs. bortezomib, cyclophosphamide and dexamethasone on outcomes in patients with multiple myeloma undergoing stem cell transplantation. Status: Manuscript Preparation**.** Manuscript was circulated to the writing committee. Goal: Manuscript Submission by June 2021.

c. **MM19-02** Maintenance therapy after second autologous hematopoietic cell transplantation for multiple myeloma. Status: Analysis**.** Datafile completed, PhD working on multivariable analysis. Goal: Manuscript preparation by June 2021.

d. **MM19-03** Second autologous stem cell transplantation as salvage therapy for relapsed or refractory immunoglobulin light chain amyloidosis. Status: Analysis**.** Dataset cleaned and univariable analysis completed. Protocol to be presented soon at the statistical meeting. Goal: Manuscript Submission by June 2021.

e. **MM20-01** Outcomes after autologous hematopoietic cell transplantation in POEMS syndrome. Status: Protocol Development. Supplemental data request sent to high POEMS transplant volume centers to gather information on risk factors. Goal: Manuscript Preparation by June 2021.

f. **MM20-02** Risk factors for and characteristics of secondary primary malignancies following autologous hematopoietic cell transplant for multiple myeloma. Status: Protocol Development. Protocol to be presented at the stats meeting. Goal: Data file preparation by June 2021**.**

g. **MM20-03** Impact of bortezomib-based versus lenalidomide maintenance therapy on outcomes of patients with high-risk multiple myeloma. Status: Protocol Development. Protocol to be presented at the stats meeting. Goal: Data file preparation by June 2021.

PUBLICATIONS, SUBMITTED PAPERS, PRESENTATIONS

a. **MM18-02** Dhakal B, D'Souza A, Callander N, Chhabra S, Fraser R, Davila O, Anderson K, Assal A, Badaway SM, Berdeja J, Cerny J, Comenzo R, Chakraborty R, Peter Gale R, Kamble R, Kharfan-Dabaja MA, Krem MM, Ganguly S, Janakiram M, Kansagra A, Munker R, Murthy HS, Patel S, Kumar S, Shah N, Qazilbash M, Hari P. Novel prognostic scoring system for autologous hematopoietic cell transplantation in multiple myeloma. British Journal of Haematology. doi:10.1111/bjh.16987. Epub 2020 Oct 23. Published with editorial.

b. **M18-01** Badar T, Hari P, Dávila O, Fraser R, Wirk B, Dhakal B, Freytes CO, Rodriguez Valdes C, Lee C, Vesole DH, Malek E, Hildebrandt GC, Landau H, Murthy HS, Lazarus HM, Berdeja JG, Meehan KR, Solh M, Diaz MA, Kharfan-Dabaja MA, Callander NS, Farhadfar N, Bashir Q, Kamble RT, Vij R, Munker R, Kyle RA, Chhabra S, Hashmi S, Ganguly S, Jagannath S, Nishihori T, Nieto Y, Kumar S, Shah N, D'Souza A. African Americans with translocation t(11;14) have superior survival after autologous hematopoietic cell transplantation for multiple myeloma in comparison with Whites in the United States. Cancer. doi:10.1002/cncr.33208. Epub 2020 Sep 23. Published with editorial.

c. **MM18-03a** Munshi PN, Vesole D, Jurczyszyn A, Zaucha JM, St. Martin A, Davila O, Agrawal V, Badawy SM, Battiwalla M, Chhabra S, Copelan E, Kharfan-Dabaja MA, Farhadfar N, Ganguly S, Hashmi S, Krem MM, Lazarus HM, Malek E, Meehan K, Murthy HS, Nishihori T, Olin RL, Olsson RF, Schriber J, Seo S, Shah G, Solh M, Tay J, Kumar S, Qazilbash MH, Shah N, Hari PN, D'Souza A. Age no bar: A CIBMTR analysis of elderly patients undergoing autologous hematopoietic cell transplantation for multiple myeloma. Cancer. doi:10.1002/cncr.33171. Epub 2020 Sep 23. Published with editorial.

d. **MM18-04** Hagen P, D'Souza A, Hari P, Davila O, Zhang M-J, Vesole D, Smith SE, Rodriguez TE, Stiff PJ. Busulfan, melphalan, and bortezomib compared to melphalan as a high dose regimen for autologous hematopoietic stem cell transplantation in multiple myeloma: Long term follow up of a novel high dose regimen. Leukemia & Lymphoma. doi:10.1080/10428194.2020.1811275. Epub 2020 Aug 31.

e. **MM17-01** Dhakal B, Patel S, Girnius S, Bachegowda L, Fraser R, Davila O, Kanate AS, Assal A, Hanbali A, Bashey A, Pawarode A, Freytes CO, Lee C, Vesole D, Cornell RF, Hildebrandt GC, Murthy HS, Lazarus HM, Cerny J, Yared JA, Schriber J, Berdeja J, Stockerl-Goldstein K, Meehan K, Holmberg L, Solh M, Diaz MA, Kharfan-Dabaja MA, Farhadfar N, Bashir Q, Munker R, Olsson RF, Gale RP, Bayer R-L, Seo S, Chhabra S, Hashmi S, Badawy SM, Nishihori T, Gonsalves W, Nieto Y, Efebera Y, Kumar S, Shah N, Qazilbash M, Hari P, D'Souza A. Hematopoietic cell transplantation utilization and outcomes for primary plasma cell leukemia in the current era. Leukemia. doi:10.1038/s41375-020-0830-0. Epub 2020 Apr 2. PMC7572530.

f. **MM17-02** Cornell RF, Fraser R, Costa L, Goodman S, Estrada-Merly N, Lee C, Hildebrandt G, Gergis U, Farhadfad N, Freytes CO, Kamble RT, Krem M, Kyle RA, Lazarus HM, Marks DI, Meehan K, Patel SS, Ramanathan M, Olsson RF, Wagner JL, Kumar S, Qazilbash MH, Shah N, Hari P, D'Souza A. Bortezomib-based induction is associated with superior outcomes in light chain amyloidosis patients treated with autologous hematopoietic cell transplantation regardless of plasma cell burden. Transplant and Cellular Therapy. doi: http//doi.org/10.1016/j.jtct.2020.11.018. Epub 2020 Dec 15.

g. **MM17-02** The impact of bortezomib based induction therapy vs no induction therapy on outcomes for light chain amyloidosis. *Submitted. Poster presentation with discussion at the ASCO 2020 Annual Meeting.*

h. **MM18-03b** Utilization and outcomes of autologous hematopoietic cell transplant in elderly multiple myeloma patients aged 75 years and older in the US. *Oral presentation at the TCT meeting 2021.*

i. **MM19-01** Impact of induction therapy with bortezomib, lenalidomide and dexamethasone vs. bortezomib, cyclophosphamide and dexamethasone on outcomes in patients with multiple myeloma undergoing stem cell transplantation. *Poster presentation at the ASH 2020 Annual Meeting.*

MM18-03b Utilization and outcomes of autologous hematopoietic cell transplant in elderly multiple myeloma patients aged 75 years and older in the US. *Oral presentation at the TCT 2021 Annual Meeting.*

MINUTES AND OVERVIEW PLAN
CIBMTR WORKING COMMITTEE FOR PLASMA CELL DISORDERS AND ADULT SOLID TUMORS
Orlando, FL
Thursday, February 20, 2020, 12:15 – 2:15 pm

