Not for publication or presentation

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A G E N D A
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**
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Statistician:	**Omar Dávila Alvelo, MS, CIBMTR Statistical Center, Milwaukee, WI; Telephone: 414-805-0686; E-mail: odavila@mcw.edu**

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1. **Introduction**
   a. Minutes and Overview Plan from February 2018 meeting (Attachment 1)
   b. Introduction of incoming co-Chair: Muzaffar Qazilbash, MD (2019 - 2024)
   c. Outgoing Chair: Tomer Mark, MD

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

3. **Presentations, published or submitted papers**
   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)

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) **Submitted**

b. **MM16-01a** Staging Systems for Newly Diagnosed Myeloma Patients Undergoing Autologous Hematopoietic Cell Transplantation: The Revised International Staging System Shows the Most Differentiation between Groups. (E Scott/S Kumar). **Published**

c. **MM16-01b** Revised-International Staging System (R-ISS) is Predictive and Prognostic for Early Relapse (<24 months) after Autologous Transplantation for Newly Diagnosed Multiple Myeloma (MM) (S Kumar/E Scott). **Published**

d. **MM16-02** Outcomes of Haploidentical Transplantation in Patients with Relapsed Multiple Myeloma: An EBMT/CIBMTR Report (F Sahebi / L Garderet / A Kanate/N Shah/Q Bashir/S Ciurea) **Published**

e. **MM17-01** Hematopoietic cell transplantation for primary plasma cell leukemia in the era of novel agents (S Girnius/S Patel/L Bachegowda/B Dhakal) **Analysis**

f. **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) **Delay owing to IT**

g. **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) **Manuscript preparation**

h. **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) **Protocol Development**

i. **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) **Datafile Preparation**

j. **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) **Analysis**

5. Future/proposed studies

Solid Tumors:

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

Amyloidosis:

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

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)

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)

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)

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)

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)

Dropped proposed studies

a. **PROP 1809-04** Outcomes of stem cell transplant for HIV positive patients with Plasma cell dyscrasias PCD (multiple myeloma, plasma cell leukemia) as compared to PCD patients without HIV. *Dropped due to small numbers and feasibility.*
b. **PROP 1810-09** Post-transplant outcomes in patients with gain of 1q21 abnormality in a risk stratification analysis. *Dropped due to overlap with recent publication. Post-Transplant Outcomes in High-Risk Compared with Non-High-Risk Multiple Myeloma: A CIBMTR Analysis. Biol Blood Marrow Transplant. 2016 Oct;22(10):1893-1899.*
c. **PROP 1811-64** Incidence of Second Primary Malignancies in Patients with Light Chain Amyloidosis who Undergo Autologous Hematopoietic Cell Transplantation. *Dropped due to small numbers and feasibility.*
d. **PROP 1811-99** Conditional Survival after Upfront Autologous Stem Cell Transplantation for Plasma Cell Disorders. *Dropped due to low scientific impact among submitted proposals*.
e. **PROP 1811-188** Assessing the Disparity between Enrolled Multiple Myeloma Patients Transplanted on Randomized Clinical Trial and the Real World Data. *Dropped due to low scientific impact among submitted proposals.*
f. **PROP 1811-98** KRD vs. VRD induction in transplant eligible multiple myeloma patients undergoing autologous stem cell transplantation. *Dropped due to small numbers and feasibility.*
g. **PROP 1811-62** Impact of pre-transplant cardiovascular disease on autologous transplant outcomes in patients with multiple myeloma > age 60. *Dropped due to small numbers and feasibility.*
h. **PROP 1811-104** Stem Cell Mobilization after Extensive Prior Therapy in Multiple Myeloma. *Dropped due to low scientific impact and inability to complete the proposed objectives with CIBMTR data.*
i. **PROP 1811-46** Tandem versus single autologous stem cell transplantation in high risk multiple myeloma patients. *Dropped due to low scientific impact among submitted proposals.*
j. **PROP 1811-79** Impact of Allogeneic Transplantation in High-Risk Multiple Myeloma as Compared with Autologous Transplantation. *Dropped due to low scientific impact among submitted proposals.*
k. **PROP 1811-103** Outcomes Following Delayed Autologous Stem Cell Transplant for Multiple Myeloma. *Dropped due to low scientific impact among submitted proposals and inability to complete the proposed objectives with CIBMTR data*
l. **PROP 1811-120** Early versus Late Autologous Stem Cell Transplant in High Risk Multiple Myeloma. *Dropped due to low scientific impact among submitted proposals and inability to complete the proposed objectives with CIBMTR data*.

