Not for publication or presentation

MINUTES AND OVERVIEW PLAN
CIBMTR WORKING COMMITTEE FOR PLASMA CELL DISORDERS AND ADULT SOLID TUMORS
Houston, Texas
Saturday, February 23, 2019, 12:15 – 2:15 pm

Co-Chair:	**Tomer Mark, MD, University of Colorado Hospital, Aurora, CO; Telephone: 720-848-3389; E-mail: tomer.mark@ucdenver.edu**
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**

1. Introduction

The CIBMTR Plasma Cell Disorders and Adult Solid Tumors Working Committee was called to order at 12:15PM on Saturday, February 23rd, by Dr. D'Souza. Dr. D'Souza introduced the committee leadership and welcomed the committee participants. Dr. D'Souza acknowledged Dr. Tomer Mark, who unfortunately could not be present for the meeting, for all his effort during the past years as Co-Chair. Dr. D'Souza introduced Dr. Muzaffar Qazilbash as the newly appointed Chair for the Working Committee starting March 1, 2019. Dr. D'Souza introduced the committee goal and expectations to the audience and reviewed presentations, publications and submitted papers in 2018. Dr. D'Souza gave update on the current status of ongoing studies and their goals for July 2019. Dr. D'Souza presented and explained the Advisory Committee Metrics, for which the committee received outstanding grade in 2018. Dr. Hari discussed important details about how the committee works, CIBMTR study development cycle and explained the different sources of CIBMTR data collection (TED and CRF). Dr. Hari also discussed future priorities of the committee: revision of plasma cell disorders forms to include new drugs, more details on POEMS, MGRS- VEGF, MRD, therapies at relapse, imaging (PET) information. Dr. Hari clarified the voting process to the audience and explained the PI's rule of conduct on the study cycle: timely completion of abstract, slides, and manuscript after the analysis is completed. If the PI does not write the first draft of the manuscript, after 3 requests, the paper will be reassigned i.e. the person who writes the manuscript will be the first author. The CIBMTR statistical resource was clarified to the audience. The average time to complete a study is 2-3 years upon statistical hour allocation and other competing projects.

2. Accrual summary (Attachment 2)

Due to the full agenda the accrual summary of registration and research cases between 1990 and 2018 were not presented to the committee but were available as part of the Working Committee attachments. The accrual summary provides information about the number of patients available in the registration level and research level for potential studies. As of December 2018, 80,342 plasma cell disorder cases were reported at the registration only level and 14,725 cases at the research level to the CIBMTR for first autologous transplant. For first allogeneic transplants, these numbers are 4,908 cases and 2,026 cases respectively.

3. Presentations, published or submitted papers

Dr. D'Souza presented the following publications and presentations from the committee's work during this year.

a. **MM14-01** M Qayed, D Kilari, T Olson, KY Chiang, A D'Souza, P Hari. Characteristics and outcomes of patients with refractory germ cell tumor undergoing autologous hematopoietic stem cell transplantation. **Presented at GU-ASCO 2018. Submitted**

b. **MM16-01a** E Scott, P Hari, S Kumar, Y Nieto, T Mark, S Kumar, C Gasparetto, A D'Souza. Staging Systems for Newly Diagnosed Myeloma Patients Undergoing Autologous Hematopoietic Cell Transplantation: The Revised International Staging System Shows the Most Differentiation between Groups. ***Biology of Blood and Marrow Transplantation. 2018 Dec;24(12):2443-2449. doi:10.1016/j.bbmt.2018.08.013. Epub 2018 Aug 21.***

c. **MM16-01b** S Kumar, A D'Souza, E Scott, C Gasparetto, S Kumar, T Mark, Y Nieto, P Hari. Revised-International Staging System (R-ISS) is Predictive and Prognostic for Early Relapse (<24 months) after Autologous Transplantation for Newly Diagnosed Multiple Myeloma (MM). ***Biology of Blood and Marrow Transplantation. 2018 Dec 20. pii: S1083-8791(18)30963-7. doi: 10.1016/j.bbmt.2018.12.141.***

d. **MM16-02** F Sahebi, L Garderet, A Kanate, N Shah, Q Bashir, S Ciurea. Outcomes of Haploidentical Transplantation in Patients with Relapsed Multiple Myeloma: An EBMT/CIBMTR Report. ***Presented at EBMT 2018. Biology of Blood and Marrow Transplantation. doi:10.1016/j.bbmt.2018.09.018. Epub 2018 Sep 20.***

e. **MM18-01** Racial Discrepancy in Clinical Outcomes of Multiple Myeloma Patients with and without t(11;14) Genetic Abnormality (D Sivaraj /A Krishnan /C Gasparetto). ***Analysis complete***