Co-Chair:	**Muzaffar Qazilbash, MD, MD Anderson Cancer Center, Houston, TX; Telephone: 713-745-3458; E-mail: mqazilba@mdanderson.org**
Co-Chair:	**Shaji Kumar, MD, Mayo Clinic Rochester, Rochester, MN; Telephone: 507-284-2017; E-mail: kumar.shaji@mayo.edu**
Co-Chair:	**Nina Shah, MD, University of California, San Francisco, CA; Telephone: 415-514-6354; E-mail: nina.shah@ucsf.edu**
Scientific Director:	**Parameswaran Hari, MD, MS, CIBMTR Statistical Center, Milwaukee, WI; Telephone: 414-805-4613; E-mail: phari@mcw.edu**
Assistant Scientific Director:	**Anita D'Souza, MD, MS, CIBMTR Statistical Center, Milwaukee, WI; Telephone: 414-805-0637; E-mail: anitadsouza@mcw.edu**
Statistical Directors:	**Raphael Fraser, PhD, CIBMTR Statistical Center, Milwaukee, WI; Telephone: 414-955-4849; E-mail: rfraser@mcw.edu**
Statistician:	**Omar Dávila Alvelo, MS, CIBMTR Statistical Center, Milwaukee, WI; Telephone: 414-805-0686; E-mail: odavila@mcw.edu**
Statistician:	**Noel Estrada-Merly, MS, CIBMTR Statistical Center, Milwaukee, WI; Telephone: 414-805-0692; E-mail: nestrada@mcw.edu**

---

1. Introduction

The Plasma Cell Disorders Working Committee (PCDWC) met on Thursday, February 20, 2018 at 12:15 p.m. The chairs, scientific director and statisticians were all presented at the meeting. Attendees were asked to have their name badges scanned at the front gate for attendance purpose and to maintain the committee membership roster.

As scientific director of the PCDWC, Dr. Parameswaran Hari welcomed the attendees on behalf of the working committee leadership and started the welcome presentation by introducing each member of the working committee leadership, then explained how to gain and maintain membership, the goals and expectations of the working committee. Dr. Hari also introduced Dr. Ibrahim Yakoub as the EBMT Chair, who was unfortunately not present at the meeting. Dr. Hari also made the announcement to the members present that he would be stepping down as Scientific Director after many years of service to the committee. Dr. Anita D'Souza would take over as the Scientific Director to continue the mission and work of the committee. Dr. Hari continued by emphasizing that each proposal was given 5 minutes for presentation and 5 minutes for discussion, and the voting scores will be used as a critical recommendation by the leadership. Dr. D'Souza continued the presentation explaining the rules of authorship, and PI's rules of conduct; emphasizing the timely completion of draft manuscript. Dr. D'Souza explained that if the PI does not write the first draft of the manuscript, after 3 requests, the paper will be reassigned, and the person who writes the manuscript will be the first author. Dr. D'Souza then presented the studies in progress and explained the Advisory Committee Metrics. Lastly, Dr. D'Souza discussed important details about the CIBMTR study development cycle and explained the different sources of CIBMTR data collection (TED and CRF).

2. Accrual summary

The accrual summary was reference by Dr. D'Souza for review but not formally presented. The link to the full accrual summary was available online as part of the attachments. The accrual summary provides information about the number of patients available in the registration level (TED) and research level (CRF) for potential studies

3. Presentations, Published or Submitted Papers

Dr. D'Souza went through the published or submitted papers in 2019, as well as abstracts that have been presented at various conferences, mentioning that it was a very productive year and emphasized the high metrics of the committee. At the time, one study was published, and five abstracts were presented or accepted for presentation. These include:

a. **MM14-01** Autologous Transplantation for Germ Cell Tumors: Improved Outcomes over 3 decades. **Published in BBMT**
b. **MM17-01** Hematopoietic cell transplantation utilization and outcomes for primary plasma cell leukemia in the current era. **Presented at ASH 2019 as an oral. Manuscript submitted**
c. **MM18-01** The t(11;14) abnormality confers superior survival in African Americans undergoing autologous hematopoietic cell transplantation for multiple myeloma. **Submitted**
d. **MM18-02** Novel Prognostic Scoring System for Autologous Hematopoietic Cell Transplantation in Multiple Myeloma. **Presented at ASH 2019 as an oral. Manuscript in preparation**
e. **MM18-03** To compare the outcomes in young patients with multiple myeloma at diagnosis undergoing autologous or allogeneic hematopoietic stem cell transplant (HCT) with older patients: progression-free and overall survival in a case match analysis. **Presented at ASH 2019 as an oral. Selected as 1 of 5 disparities-focused abstract by ASH for media release. Manuscript in preparation**
f. **MM18-04** Busulfan, Melphalan, and Bortezomib versus High-Dose Melphalan as a Conditioning Regimen for Autologous Hematopoietic Stem Cell Transplantation in Multiple Myeloma: Long Term Follow Up of a Novel Conditioning Regimen **Presented at ASH 2019 as a poster. Manuscript submitted**

4. Studies in Progress

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

a. **MM17-01** Hematopoietic cell transplantation utilization and outcomes for primary plasma cell leukemia in the current era (S Girnius/S Patel/L Bachegowda/B Dhakal) Submitted. The goal of the study is to publish paper by June 2020.
b. **MM17-02** The Impact of Bortezomib Based Induction Therapy vs No Induction Therapy on Outcomes for Light Chain Amyloidosis (R Cornell/S Goodman/L Costa) Analysis. The goal of this study is to submit manuscript by June 2020.
c. **MM18-01** The t(11;14) abnormality confers superior survival in African Americans undergoing autologous hematopoietic cell transplantation for multiple myeloma (T Badar) Submitted. The goal of the study is to publish paper by June 2020.
d. **MM18-02** Deriving a prognostic score for patients undergoing high dose therapy and autologous SCT for myeloma and examining validity of this in long-term exceptional responders (A Hall/B Dhakal/Z Gahvari/S Chhabra/N Callander) The goal is to submit paper by March 2020.
e. **MM18-03** To compare the outcomes in young patients with multiple myeloma at diagnosis undergoing autologous or allogeneic hematopoietic stem cell transplant (HCT) with older patients: progression-free and overall survival in a case match analysis (P Munshi/A Jurczyszyn/J Zaucha/D Vesole) Manuscript in preparation. The goal is to submit paper by March 2020.
f. **MM18-04** Busulfan, Melphalan, and Bortezomib versus High-Dose Melphalan as a Conditioning Regimen for Autologous Hematopoietic Stem Cell Transplantation in Multiple Myeloma: Long Term Follow Up of a Novel Conditioning Regimen (P Hagen/P Stiff) Submitted. The goal of the study is to publish paper by March 2020.

g. **MM19-01** Impact of Induction Therapy with VRD vs. VCD on Outcomes in Patients with Multiple Myeloma Undergoing Stem Cell Transplantation (S Sidana/M Norkin/S Kumar/S Giralt) Protocol Development. The goal of this study is to have the protocol finalized by April 2020 and proceed to analysis.
h. **MM19-02** Maintenance therapy after second autologous hematopoietic cell transplantation for Multiple Myeloma. (O Pasvolsky/ M Yeshurun U Rozovski/ L Alon) Protocol Development
i. **MM19-03** Second autologous stem cell transplantation as salvage therapy for relapsed or refractory AL amyloidosis (C Tan/H Fung) Protocol Development. The goal of this study is to have the protocol finalized by October 2020 and proceed to analysis.