m. **PROP 1811-138** Outcomes of upfront versus delayed melphalan conditioned autologous transplant in patients with multiple myeloma. *Dropped due to low scientific impact among submitted proposals and inability to complete the proposed objectives with CIBMTR data*.
n. **PROP 1811-102** Outcomes after ASCT in Patients with High Risk Myeloma Defined by Novel Parameters (gain 1q, double hit or triple hit multiple myeloma). *Dropped due to overlap with recent publication. Post-Transplant Outcomes in High-Risk Compared with Non-High-Risk Multiple Myeloma: A CIBMTR Analysis. Biol Blood Marrow Transplant. 2016 Oct;22(10):1893-1899.*
o. **PROP 1811-93** Outcomes of autologous vs. allogeneic hematopoietic stem cell transplantation (HCT) for Waldenstrom's macroglobulinemia. *Dropped due to overlap with recent publication. Allogeneic Transplantation for Relapsed Waldenstrom Macroglobulinemia and Lymphoplasmacytic Lymphoma. Biol Blood Marrow Transplant. 2017 Jan;23(1):60-66.*

MINUTES AND OVERVIEW PLAN
CIBMTR WORKING COMMITTEE FOR PLASMA CELL DISORDERS AND ADULT SOLID TUMORS
Salt Lake City, Utah
Wednesday, February 21, 2018, 2:45 – 4:45 pm

Co-Chair:	**Cristina Gasparetto, MD, Duke University Medical Center, Durham, NC; Telephone: 919-668-1017; E-mail: cristina.gasparetto@duke.edu**
Co-Chair:	**Yago Nieto, MD, MD Anderson Cancer Center, Houston, TX; Telephone: 713-792-2466; E-mail: ynieto@mdanderson.org**
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**
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 2:45 PM on Wednesday, February 21st, by Dr. D'Souza. Dr. D'Souza introduced the committee leadership and welcomed the committee participants. Drs. D'Souza acknowledged Drs. Gasparetto and Nieto for all of their efforts during the past years as Co-Chairs and were presented with a gift. Dr. D'Souza introduced Dr. Nina Shah as the newly appointed Chair for the Working Committee starting March 1, 2018. Dr. D'Souza introduced the committee goal and expectations to the audience and reviewed previous meeting presentations, published/submitted papers in 2017. Dr. Hari discussed important details about how the committee works and discussed future priorities of the committee: eg. Revision of plasma cell disorders forms to include new drugs, R-ISS, MRD, imaging (PET) and plan for forms revision for the plasma cell disorders. 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 2017 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 2017, 73,201 plasma cell disorder cases were reported at the registration level and 13,103 cases at the research level to the CIBMTR for (first) autologous transplant. For first allogeneic transplants, these numbers are 4,842 cases and 1,956 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. P***oster presentation at GU-ASCO 2018.***

b. **MM14-02** A Mahindra, C Gasparetto, M Fei, A Krishnan, J Huang, M Tomer, P Hari, Y Nieto, A D'Souza. Autologous hematopoietic cell transplantation in patients with renal insufficiency. ***Bone Marrow Transplantation. 2017 Sep 18; 52 (12): 1616–1622.***

c. **MM14-03** S Kumar, A Dispenzieri, R Fraser, J Huang, C Gasparetto, A Krishnan, T Mark, Y Nieto, A D'Souza, P Hari. Trends in survival outcomes among patients relapsing early after autologous stem cell transplantation for multiple myeloma. ***Leukemia. doi:10.1038/leu.2017.331. Nov 2017.***

d. **MM15-02** M Sharma, A Krishnan, B Bruno, N Tank et. al. Post-relapse Survival Rates after Tandem Auto-HSCT vs. Auto/Allo-HSCT in Multiple Myeloma. ***Biology of Blood and Marrow Transplantation. doi: 10.1016/j.bbmt.2017.10.024, Oct 2017.***