4. Studies in progress (Attachment 3)

Dr. D'Souza introduced the following studies in progress and goal by July 2019.

a. **MM14-01: Characteristics and Outcomes of patients with refractory germ cell tumor undergoing autologous hematopoietic stem cell transplantation** (M Qayed/D Kilari/ T Olson/ KY Chiang/P Hari). The primary aim of the study is to determine the overall outcomes of patients with testicular and extragonadal GCT (excluding intracranial tumors) who underwent high-dose chemotherapy and autologous SCT. The paper has been submitted. The goal of the study is to publish paper by June 2019.

b. **MM17-01: Hematopoietic cell transplantation for primary plasma cell leukemia in the era of novel agents** (S Girnius/S Patel/L Bachegowda/B Dhakal). This study looks to evaluate transplant outcomes of patients aged ≥ 18 years with pPCL who underwent autologous HCT and allogeneic. Analysis is underway. The goal of the study is to complete analysis by July 2019.

c. **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) This study looks to compare pre-transplant bortezomib-based induction therapy with no induction therapy prior to autologous hematopoietic cell transplantation and evaluate transplant outcomes in patients with light chain (AL) amyloidosis. Study is delayed pending IT updates with data retrieval for AL amyloidosis. The study will only be started once data is available to the WC.

d. **MM18-01: Racial Discrepancy in Clinical Outcomes of Multiple Myeloma Patients with and without t(11;14) Genetic Abnormality** (D Sivaraj /A Krishnan /C Gasparetto) This study looks to assess the effects

of t(11;14) on survival outcomes between African American and non-African American with multiple myeloma who underwent high dose melphalan plus autologous hematopoietic cell transplantation. The study is in manuscript preparation phase. The goal is to submit paper by June 2019.

e. **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) This study looks to identify pre-transplant factors that can help develop a prognostic score at the time of transplant. The purpose of this score is to help predict outcomes in transplant eligible myeloma patients and help predict a group of patients at high risk of early relapse as well as "exceptional responders" with extremely long responses to high dose melphalan. The study is in protocol development. The goal is to finalize datafile by May 2019 and proceed to analysis.

f. **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) This study looks to compare the outcomes of autologous and allogeneic HCT in patients with MM < 50 years in different age groups (20-39 years and 40-49 years) with patients ≥ 50 years (50-59 years, 60-69 and ≥ 70). The study is in datafile preparation. The goal is to finalize datafile and analysis by April 2019.

g. **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) This study looks to update the outcomes among multiple myeloma patients treated on a phase I/II BUMELVEL cohort and a CIBMTR MEL 200 control cohort. The goal for this study is to complete the analysis by April 2019.

5. Future/proposed studies

This year, we received 25 proposals, 10 of which were invited to present at the meeting (including 1 merge of 3 proposals with similar research objectives). After the introduction of the voting process, the following new proposals were presented and voted on. Dr. Shah introduced the first 4 proposals.

a. **PROP 1811-58** Outcomes of Autologous Hematopoietic Cell Transplantation for Relapsed/Refractory Germ Cell Tumors in Females (Sagar Patel/Navneet Majhail) (Attachment 4)

Dr. Patel presented the proposal on behalf of the group. This study hypothesizes that outcomes of autologous hematopoietic cell transplantation for relapsed/refractory germ cell tumors in females are comparable to those with males with testicular germ cell tumors. There are 98 female patients (13 in CRF) who underwent AutoHCT for germ cell tumor from 2008-2017. The audience had concerns regarding the low number of CRF patients in the database, and how we will be able to draw clear conclusions due to this limitation. The proposal also wanted to limit the population to adults ≥ 18 years, but over 50% of the population was below 18 years of age.