5. Future/Proposed Studies

Dr. D'Souza thanked the investigators whose proposals were submitted but not selected for presentation, emphasizing that the majority were dropped due to overlaps with current studies and data availability issues. Also reiterated the voting process. Dr. Muzaffar Qazilbash introduced the presenter for the first 2 proposals.

a. **PROP 1911-95** Serum Free light Chain measurement following Autologous Hematopoietic Cell Transplantation is predictive of outcomes in Multiple Myeloma. (Murthy/Kharfan-Dabaja/Kumar)
Dr. Hemant Murthy presented the proposal. The goals of the proposal are to: 1) assess the impact of autologous HCT patients' normalization of serum free light chain ratio (sFLC) at day +100 with clinical outcomes (relapse, PFS and OS). Also, to analyze the impact of % change in involved FLC from baseline and day +100 with outcomes and to analyze disease and patient characteristics that are associated with the normalization of sFLC ratio. The PI hypothesized that normalization of serum free light chain following HCT predicts superior PFS and OS in multiple myeloma. There were 2,946 patients (~45% of CRF patients) which contained available information on sFLC at diagnosis and 100-days from 2008 to 2018. Dr. Murthy suggested that sFLC could potentially be considered a surrogate marker of long-term outcomes and the CIBMTR would help to complete the largest study reported on the role of sFLC. Proposal presentation was opened for comments and questions. A comment was made on the possible exclusion of patients with renal dysfunction. A member of the audience was concerned on normalization ratio and how it is affected by treatment. A question was asked on the possibility to stratify the analysis based on the (sFLC) ratio. Dr. Murthy commented on 100-days as an inflection point and its relationship with maintenance therapy, explaining that at this point maintenance strategies are developed, and ratio may not be affected by it. A comment was made on patients with abnormal normalization ratio, which tend to seek bortezomib. Couple of audience members commented on whether to include at transplant timepoint in the timepoints to evaluate (sFLC) ratio but this was not available. Additional time points after day 100 were also of interest, e.g. day 180, but this would not be available. Last comment was made on the different tests for calculating the sFLC ratio and the variability of results.
b. **PROP 1911-96** Prexisting malignancy as risk factor for development of new primary malignancy following Autologous Stem Cell Transplantation and Maintenance therapy in Multiple Myeloma (Murthy/Kharfan-Dabaja/Kumar)
Dr. Hemant Murthy presented the proposal. The goals of the proposal are to 1) assess the cumulative incidence of new post-transplant malignancy and new secondary hematologic malignancy in patients who have a pre-existing malignancy reported prior to the diagnosis of MM,2) determine if the presence of pre-existing malignancy increased the risk of developing new post-transplant malignancy in patients who have undergone autologous stem cell transplantation for multiple myeloma compared to those without preexisting malignancy. The hypotheses are: 1) that in patients with MM and prior history of malignancy who receive Auto-SCT the incidence and risk of developing new post-transplant malignancy and new secondary hematologic malignancy is increased; 2) maintenance therapy increases incidence of both new post-transplant malignancy and secondary hematologic malignancy compared with those with no maintenance. Between 2008 to 2018, there were 534 multiple myeloma cases undergoing first

autologous stem cell transplants with a history of prior malignancies. Dr. Murthy emphasized that this study could help guide pre-transplant decision and post-transplant choice of maintenance therapy. He emphasized the importance of the CIBMTR in order to conduct this study which would not be able to be conducted in other registries.

Proposal presentation was opened for comments and questions. A concern was raised on the timeline of prior malignancies to transplant. Another member questioned what kind of new malignancies where going to be included. Dr. Hari replied that we gather all malignancies in our forms except for skin cancers. A comment was made on the possibility of adding patients without prior solid tumors to compare the incidence of new malignancies. A member of the audience questioned on the availability of information of family incidence of malignancies. This would not be available. Dr. Hari responded that prospectively people tend to forget to report a malignancy. A concern was raised on the low numbers of new malignancies. A member of the audience pointed out the lack of information on treatment of the prior malignancy as a limitation to this study. Lastly, an audience member asked what the risk of new malignancy is on the group who received maintenance therapy.

c. **PROP 1911-123** Outcomes after autologous hematopoietic cell transplantation in POEMS syndrome. (Kansagra/Cornell/Dispenzieri)

Dr. Shaji Kumar presented the proposal on behalf of Dr. Ankit Kansagra. The goals of the proposal are: 1) to evaluate AHCT use in POEMS and determine disease status, hematopoietic recovery rates, and clinical outcomes; 2) to identify prognostic markers of survival after AHCT and create a predictive scoring system; and 3) to evaluate the role of induction vs no-induction therapy on outcomes. This study hypothesizes that autologous hematopoietic cell transplantation (AHCT) will demonstrate low transplant related mortality and prolonged progression free survival when used as treatment for patients with POEMS syndrome. There were 418 patients with POEMS patients >18 years of age, undergoing HDT/ASCT and reported to CIBMTR from 2000-2018 and about 14% of these patients are from the CRF track. Dr. Kumar emphasized the importance of using CIBMTR data to evaluate the role of AHCT in patients with POEMS.

First question asked on the availability of information on neurologic responses. A concerned was raised on the possible misclassification on the diagnosis of POEMS syndromes. Dr. Hari commented on the availability of path reports to confirm the diagnosis for some patients, but we would have to trust centers classification. A comment was made on availability of maintenance therapy for these patients. Dr. D'Souza responded that this information is available only on CRF patients. Other comments were made on the availability of information on initial treatment and mobilization failure. Dr. Kumar clarified that we would only have data on patients who underwent transplant.

Dr. Kumar introduced the next presenter and study.

d. **PROP1910-21/PROP1911-141/PROP1911-228/PROP1911-44** <u>Combined proposal:</u> Risk factors for and characteristics of secondary primary malignancies following autologous hematopoietic cell transplant for multiple myeloma

Dr. Brittany Ragon presented the combined proposal on behalf of all groups who proposed similar concepts. The goals of the proposal are: 1) to determine the cumulative incidence of second primary malignancies (SPM), and secondary hematological malignancies (SHM); 2) to compare overall survival (OS) in patients with SPM and SHM compared to those without SPM and SHM; 3) to identify patient and disease characteristics that predict an increased risk of developing SPM/SHM and 4) to determine the risk of SPM/SHM when post auto-HCT lenalidomide therapy is utilized. They hypothesize that multiple myeloma (MM) patients undergoing autologous hematopoietic cell transplant (auto-HCT), post-transplant therapies can modify the risk of second primary malignancies (SPM), including the risk of secondary hematological malignancies (SHM) and that patients who develop SPM following auto-HCT for MM have an inferior overall survival compared to those who do not develop SPM.

Proposal presentation was opened for comments and questions. A concern was raised on the duration of lenalidomide. A member of the audience asked if cytogenetic abnormalities tested via FISH are captured in the forms. Dr. D'Souza replied that we collect that information, and we also have the reports on abnormalities. A concern was raised on the recurrence of SPM. A member of the audience suggested to look on the availability of SHM after an allogeneic transplant.
Dr. Nina Shah introduced the last presenter.

e. **PROP1911-134/PROP1911-237/PROP1911-26** Combined proposal: Impact of bortezomib-based vs. lenalidomide maintenance therapy on outcomes of patients with high-risk multiple myeloma.
Dr. Naresh Bumma presented the combined proposal on behalf of all groups who proposed similar concepts. The goals of the proposal are 1) to evaluate outcomes after novel agent induction, autologous stem cell transplant (ASCT) and maintenance therapy in patients with high-risk multiple myeloma (MM) compared to patients with standard risk disease; 2) evaluate progression free survival (PFS) in patients with high-risk MM receiving lenalidomide only maintenance vs. bortezomib-based (alone or in combination) consolidation/maintenance after ASCT; 3) evaluate overall survival (OS) in patients with high-risk MM receiving lenalidomide only maintenance vs. bortezomib-based (alone or in combination) consolidation/maintenance after ASCT.
The hypothesis is that lenalidomide single agent as maintenance therapy is associated with inferior progression free survival in high-risk myeloma patients (defined as deletion 17p/monosomy 17, t(4;14), t(14;16), t(14;20) or gain 1q on FISH). Between years 2014 to 2018 there were 3879 patients who underwent ASCT after first induction from which 1246 were classified as high risk and 80.4% received post ASCT therapy. Dr. Bumma emphasized that there is limited information comparing lenalidomide alone to other maintenance regimens in high risk MM. Hence, this study will help to determine post ASCT therapy for patients with high risk MM.
First comment was on the availability on dual maintenance therapies, Dr. D'Souza replied that we collect that information. Another comment was made on follow-up since Dr. Bumma planned 2019 could be possibly included in the proposal. Dr. D'Souza replied that study should be done until 2018 since we would not have complete data reporting for 2019 yet. A member suggested the possible analysis of double hits on cytogenetics. A concern was raised on a possible center effect between high risk cytogenetics and the intent of treatment. Other member commented on the small differences found in different studies that compared the use of Bortezomib.