e. **MM15-03** J Schriber, P Hari, KW Ahn, M Fei, L Costa, M Kharfan-Dabaja, M Angel-Diaz, RP Gale, S Ganguly, S Girnius, S Hashmi, A Pawarode, D Vesole, P Wiernik, BM Wirk, D Marks, T Nishihori, R Olsson, S Usmani, T Mark, Y Nieto, A D'Souza. Significant Differences in Stem Cell Transplant Utilization Rates (STUR) of Autologous Hematopoietic Cell Transplant (AHCT) in Multiple Myeloma (MM) Based on Ethnicity without Differences in Efficacy: a CIBMTR Report. ***Cancer. Aug 15; 123 (16): 3141-3149.***

f. **MM16-01a** E Scott, P Hari, S Kumar, Y Nieto, T Mark, S Kumar, C Gasparetto, A D'Souza. Validation of the R-ISS and IMWG-2014 classification in multiple myeloma patients undergoing high dose melphalan autologous stem cell transplant registered with the CIBMTR. ***Poster presentations at the American Society of Hematology, Dec 2017.***

g. **MM16-01b** S Kumar, A D'Souza, E Scott, C Gasparetto, S Kumar, T Mark, Y Nieto, P Hari. Revised-International staging system is independently predictive and prognostic for early relapse after upfront autologous hematopoietic cell transplantation (AHCT) for Newly Diagnosed Multiple Myeloma. ***Poster presentations at the American Society of Hematology, Dec 2017.***

h. **MM16-02** A Kanate, N Shah, Q Bashir, S Ciurea. Alternative donor allogeneic hematopoietic transplantation strategies for multiple myeloma in adult patients: Haploidentical related donor transplantation. EBMT collaborative study. ***Accepted for oral presentation at EBMT-meeting 2018.***

i. **SC16-03** A D'Souza, J Huang, M Fei, P Hari. Trends in Pre- and Post-Transplant Therapies Prior to First Autologous Hematopoietic Cell Transplantation Among Patients with Multiple Myeloma in the United States, 2004-2014. ***Leukemia. 2017 Sep; 31 (9):1998-2000.***

4. Studies in progress (Attachment 3)

Dr. D'Souza introduced the following studies in progress and goal by July 2018.

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 goal of the study is to work on data file preparation after 2017 BMT Tandem meeting. Manuscript is underway. The goal of the study is to submit manuscript by April 2018.

b. **MM16-01a** Validation of the R-ISS and IMWG-2014 classification in multiple myeloma patients undergoing high dose melphalan autologous stem cell transplant registered with the CIBMTR (E Scott/S Kumar). This study assess the IMWG-2014 and the newly recommended R-ISS based outcome from CIBMTR database and validate the prognostic significance (response rate, progression free and overall survival) in patients that received an autologous hematopoietic cell transplant for multiple myeloma registered with the CIBMTR. Manuscript was submitted to JCO in early February.

c. **MM16-01b** Revised-International staging system is independently predictive and prognostic for early relapse after upfront autologous hematopoietic cell transplantation (AHCT) for Newly Diagnosed Multiple Myeloma (S Kumar/E Scott). This study will assess the ability of R-ISS at diagnosis to predict for early relapse and its independent prognostic effect on post relapse survival after an early relapse. Manuscript is underway. The goal of the study is to submit manuscript by April 2018.

d. **MM16-02** Alternative donor allogeneic hematopoietic transplantation strategies for multiple myeloma in adult patients: Haploidentical related donor transplantation. EBMT collaborative study (A Kanate/N Shah/Q Bashir/S Ciurea). This is a collaborative study with EBMT that will describe the post-transplantation outcomes in patients with MM undergoing haploidentical allo-HCT. The goal of the study is to submit manuscript by July 2018.

e. **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 . Study is in supplemental data collection of key variables to be analyzed from the top 15 centers of the population. Analysis will be done once the information is gathered. We anticipate completing supplemental data collection by March 2018 and finalizing data file preparation by July 2018. The goal of the study is to finalize analysis and manuscript preparation by July 2019.

f. **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. Protocol development is in progress. We anticipate finalizing protocol by July 2018 and start working on data file preparation. The goal of the study is to finalize analysis and manuscript preparation by July 2019.

Future/proposed studies

5. This year, we received 19 proposals, 11 of which were invited to present at the meeting (including 2 merged proposals with similar research objectives). After the introduction of the voting process, the following new proposals were presented and voted on. Dr. Kumar introduced the first three proposals.