<u>Amyloidosis:</u>

b. **PROP 1811-168** Second autologous stem cell transplantation as salvage therapy for relapsed or refractory AL amyloidosis (Carlyn Tan/Henry Fung) (Attachment 5)

Dr. Tan presented the proposal on behalf of the group. This study hypothesizes that second course of high-dose therapy and autologous stem cell transplant as salvage therapy results in improvement in the progression free survival and overall survival of patients with relapsed/refractory AL amyloidosis. There are 90 patients (27 in CRF) who underwent 2nd HCT from Amyloidosis from 1999-2016. The audience had suggestions including allowing coexistent Multiple Myeloma patients, organ involvement information available for 1st and 2nd HCT, limit population to year of transplant > 2006 since there where no relevant drugs before this year for amyloidosis, and the role of tandem transplants in this population.

Multiple Myeloma:

c. **PROP 1811-49** Serum Free light Chain ratio at Day +100 and Day + 180 following Autologous Hematopoietic Cell Transplantation is predictive of outcomes in Multiple Myeloma (Hemant Murthy/Nosha Farhadfar/John Wingard) (Attachment 6)
Dr. Murthy presented the proposal on behalf of the group. This study hypothesizes that normalization of serum free light chain ratio at day +100 and day +180 following autologous hematopoietic cell transplantation is independently predictive of superior progression free and overall survival in multiple myeloma. There are 4,586 patients in CRF who underwent AutoHCT for multiple myeloma from 2008-2016 but only approximately third of these at FLC ratio available at baseline and day 100. The audience had questions regarding the handling of patients with normal light chain ratio before transplant, limitation of only one end point (day 100) as predictor of outcomes, and to consider the use of absolute amount of free light chain instead of the ratio.

d. **PROP 1811-108** Maintenance therapy after second autologous hematopoietic cell transplantation for Multiple Myeloma (Oren Pasvolsky /Moshe Yeshurun/Uri Rozovski/Liat Shargian-Alon) (Attachment 7)
Dr. Kumar presented the proposal on behalf of the group. This study hypothesizes that maintenance therapy may prolong progression free survival and overall survival after second AutoHCT. There are 500 patients in CRF who underwent 2nd AutoHCT for Multiple Myeloma from 2008 - 2016. The audience had questions about the limitation of not knowing the specific reason why the patient received or did not receive maintenance therapy thereby not being able to draw clear conclusions, possible stratification of patients by response after 1st HCT, role of tandem transplants, possible stratification of patients by year of transplant, and conditioning regimen given (other than melphalan).

Dr. Kumar introduced the last 3 proposals.

e. **PROP 1811-05** Outcomes for patients with Multiple Myeloma treated with Autologous or Syngeneic Allogenic Stem Cell Transplantation (Andrew Pham /Anuj Mahindra) (Attachment 8)
Dr. Pham presented the proposal on behalf of the group. This study hypothesizes that autologous stem cell transplant will still be shown to provide benefit to patients with multiple myeloma and that syngeneic transplantation will be demonstrated to be safe and efficacious as well. There are 55 patients who underwent syngeneic AlloHCT and 4,624 who underwent AutoHCT from 2008 - 2016. The audience questioned the low number of patients in syngeneic group therefore not being able to draw clear conclusions, as well as lack of novelty since the CIBMTR has published this type of analysis in the past.

f. **PROP 1810-06/1811-117/1811-153** Comparison of real-world experience of maintenance strategies in multiple myeloma patients after autologous stem cell transplantation (Dhakal Binod/ Shebli Atrash/ Gayathri Ravi/ Ehsan Malek/ Peter Voorhees) (Attachment 9)
Dr. Ravi presented the proposal on behalf of the group. This study hypothesizes that Lenalidomide based maintenance is superior to non-lenalidomide based maintenance. There are 4,834 patients who underwent AutoHCT with maintenance therapy information available from 2008 - 2016. The audience had questions regarding the information available of specific drugs given as consolidation or maintenance therapy, cytogenetics information available, and effect of patients enrolled in clinical trials during this time period.