24 additional proposals were submitted but not presented as listed below:

a. **PROP1911-03** The impact of response kinetics on outcomes while on lenalidomide maintenance after autologous hematopoietic cell transplantation in multiple myeloma. *Dropped Reason - Feasibility*
b. **PROP1911-07** Transplant outcomes in multiple myeloma-associated AL amyloidosis *Dropped Reason - Insufficient score to proceed among submitted proposals*
c. **PROP1911-107** Impact of Melphalan dose on outcomes following autologous stem cell transplantation in light chain amyloidosis with renal involvement in young vs. older patients. *Dropped Reason - Insufficient score to proceed among submitted proposals*
d. **PROP1911-117** The effect of coexistent amyloid and multiple myeloma in patients undergoing autologous stem cell transplant*. Dropped Reason - Insufficient score to proceed among submitted proposals*
e. **PROP1911-122** Growth Factors vs. Growth Factors + Chemotherapy in Peripheral Blood Stem Cell Mobilization for Autologous Hematopoietic Stem Cell Transplantation in Multiple Myeloma Patients. *Dropped Reason - Overlap with SC15-04*
f. **PROP1911-130** Melphalan dosing in the setting of advanced age and comorbidity. *Dropped Reason - Overlap with MM18-03*
g. **PROP1911-17** Comparison of high dose melphalan with 1 day vs. 2day regimen followed by autologous hematopoietic cell transplantation in patients with multiple myeloma. *Dropped Reason - Feasibility*

h. **PROP1911-177** To compare the outcomes of upfront autologous hematopoietic stem cell transplant using melphalan 200mg/m2 to melphalan <200mg/m2 in young and older patients with renal insufficiency and multiple myeloma in the US. *Dropped Reason - Overlap with MM14-03*
i. **PROP1911-180** Success and safety of re-mobilization of stem cell for patients with Multiple Myeloma who have previously undergone autologous stem cell transplant. *Dropped Reason - Feasibility*
j. **PROP1911-186** Evaluation of factors predictive of successful outcomes in allogeneic hematopoietic cell transplantation for multiple myeloma. *Dropped Reason - Feasibility*
k. **PROP1911-189** The Mayo 2012 and European 2015 Staging Systems for Systemic Light Chain Amyloidosis Predict Survival following High Dose Melphalan and Autologous Stem Cell Transplantation Irrespective of Transplant Center Experience. *Dropped Reason - Feasibility*
l. **PROP1911-230** Outcomes with an intensified conditioning regimen of BCNU/melphalan compared with melphalan alone in myeloma patients not achieving deep hematologic response prior to ASCT. *Dropped Reason - Insufficient score to proceed among submitted proposals*
m. **PROP1911-255** Outcome of patients with Multiple Myeloma undergoing Autologous (AHCT) and Allogeneic Stem Cell Transplantation (Allo-HCT) stratified by Lactate Dehydrogenase (LDH). *Dropped Reason - Feasibility*
n. **PROP1911-269** Study the Impact of Bone marrow microenvironment using thrombocytopenia and anemia as a surrogate marker in Multiple Myeloma patients undergoing autologous stem cell transplant. *Dropped Reason - Insufficient score to proceed among submitted proposals*
o. **PROP1911-29** KRD vs. VRD induction in transplant eligible multiple myeloma patients undergoing autologous stem cell transplantation. *Dropped Reason - Feasibility*
p. **PROP1911-37** Predictors and Prognostic Impact of Early Relapse After Salvage Second Autologous Hematopoietic Cell Transplantation for Relapsed. *Dropped Reason - Insufficient score to proceed among submitted proposals*
q. **PROP1911-43** Assessing outcomes of patients with AL amyloidosis with t(11;14) after autologous stem cell transplant. *Dropped Reason - Insufficient score to proceed among submitted proposals*
r. **PROP1911-62/PROP1911-65** Outcomes of autologous hematopoietic cell transplantation in multiple myeloma with pre-existing monoclonal gammopathy of unknown significance, smoldering myeloma or solitary plasmacytoma. *Dropped Reason - Insufficient score to proceed among submitted proposals*
s. **PROP1911-71** Evaluation of the outcomes of the use of allogeneic stem cell transplant in refractory or relapsed systemic amyloid light chain amyloidosis. *Dropped Reason - Insufficient score to proceed among submitted proposals*
t. **PROP1911-84** Efficacy analysis of melphalan dose reduction in multiple myeloma patients undergoing autologous transplant in the era of novel agent induction and maintenance. Dropped Reason - Insufficient score to proceed among submitted proposals
u. **PROP1911-94** Outcomes of HIV+ Patients undergoing Autologous HCT for Multiple Myeloma. *Dropped Reason – Feasibility*
v. **PROP1911-213** Comparing outcomes of maintenance therapies after autologous stem cell transplant (SCT) in patients with multiple myeloma. *Dropped Reason -Insufficient score to proceed among submitted proposals*
w. **PROP1910-03** Optimal conditioning regimen for relapsed Multiple Myeloma, prior to second salvage autologous hematopoietic stem cell transplant. *Dropped Reason- Insufficient score to proceed among submitted proposals*

The meeting was adjourned at **2:00** p.m. Dr. Kumar asked the audience to give an applause and thank Dr. Hari for his contributions.

6. Other Business

The chairs of the working committee, scientific director and statisticians had a post-WC meeting afterwards. After the new proposals were presented, each attendee had the opportunity to vote the proposals using the

provided voting sheets. Based on the voting results, current scientific merit and impact of the studies on the field, the following studies were decided to move forward as the committee's research portfolio for the upcoming year:

a. **MM20-01: PROP 1911-123** Outcomes after autologous hematopoietic cell transplantation in POEMS syndrome (Kansagra/Cornell/Dispenzieri/Kumar)
b. **MM20-02: PROP 1910-21/ PROP 1911-141/ PROP 1911-228/ PROP 1911-44** Risk factors for and characteristics of secondary primary malignancies following autologous hematopoietic cell transplant for multiple myeloma (Ragon/George/Gowda/Shah/Usmani). Invite Dr. Murthy to the Writing Committee since **PROP 1911-96** included many overlaps with the study, and prior malignancy was a variable we could add to this study and include within this protocol.
c. **MM20-03: PROP 1911-134/ PROP 1911-237/ PROP 1911-26** Impact of bortezomib-based vs. lenalidomide maintenance therapy on outcomes of patients with high-risk multiple myeloma (Bumma/Dhakal/Sidana)