Multiple Myeloma:

a. **PROP 1709-02** Prognostic Scoring System of Outcomes in Patients Undergoing Autologous Stem Cell Transplantation for Multiple Myeloma (Dhakal Binod/Chhabra Saurabh) (Attachment 4)
Dr. Hari presented the proposal on behalf of the team. The purpose of the study is to do a prognostic score for Multiple Myeloma patients using the patient's information prior to transplant rather than at diagnosis, as all of the other prognostics scores are base from. There are 4,705 patients who underwent peripheral blood and melphalan based first Auto HCT for Multiple Myeloma from 2008-2016. There were some concerns regarding the time period in which the study is considering (2008-2016) since there where big changes in the practice during that period (example: FISH, novel agents, maintenance therapy, etc.). The suggestion was to use a period in which the modern treatment can be captured (e.g. ≥ 2010). The issue with this suggestion is that there will not be enough events if we limit the population to the most recent years.

b. **PROP 1710-23** Racial Discrepancy in Clinical Outcomes of Multiple Myeloma Patients Harboring t(11;14) Genetic Abnormality (Dharshan Sivaraj/Amrita Krishnan/Cristina Gasparetto) (Attachment 5)
Dr. Sivaraj presented the proposal on behalf of the group. The purpose of this study is to examine patient characteristics and survival outcomes between African American (AA) and non-African American (nAA) with t(11;14). There are 118 AA vs. 302 nAA adult patients with t(11;14) who underwent first auto transplant from 2005-2016. There was some concern about why limit only to AA and not explore other races. It was explained that CIBMTR has looked at different races but there were too few patients in the other races groups.

c. **PROP 1711-20** 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 (Pashna Munshi/ Artur Jurczyszyn/ Jan Maciej Zaucha/ David Vesole) (Attachment 6)
Dr. Munshi presented the proposal on behalf of the group. The purpose of this study is to look at outcomes in young and very young MM patients compared to older patients undergoing first Auto or Allogeneic HCT in the era of modern agents. There are 6,797 patients in the registry from 2005-2016 divided between 5 age groups (20-39 vs. 40-49 vs. 50-59 vs. 60-69 vs. ≥70), 247 receiving allogeneic transplant and 6,550 receiving autologous transplant. There were no questions from the audience for this proposal.

Dr. Tomer Mark introduced the following 3 proposals

d. **PROP 1711-37** Outcomes of autologous stem cell transplantation in patients with primary refractory multiple myeloma (Rajshekhar Chakraborty/ Jack Khouri/ Hien Liu/ Navneet Majhail) (Attachment 7)
Dr. Chakraborty presented the proposal on behalf of the group. The purpose of this study is to assess post-transplant response on patients with <PR prior to HCT. There are 349 patients with < PR who underwent first upfront PB Auto HCT and received novel agent from 2005-2016. Comments were received about how many lines of induction were given, how many patients received second HCT, and patients who were unable to mobilize. There was also some concern about overlap between other similar study done in the CIBMTR who looks at this population from 1995-2010. It was suggested to try to reduce the overlap between both studies as much as possible

e. **PROP 1711-90** Prior solid malignancy as risk factor for development of Secondary Primary Malignancy following Autologous Stem Cell Transplantation and Maintenance therapy in Multiple Myeloma

(Hemant Murthy/ Johnathan Kaufman) (Attachment 8)
Dr. Murthy presented the proposal on behalf of the group. The purpose of this study is to determine if the presence of prior solid tumor malignancy increase the risk of developing secondary primary malignancy. There are 3,957 adult patients who underwent PB auto HCT for MM from 2008-2015 divided in the following groups No tumor/no maintenance vs. no tumor/maintenance vs. Tumor/no maintenance vs. tumor/maintenance (2,498 vs. 1,142 vs. 224 vs. 93 respectively).Comments were received about other possible risk factors other than prior solid malignancy, the importance of Lenalidomide and how it was administered, and how much data is available for prior malignancy.