g. **PROP 1812-07** Impact of Induction Therapy with VRD vs. VCD on Outcomes in Patients with Multiple Myeloma Undergoing Stem Cell Transplantation (Surbhi Sidana/Maxim Norkin/Shaji K. Kumar/ Sergio Giralt) (Attachment 10)

Dr. Sidana presented the proposal on behalf of the group. This study hypothesizes that patients with newly diagnosed multiple myeloma receiving bortezomib- cyclophosphamide-dexemethasone (VCD) based chemotherapy prior to AutoHCT have similar progression free survival compared to those receiving bortezomib-lenalidomide- dexamethasone (VRD) based induction, after adjusting for other prognostic factors. There are 796 patients who received VRD and 291 patients who received VCD prior to AutoHCT for MM from 2010 - 2016. The audience had question regarding dose of chemotherapy given prior to transplant, results from trials that shown VRD is better than VCD, possibility of limiting population to patients with renal deficiencies, how many patients received tandem transplants, and information about maintenance and consolidation therapy.

The Plasma Cell and Adult Solid Tumors working committee meeting came to a close at 2:00 PM. The committee leadership met with members of the committee and answered questions. Each participant in the meeting had the opportunity to rate each proposal using paper ballots. Based on the voting results, the following studies will move forward as the committee's research portfolio for the upcoming year:

PROP 1812-07 Impact of Induction Therapy with VRD vs. VCD on Outcomes in Patients with Multiple Myeloma Undergoing Stem Cell Transplantation (Surbhi Sidana/Maxim Norkin/Shaji K. Kumar/ Sergio Giralt)

PROP 1811-108 Maintenance therapy after second autologous hematopoietic cell transplantation for Multiple Myeloma (Oren Pasvolsky /Moshe Yeshurun/Uri Rozovski/Liat Shargian-Alon)

PROP 1811-168 Second autologous stem cell transplantation as salvage therapy for relapsed or refractory AL amyloidosis (Carlyn Tan/Henry Fung)

Not for publication or presentation

Working Committee Overview Plan for 2019 - 2020

Study number and title	Current status	Goal with date	Total hours to complete	Total hours to goal	Hours allocated to 6/30/2019	Hours allocated 7/1/2019-6/30/2020	Total Hours allocated
MM17-01: Hematopoietic cell transplantation for primary plasma cell leukemia in the era of novel agents	Manuscript Prep	Submission - May 2019	70	**70**	70	10	**80**
MM17-02: The Impact of Bortezomib Based Induction Therapy vs No Induction Therapy on Outcomes for Light Chain Amyloidosis	Deferred	Manuscript prep - April 2020	280	**210**	0	210	**210**
MM18-01: Racial Discrepancy in Clinical Outcomes of Multiple Myeloma Patients with and without t(11;14) Genetic Abnormality	Manuscript Prep	Submission – June 2019	50	**50**	50	10	**60**
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	Protocol Development	Submission - June 2020	310	**310**	240	70	**310**
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:	Datafile prep	Submission - May 2019	160	**160**	90	70	**160**

progression-free and overall survival in a case match analysis							
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	Datafile prep	Published - Jan 2020	40	**40**	40	10	**50**
MM19-01: Impact of Induction Therapy with VRD vs. VCD on Outcomes in Patients with Multiple Myeloma Undergoing Stem Cell Transplantation	Protocol pending	Analysis - March 2020	330	**200**	0	200	**200**
MM19-02: Maintenance therapy after second autologous hematopoietic cell transplantation for Multiple Myeloma	Protocol pending	Analysis - May 20	330	**200**	0	200	**200**
MM19-03: Second autologous stem cell transplantation as salvage therapy for relapsed or refractory AL amyloidosis	Protocol pending	Datafile prep - June 2020	290	**100**	0	100	**100**

Oversight Assignments for Working Committee Leadership (March 2019)

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
Nina Shah:	**MM17-02:** Bortezomib induction therapy for light chain amyloidosis **MM18-02:** Prognostic score system **MM18-03:** Compare young vs. old MM patients
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