Not for publication or presentation ***Attachment 1***

Working Committee Overview Plan for 2020-2021

Study number and title	Current status	Goal with date	Total hours to complete	Total hours to 2021 goal	Hours allocated to 6/30/20	Hours allocated 7/1/20-6/30/21	Total Hours allocated
MM17-01: Hematopoietic cell transplantation for primary plasma cell leukemia in the era of novel agents	Submitted	Published – July 2020	0	**0**	0	0	**0**
MM17-02: The Impact of Bortezomib Based Induction Therapy vs No Induction Therapy on Outcomes for Light Chain Amyloidosis	Analysis	Submitted – July 2020 Published – July 2021	80	**80**	70	10	**80**
MM18-01: Racial Discrepancy in Clinical Outcomes of Multiple Myeloma Patients with and without t(11;14) Genetic Abnormality	Submitted	Published – July 2020	0	**0**	0	0	**0**
MM18-02: Deriving a prognostic score for patients undergoing high dose therapy and autologous SCT for myeloma and examining validity of this in long-term exceptional responders	Manuscript Prep	Published – July 2021	10	**20**	10	10	**20**
MM18-03: To compare the outcomes in young patients with multiple myeloma at diagnosis undergoing autologous or allogeneic hematopoietic stem cell transplant (HCT) with older patients: progression-free and overall survival in a case match analysis	Manuscript Prep	Published – July 2021	10	**20**	10	10	**20**
MM18-04: Busulfan, Melphalan, and Bortezomib versus High-Dose Melphalan as a Conditioning Regimen for Autologous Hematopoietic Stem Cell Transplantation in Multiple Myeloma: Long Term Follow Up of a Novel Conditioning Regimen	Submitted	Published – July 2020	0	**0**	0	0	**0**
MM19-01: Impact of Induction Therapy with VRD vs. VCD on Outcomes in Patients with Multiple Myeloma Undergoing Stem Cell Transplantation	Protocol Development	Submitted – March 2021	280	**280**	150	130	**280**
MM19-02: Maintenance therapy after second autologous hematopoietic cell transplantation for Multiple Myeloma	Protocol Development	Manuscript Prep – July 2021	280	**210**	150	60	**210**

MM19-03: Second autologous stem cell transplantation as salvage therapy for relapsed or refractory AL amyloidosis	Protocol Development	Submitted – March 2021	290	**290**	100	190	**290**
MM20-01: Outcomes after autologous hematopoietic cell transplantation in POEMS syndrome	Protocol Pending	Manuscript Prep – July 2021	330	**260**	0	260	**260**
MM20-02: Risk factors for and characteristics of secondary primary malignancies following autologous hematopoietic cell transplant for multiple myeloma	Protocol Pending	Data File Preparation – July 2021	330	**100**	0	100	**100**
MM20-03: Impact of bortezomib-based vs. lenalidomide maintenance therapy on outcomes of patients with high-risk multiple myeloma	Protocol Pending	Data File Preparation – July 2021	330	**100**	0	100	**100**

Working Assignments for Working Committee Leadership (March 2020)	
Shaji Kumar:	**MM17-01:** HCT for primary plasma cell leukemia **MM18-01:** Racial discrepancy in MM patients with t(11;14) **MM19-01:** VRD vs. VCD as induction for MM patients **MM20-02:** Risk factors for and characteristics of secondary primary malignancies following autologous hematopoietic cell transplant for multiple myeloma
Nina Shah:	**MM17-02:** Bortezomib induction therapy for light chain amyloidosis **MM18-02:** Prognostic score system **MM18-03:** Compare young vs. old MM patients **MM20-01:** Outcomes after autologous hematopoietic cell transplantation in POEMS syndrome
Muzaffar Qazilbash:	**MM18-04:** BuMelVel vs High dose Mel in MM **MM19-02:** Maintenance therapy after second AutoHCT for MM **MM19-03:** Second AutoHCT for AL Amyloidosis **MM20-03:** Impact of bortezomib-based vs. lenalidomide maintenance therapy on outcomes of patients with high-risk multiple myeloma

Proposal: 2010-132

Title:
Characteristics and outcomes of adolescent and young adults with multiple myeloma after autologous hematopoietic stem cell transplant

Christin B. DeStefano, MD, christin.destefano@usuhs.edu, David Grant USAF Medical Center, Uniformed Services University (Junior investigator)
Steven J. Gibson, MD, steven.j.gibson24.mil@mail.mil, Walter Reed National Military Medical Center

Research hypothesis:
The central hypotheses of this project are that: 1) early autologous stem cell transplant (autoHCT) is commonly used among adolescents and young adults (AYAs) with multiple myeloma (MM) and 2) long-term survival, rates of second primary malignancies (SPMs) and infectious complications differ in AYAs post- autoHCT than AYAs treated without autoHCT and older adults who are status post autoHCT.

Specific aims:
- **Aim 1: To describe patient and disease related characteristics of AYAs with MM treated with early high dose melphalan and autoHCT.** We request data from the CIBMTR on AYAs (age 15-39) treated with melphalan-only conditioning therapy and early autoHCT (within the 12 months) from 2000-2018. We will characterize: 1) patient-related factors at diagnosis such as age, gender, race, ethnicity, socioeconomic data, HCT-CI, year of diagnosis, and country/state of residence, 2) disease-related factors such as ISS or R-ISS stage (including baseline albumin, B2-microglobulin, LDH, and cytogenetics via FISH and karyotype), MM subtype, presence of extramedullary plasmacytomas, and best hematologic response to induction therapy and 3) treatment factors including induction therapy regimen, post-transplant consolidation and maintenance therapy, and receipt of radiotherapy pre-transplant. We will compare certain patient-related factors among the CIBMTR early autoHCT cohort with AYAs diagnosed with MM during the same time frame from the SEER-18 database, to see if AYA patients of certain demographic or socioeconomic backgrounds are more likely to receive autoHCT. CIBMTR collects data on roughly 80% of autologous transplants performed in the United States (U.S.), while SEER-18 covers about 28% of the U.S. and is comprised of a nationally representative patient population.
- **Aim 2: To characterize responses to autoHCT, survival outcomes, SPMs, and infections of AYA MM patients after autoHCT.** From the CIBMTR AYA MM population who received early autoHCT within 12 months of diagnosis (as described in Aim 1), we will assess post-autoHCT treatment outcomes. We will assess: 1) best hematologic response to autoHCT, progression free survival (PFS, defined as time from autoHCT to initiation of second line therapy), and overall survival (OS), 2) incidence of SPMs, 3) incidence of infection complications, and 4) cause of death. Within the CIBMTR cohort, we will assess how patient-related factors, disease-related factors, and treatment factors impact survival, SPMs, and infections.
    a. **To compare outcomes of AYA MM patients after autoHCT with outcomes of older adult MM patients after autoHCT, AYA MM patients treated without autoHCT, and AYA MM patients unselected for treatment.** We will request a comparator arm from CIBMTR consisting of patients age 40-60 diagnosed with MM between 2000-2018 who also received an early autoHCT after melphalan only conditioning, and who are matched by year of diagnosis, age, gender, race, ethnicity, ISS or R-ISS, MM subtype, cytogenetic risk, induction therapy, best response to induction, and post-transplant maintenance. We will compare best responses to

autoHCT, PFS, OS, SPMs, major infections, and cause of death. We will also create comparator arms encompassing AYA MM patients treated without early autoHCT from the American Society of Clinical Oncology (ASCO)'s CancerLinq multiple myeloma registry, and AYA MM patients unselected for treatment from the SEER-18 database. Using these two comparator arms, we will compare disease-specific survival, OS, incidence of SPMs, major infections, and cause of death with AYA MM patients treated with early autoHCT from the CIBMTR database.

Scientific impact:

AYAs with cancer are defined as individuals between age 15-39 at the time of diagnosis, and this patient population is of interest from a Department of Defense perspective as most active duty service members with cancer are AYAs. AYAs with multiple myeloma (MM) are of particular interest given the association of monoclonal gammopathies with military-relevant exposures such as Agent Orange, pesticides, and aerosolized carcinogens released during the World Trade Center disaster (1-3).

AYAs with MM have better survival outcomes than older patients, especially among those with good initial prognostic factors (4-6). Post-transplant outcomes among AYAs with MM have not been well characterized. It will be interesting to assess how baseline characteristics such as race, ethnicity, and socioeconomic status impact likelihood of receiving autoHCT as well as post-transplant survival, and will provide insight into potential barriers to healthcare access if racial, ethnic, or socioeconomic differences are noted. Data for a one-time analysis provided recently by the CIBMTR revealed that there were 1,142 AYA MM patients treated with autoHCT from 2008-2018, suggesting that autoHCT is a relatively common practice despite AYAs being under-represented in autoHCT MM studies such as IFM-2009 (7). Additionally, AYAs might be more likely to have hereditary predispositions to their MM (8-11), and therefore it is unclear if complications of early autoHCT (such as SPMs) offset their improved survival. A recent CIBMTR study assessed characteristics and outcomes of elderly patients (>70 years old) who underwent autoHCT and found no differences when compared to those 60-69 years old (12). Herein we aim to assess characteristics and outcomes of AYA patients treated with early autoHCT and determine if there are differences when compared to their older counterparts, AYAs treated without autoHCT, and background AYA MM patients unselected for treatment.

We will characterize post-transplant survival as well as complications to include infection and SPM development. Previous studies using SEER data found SPMs to represent around 5% of deaths among AYAs with MM, with acute myeloid leukemia, non-Hodgkin lymphoma, and lung cancer being the most common (standardized incidence ratio 14.6, 5.3, and 4.9, respectively) (13). However, the influence of induction therapy, early auto-HCT and post-transplant therapy among AYAs is unknown, as is the incidence of SPMs and infections. The combination of melphalan and lenalidomide has been shown to heighten the risk of therapy related myeloid neoplasms in an analysis involving standard MM patients (not AYAs), yet this SPM risk is counter-balanced by a large survival benefit (14, 15). If AYAs appear to have an even higher risk of SPMs after early autoHCT, this could provide rationale for a future study utilizing biospecimens from the NMDP Research Sample Repository to assess germline predisposition and underlying clonal hematopoiesis mutations among those AYAs who developed SPMs. This analysis may also provide valuable information on how timing of transplant, especially among those who are considered high-risk, affects survival outcomes given that one-time CIBMTR analysis shows the vast majority (80%) of AYAs receive transplant within the first year of MM diagnosis.

Lastly, infection remains a significant cause of morbidity among autoHCT recipients, with OS being worse among those with early infections (HR 1.54, [1.03-2.30]) (16). In the same SEER analysis, infections (to include HIV) were reported at 3.6% as cause of death in the AYA MM population (13). We will characterize what types of infections are most prevalent in the AYA post-transplant, and aim to identify any risk factors increasing this risk and creating an area for potential intervention in the future.

Scientific justification:
MM is an incurable disease of the elderly with less than 1% of cases diagnosed in those under 30 years old (17). The AYAs with MM have been found to live longer, with an increased risk for SPMs, reproductive issues, and therapy-related cardiotoxicity (18). Overall survival among all MM patients continues to increase, with AYAs having a median disease-specific survival of 15 years in recent SEER analysis (13). When looking at survival by year of diagnosis, there was a 61% reduction in risk of death among those diagnosed between 2012-2017 when compared to 2000-2005 (13), likely a reflection of novel therapies like lenalidomide and proteasome inhibitors. Survival analyses in the AYA population assessing patient characteristics and outcomes after high dose melphalan/early autoHSCT have not been performed, and hence an unmet need persists. Aim 1 of this proposal will help identify characteristics of AYA MM patients selected to undergo early autoHCT and could unveil healthcare disparities in access to stem cell transplantation based on race/ethnicity and socioeconomic status. Aim 2 will identify benefits and long-term risks (SPMs, infections) associated with autoHCT among AYA MM patients. Aim 3, with our comparator arms, will allow us to better understand the role of autoHCT in the management of AYA MM patients, particularly the benefits and risks attributable to transplant. From a military standpoint, this study could provide information to better guide treating physicians caring for AYA military members and Veterans afflicted with myeloma.

Patient eligibility population:
Patients age 15-39 years old at the time of MM diagnosis who were diagnosed between 2000-2018 and who received early autologous stem cell transplant (within the first 12 months of diagnosis) with melphalan-only conditioning.

Data requirements:
Supplemental data will be requested from Plasma Cell Disorders (Multiple Myeloma) pre-infusion and post-HCT data, and includes the following variables: baseline albumin, b2-microglobulin, cytogenetics (FISH and karyotype), presence of extramedullary plasmacytomas, induction therapy, best response to induction therapy, and post-transplant therapy (consolidation, maintenance, and 2nd line therapy after relapse).

Sample requirements:
None

Study design:
This is a retrospective cohort study utilizing data from the CIBMTR. Inclusion criteria includes patients 15-39 years of age at the time of MM diagnosis (ICD-O code 9732/3) between 2000-2018 who received early autoHCT (within the first 12 months of MM diagnosis) and melphalan only conditioning. Variables to be assessed include patient-related, disease-related and treatment-related variables as described in Aim 1. Endpoints being assessed include best response to autoHCT, PFS, OS, incidence of SPMs and infections, and cause of death (death attributable to myeloma versus SPM versus infection). Analyses will be conducted with STATA for Windows Version 14.2; data will be censored at time of death or loss to follow up. Kaplan-Meier curves will be generated to illustrate the probability of mortality over time in groups with different characteristics. Individual variables will be compared via log rank tests, and Cox proportional hazard regression models will be constructed using predictors with *p* values of .25 or less and/or those specified as important *a priori*. Model fit will be assessed with Akaike's information

criterion and Snell residuals. Assumptions of the Cox proportional hazards model will be evaluated with log-time.

Non-CIBMTR data source:
None.

Conflicts of interest:
None

References:

1. Landgren O, Kyle RA, Hoppin JA, Beane Freeman LE, Cerhan JR, Katzmann JA, et al. Pesticide exposure and risk of monoclonal gammopathy of undetermined significance in the Agricultural Health Study. Blood. 2009;113(25):6386-91.
2. Landgren O, Shim YK, Michalek J, Costello R, Burton D, Ketchum N, et al. Agent Orange Exposure and Monoclonal Gammopathy of Undetermined Significance: An Operation Ranch Hand Veteran Cohort Study. JAMA Oncol. 2015;1(8):1061-8.
3. Landgren O, Zeig-Owens R, Giricz O, Goldfarb D, Murata K, Thoren K, et al. Multiple Myeloma and Its Precursor Disease Among Firefighters Exposed to the World Trade Center Disaster. JAMA Oncol. 2018;4(6):821-7.
4. Blade J, Kyle RA, Greipp PR. Presenting features and prognosis in 72 patients with multiple myeloma who were younger than 40 years. Br J Haematol. 1996;93(2):345-51.
5. Ludwig H, Durie BG, Bolejack V, Turesson I, Kyle RA, Blade J, et al. Myeloma in patients younger than age 50 years presents with more favorable features and shows better survival: an analysis of 10 549 patients from the International Myeloma Working Group. Blood. 2008;111(8):4039-47.
6. Jurczyszyn A, Davila J, Kortum KM, Jayabalan DS, Vij R, Fiala M, et al. Multiple myeloma in patients up to 30 years of age: a multicenter retrospective study of 52 cases. Leuk Lymphoma. 2019;60(2):471-6.
7. Attal M, Lauwers-Cances V, Hulin C, Leleu X, Caillot D, Escoffre M, et al. Lenalidomide, Bortezomib, and Dexamethasone with Transplantation for Myeloma. N Engl J Med. 2017;376(14):1311-20.
8. Hu Y, Chen W, Wang J. Progress in the identification of gene mutations involved in multiple myeloma. OncoTargets and therapy. 2019;12:4075-80.
9. Jain M, Ascensao J, Schechter GP. Familial myeloma and monoclonal gammopathy: a report of eight African American families. American journal of hematology. 2009;84(1):34-8.
10. Lynch HT, Watson P, Tarantolo S, Wiernik PH, Quinn-Laquer B, Isgur Bergsagel K, et al. Phenotypic heterogeneity in multiple myeloma families. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2005;23(4):685-93.
11. Koura DT, Langston AA. Inherited predisposition to multiple myeloma. Therapeutic advances in hematology. 2013;4(4):291-7.
12. Munshi PN, Vesole D, Jurczyszyn A, Zaucha JM, St Martin A, Davila O, et al. Age no bar: A CIBMTR analysis of elderly patients undergoing autologous hematopoietic cell transplantation for multiple myeloma. Cancer. 2020.
13. Gibson SJ TJ, DeStefano CB. A SEER and CIBMTR analysis of multiple myeloma in adolescent and young adults. American College of Physicians 2020 Tri-Service Chapter Meeting, Hematology/Oncology Breakout Session; Sep 2020; San Antonio (Virtual)2020.
14. Palumbo A, Bringhen S, Kumar SK, Lupparelli G, Usmani S, Waage A, et al. Second primary malignancies with lenalidomide therapy for newly diagnosed myeloma: a meta-analysis of individual patient data. Lancet Oncol. 2014;15(3):333-42.

15. McCarthy PL, Holstein SA, Petrucci MT, Richardson PG, Hulin C, Tosi P, et al. Lenalidomide Maintenance After Autologous Stem-Cell Transplantation in Newly Diagnosed Multiple Myeloma: A Meta-Analysis. J Clin Oncol. 2017;35(29):3279-89.
16. Rahman S, Rybicki L, Ky Hamilton B, Pohlman B, Jagadeesh D, Cober E, et al. Early infectious complications after autologous hematopoietic cell transplantation for multiple myeloma. Transplant infectious disease : an official journal of the Transplantation Society. 2019;21(4):e13114.
17. Cancer Stat Facts: Myeloma: National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program; 2020 [Available from: SEER.cancer.gov.
18. Devine H, Verina D. Young Adults with Multiple Myeloma. Seminars in oncology nursing. 2017;33(3):316-31.

Table 1. Characteristics of young adult patients who underwent first HCT for MM from 1995-2019 and registered with CIBMTR (TED level variables)

Characteristic	TED	CRF
No. of patients	1426	339
No. of centers	213	116
Median age (range) - median (min-max)	36.87 (16.72-39.99)	36.11 (16.73-38.99)
Age - no. (%)		
15-19	6 (0)	1 (0)
20-29	89 (6)	33 (10)
30-39	1023 (72)	305 (90)
Gender - no. (%)		
Male	890 (62)	199 (59)
Female	536 (38)	140 (41)
Region - no. (%)		
US	1132 (79)	298 (88)
Canada	76 (5)	12 (4)
Europe	29 (2)	3 (1)
Asia	45 (3)	5 (1)
Australia/New Zealand	20 (1)	4 (1)
Mideast/Africa	29 (2)	2 (1)
Central/South America	95 (7)	15 (4)
Race - no. (%)		
White	882 (62)	197 (58)
Black or African American	267 (19)	103 (30)
Asian	58 (4)	12 (4)
Native Hawaiian or other Pacific Islander	4 (0)	0
American Indian or Alaska Native	5 (0)	1 (0)
Other	17 (1)	0
More than one race	2 (0)	2 (1)
Missing	191 (13)	24 (7)
Karnofsky score prior to HCT - no. (%)		
90-100	692 (49)	123 (36)
< 90	343 (24)	58 (17)
Missing	391 (27)	158 (47)
HCT-CI - no. (%)		
0	468 (33)	66 (19)
1	121 (8)	22 (6)
2	166 (12)	34 (10)
=>3	269 (19)	59 (17)
Missing	401 (28)	158 (47)

Characteristic	TED	CRF
Conditioning regimen - no. (%)		
Melphalan only	1307 (92)	298 (88)
Melphalan based regimen	119 (8)	41 (12)
Melphalan dose(mg/m) - no. (%)		
MEL 140	94 (7)	88 (26)
MEL 200	936 (66)	228 (67)
Missing	396 (28)	23 (7)
Disease status prior to transplant - no. (%)		
sCR/CR	254 (18)	53 (16)
VGPR	368 (26)	68 (20)
PR	581 (41)	158 (47)
SD	102 (7)	34 (10)
PD/Relapse	63 (4)	13 (4)
Missing	58 (4)	13 (4)
Time from diagnosis to HCT - median (min-max)	7.71 (0.16-187.89)	7.24 (0.13-125.13)
Time from diagnosis to HCT - no. (%)		
< 6 months	441 (31)	104 (31)
6-12 months	624 (44)	194 (57)
12-18 months	235 (16)	28 (8)
≥24 months	116 (8)	12 (4)
Missing	10 (1)	1 (0)
Year of transplant - no. (%)		
1995	7 (0)	2 (1)
1996	9 (1)	2 (1)
1997	13 (1)	6 (2)
1998	19 (1)	13 (4)
1999	19 (1)	9 (3)
2000	32 (2)	9 (3)
2001	22 (2)	20 (6)
2002	41 (3)	10 (3)
2003	44 (3)	6 (2)
2004	47 (3)	15 (4)
2005	43 (3)	27 (8)
2006	40 (3)	29 (9)
2007	54 (4)	13 (4)
2008	50 (4)	25 (7)
2009	80 (6)	5 (1)
2010	82 (6)	5 (1)
2011	91 (6)	7 (2)
2012	85 (6)	16 (5)

Characteristic	TED	CRF
2013	89 (6)	22 (6)
2014	90 (6)	12 (4)
2015	76 (5)	14 (4)
2016	95 (7)	21 (6)
2017	83 (6)	12 (4)
2018	99 (7)	31 (9)
2019	116 (8)	8 (2)
Follow-up - median (min-max)	59.74 (3.06-268.52)	75.56 (3.03-256.91)

Table 2. Characteristics of Multiple Myeloma patients undergoing first autologous stem cell transplants from 1995 to 2019, CRF-specific variables

Characteristic	N (%)
No. of patients	339
No. of centers	117
ISS stage at diagnosis - no. (%)	
ISS stage I	97 (29)
ISS stage II	71 (21)
ISS stage III	56 (17)
Missing	115 (34)
Stage at diagnosis(ISS/DS) - no. (%)	
stage III	206 (61)
stage I-II	120 (35)
Missing	13 (4)
Immunochemical subtype - no. (%)	
IgG	169 (50)
IgA	55 (16)
Light chain	98 (29)
Non-secretory	6 (2)
Others	5 (1)
Missing	6 (2)
Hemoglobin prior to transplant - no. (%)	
< 10 g/dl	69 (20)
≥ 10 g/dl	230 (68)
Missing	40 (12)
Serum creatinine prior to transplant, mg/dl - no. (%)	
< 2 mg/dl	292 (86)
≥ 2 mg/dl	24 (7)
Missing	23 (7)

Characteristic	N (%)
Bone marrow plasma cells at diagnosis - no. (%)	
<10%	35 (10)
≥10%	222 (65)
Missing	82 (24)
Bone marrow plasma cells at transplant - no. (%)	
<10%	183 (54)
≥10%	59 (17)
Missing	97 (29)
Lines of chemotherapy - no. (%)	
1	217 (64)
≥2	88 (26)
Missing	34 (10)
Chemotherapy - no. (%)	
VTD	11 (3)
VRD	81 (24)
VCD	36 (11)
VD	30 (9)
RD	10 (3)
TD	52 (15)
VAD/similar	72 (21)
KRD	3 (1)
Daratumumab	6 (2)
Others	4 (1)
Missing	34 (10)
Intent to Maintenance therapy - no. (%)	
No	123 (36)
Yes	125 (37)
Missing	90 (27)
post-HCT therapy (for current transplant) - no. (%)	
VR +/- other	15 (4)
VC +/- other	3 (1)
V +/- other	16 (5)
R +/- other	77 (23)
K +/- other	2 (1)
Other	13 (4)
No Maintenance	123 (35)
Missing	90 (27)

Proposal: 2010-161

Title:
Outcomes of autologous hematopoietic cell transplantation for Light Chain Deposition Disease

Hamza Hashmi, MD, hashmih@musc.edu, Medical University of South Carolina, Charleston, SC
Taiga Nishihori, MD, taiga.nishihori@moffitt.org, Moffitt Cancer Center, Tampa, FL 33612

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

Specific aims:
- To determine overall survival (OS) after autologous HCT for LCDD
- To determine disease response [hematological, clinical], progression-free survival (PFS), transplant-related mortality (TRM), cumulative incidence of relapse after HCT for LCDD

Scientific impact:
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 outcomes of autologous HCT and could lead to future novel research on improving the transplant outcomes.

Scientific justification:
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/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 appears 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 organ impairment related to 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 dataset of patients undergoing autologous HCT 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 (incluidng TRM) in patients undergoing autologous HCT with advanced age renal disease and allow for better patient selection for transplant.

Patient eligibility population:
Inclusion criteria:
Adult patients (age>18 years) who received autologous HCT for LCDD from 2000 to 2019

Exclusion criteria:
None

Variables to be described: (variables to be included in the multivariate analysis are bolded)
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 or no
- **Chronic kidney disease stage:** I-II (GFR>60 ml/min) vs III (GFR 30-60 ml/min) vs IV (GFR 15-30 ml/min) vs V (GFR<15 ml/min)
- **Organ involvement** by LCDD: renal vs. cardiac vs. others
- **Need for hemodialysis prior to HCT: yes or no**
- **Renal transplant prior to HCT: yes or no**

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 % at diagnosis and prior to HCT:>10% vs 5-10% vs <5%
- Disease status (hematological) prior to transplant: Complete response [CR], partial response [PR], stable disease [SD] vs progressive disease [PD]
- **Number of prior chemotherapy lines**: continuous
- **Prior treatment: bortezmob-based vss IMID-based vs. others**
- Time from diagnosis to transplant: continuous (months)
- Prior radiotherapy: yes vs. no

Transplant related:

- **Mobilization**: G-CSF vs Plerixafor vs chemo-based
- CD34 cell dose (/recipient body weight)
- Conditioning regimen: Melphalan 200 mg/m² vs melphalan 140 mg/m² vs BEAM vs others
- Engraftment syndrome: yes vs no
- Secondary MDS post HCT: yes vs no
- **Need for hemodialysis post HCT: yes or no**
- **Renal transplant post HCT: yes vs no**
- **Use of maintenance post HCT: yes or no**

Data requirements:
None

Sample requirements:
None

Study design:
Outcomes:

- Overall survival: Time from HCT to death from any cause. Patients will be censored at the time of last follow up.
- Progression-free survival: Time from HCT 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.
- Clinical response: based on improvements in kidney function [Serum creatinine, glomerular filtration rate, creatinine clearance, progression to end-stage renal disease]
- Hematologic response: CR: negative BM, and negative immunofixation of the serum and urine; very good partial response: 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 ASCT for patients with LCDD between 2000 and 2019 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 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 also consider comparing the outcomes based on the year of HCT if there is sufficient number of cases for such evaluation to understand the impact of year of HCT in LCDD. Probabilities of renal failure requiring hemodialysis after autologous HCT will be calculated using cumulative incidence curves.

Non-CIBMTR data source:
May be needed from individual institution

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

Table 1. Characteristics of adult patients who underwent first HCT for LCDD from 2000-2019 and registered with CIBMTR (TED level variables)

Characteristic	TED	CRF
No. of patients	185	78
No. of centers	81	35
Age at HCT - median (min-max)	59.39 (23.93-77.66)	57.89 (35.79-76.44)
Age at transplant, years - no. (%)		
18-39	13 (7)	2 (3)
40-49	31 (17)	23 (29)
50-59	57 (31)	17 (22)
60-69	71 (38)	26 (33)
70+	13 (7)	10 (13)
Gender - no. (%)		
Male	102 (55)	40 (51)
Female	83 (45)	38 (49)
Region - no. (%)		
US	169 (91)	75 (96)
Canada	11 (6)	0
Mideast/Africa	1 (1)	0
Central/South America	4 (2)	3 (4)
Race - no. (%)		
Caucasian	134 (72)	53 (68)
African-American	24 (13)	21 (27)
Asian	6 (3)	2 (3)
Pacific islander	1 (1)	0
Native American	2 (1)	0
Missing	18 (10)	2 (3)
Karnofsky score prior to HCT - no. (%)		
90-100	101 (55)	32 (41)
< 90	80 (43)	44 (56)
Missing	4 (2)	2 (3)
HCT-CI - no. (%)		
0	35 (19)	15 (19)
1	13 (7)	9 (12)
2	37 (20)	14 (18)
3+	100 (54)	40 (51)
Adjusted HCT-CI scores (Renal Comorbidity excluded)- no. (%)		
0	49 (26)	22 (28)
1	19 (10)	13 (17)

Characteristic	TED	CRF
2	36 (19)	8 (10)
3+	81 (44)	35 (45)
Conditioning regimen - no. (%)		
Melphalan only	180 (97)	77 (99)
Melphalan based regimen	5 (3)	1 (1)
Melphalan dose(mg/m) - no. (%)		
MEL 140	90 (49)	30 (38)
MEL 200	95 (51)	47 (60)
Missing	0	1 (1)
Disease status prior to transplant - no. (%)		
sCR/CR	35 (19)	13 (17)
VGPR	69 (37)	31 (40)
PR	48 (26)	22 (28)
SD	24 (13)	8 (10)
PD/Relapse	4 (2)	2 (3)
Missing	5 (3)	2 (3)
Time from diagnosis to HCT - median (min-max)	7.7 (0.39-835.2)	7.25 (2.57-82.83)
Time from diagnosis to transplant - no. (%)		
<6 months	65 (35)	27 (35)
6-12 months	68 (37)	37 (47)
12-18 months	26 (14)	5 (6)
18-24 months	12 (6)	1 (1)
>24 months	14 (8)	8 (10)
Year of transplant - no. (%)		
2011	1 (1)	1 (1)
2013	5 (3)	2 (3)
2014	20 (11)	2 (3)
2015	25 (14)	5 (6)
2016	51 (28)	7 (9)
2017	36 (19)	12 (15)
2018	22 (12)	29 (37)
2019	25 (14)	20 (26)
Follow-up - median (min-max)	26.41 (2.01-96.61)	12.47 (2.8-73.09)

Selected LCDD patients from 2000-2019, Excluded no-consented patients, Excluded Embargoed centers

Table 1b. CRF-specific variables

Characteristic	CRF
No. of patients	78
Lines of chemotherapy - no. (%)	
1	56 (72)
≥2	13 (17)
Missing	9 (12)
Chemotherapy - no. (%)	
VTD	1 (1)
VRD	20 (26)
VCD	25 (32)
VD	9 (12)
RD	4 (5)
TD	2 (3)
KRD	2 (3)
Daratumumab	4 (5)
VAD/similar	1 (1)
Others	1 (1)
Missing	9 (12)
Immunochemical subtype - no. (%)	
IgG	7 (9)
IgA	4 (5)
Light chain	31 (40)
Non-secretory	25 (32)
Unknown Type	11 (14)
Serum creatinine prior to transplant, mg/dl - no. (%)	
< 2 mg/dl	53 (68)
≥ 2 mg/dl	25 (32)
Intent to Post-transplant therapy - no. (%)	
No	23 (29)
Yes	47 (60)
missing	8 (10)
post-HCT therapy (for current transplant) - no. (%)	
VR +/- other	9 (12)
V +/- other	8 (10)
R +/- other	24 (31)
Other	6 (8)
No maintenance	23 (29)
Missing	8 (10)
Post-transplant dialysis	
No	8 (10

Characteristic	CRF
Yes	2 (3)
Missing	68 (87)