f. **PROP 1711-149** Prognostic Impact of Duration of Induction Therapy before Autologous Stem Cell Transplant in Multiple Myeloma (Surbhi Sidana/ Shaji Kumar) (Attachment 9)
Dr. Sidana presented the proposal on behalf of the group. The purpose of this study is to evaluate if longer duration of induction therapy (≥ 6 months) before HCT is associated with better outcomes compared to shorter duration (< 6 months) on patients with newly diagnosed MM. There are 1,893 vs. 1,326 adult patients who underwent first upfront Auto HCT with novel agents between 2005-2016 with <6 months of induction vs. ≥6 months of induction. Comments were received about the availability of the dates for each cycle, issue with the patients who relapsed and got re-induced who may be a source of biased on the study, and the way the groups were divided suggesting shorter period of time (2 vs. 4 vs. 6 vs. >6 months) There was some concern that maybe a retrospective study is not the best option to analyze this topic and should be better done in a randomized trial.

Dr. Gasparetto introduced the following 4 proposals

g. **PROP 1711-164** Characteristics of patients with multiple myeloma who are exceptional responders to high dose therapy and autologous peripheral blood stem cell transplantation. (Natalie Callander/ Aric Hall/ Zhubin Gahvari) (Attachment 10)
Dr. Gahvari presented the proposal in behalf of the group. The purpose of this study is to analyze disease and patient specific characteristics that are associated with exceptional response on patients with MM who underwent Auto HCT. There are 342 adult patients who underwent Auto HCT for MM with PFS ≥ 7 years from 1998-2012. Comments were received about similar study that has been done by the International Myeloma Working Group, available data on time to next treatment, possible cofounding on patients with MGUS, and possible biological explanation compare to efficacy of treatment.

h. **PROP 1711-112/1711-139** Melphalan dosing in the setting of advanced age and comorbidity (Trent Peng Wang/ Lohith Gowda/ Amer Beitinjaneh/ Qaiser Bashir/ Koen van Besien) (Attachment 11)
Dr. Wang presented the proposal in behalf of the group. The purpose of this study is to evaluate the safety and efficacy outcomes of melphalan 140 mg/m^2 vs. 200 mg/m^2 between younger (< 65) and older patients (≥ 65) with MM. There are 4,119 vs 1,386 adult patients who underwent first PB auto HCT for MM with < 65 years vs. ≥ 65 years from 2005-2016. There were no questions from the audience for this proposal.

Amyloidosis:

i. **PROP 1711-34** Outcomes of Autologous Hematopoietic Cell Transplantation for Immunoglobulin Light Chain Amyloidosis with Coexistent Multiple Myeloma (Baldeep Wirk) (Attachment 12)
Dr. Wirk presented the proposal. The purpose of this study is to evaluate the outcomes of Auto HCT for patients with AL amyloidosis with coexistent MM. There are 323 vs. 135 adult patients who underwent

auto HCT from 2005-2015 with < 10% plasma cell in BM vs. ≥ 10% plasma cell in BM. Comments were received about heterogeneity on practice for induction therapy by institutions and how the study is going to account for that.

j. **PROP 1711-150** Outcomes with Second Autologous Transplant for Patients with Light Chain Amyloidosis (Surbhi Sidana/ Shaji Kumar) (Attachment 13)
Dr. Sidana presented the proposal in behalf of the group. The purpose of this study is to evaluate TRM in patients with AL amyloidosis undergoing a second autologous HCT at the time of relapse. There are 96 adult patients who underwent second auto HCT for relapsed amyloidosis from 2001-2016. Comments were received about making sure to exclude patients who received tandem transplant, and to identify patients with amyloidosis and MM since these patients might have relapsed from MM and not for amyloidosis.
The working committee meeting ended at 4:30 PM. The committee leadership met with members of the committee and answer questions.
A total of 1,050 hours of MS biostatistician time was allocated to our WC for the 2018-2019 academic year. Thus, we will be able to accept 3-4 new studies.

Working Committee Overview Plan for 2018 - 2019

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). Study is in manuscript preparation. The goal is to submit by March 2018. Hours to completion: 50 hours. 50 statistical hours were allocated for submission, 0 hours corresponding to fiscal year 2018-2019.

MM16-01a: Validation of the R-ISS and IMWG-2014 classification in multiple myeloma patients undergoing high dose melphalan autologous stem cell transplant registered with the CIBMTR (E Scott/S Kumar). Study was submitted and we plan to publish paper by June 2018. Hours to completion: 10 hours. 10 statistical hours were allocated for submission, 0 hours corresponding to fiscal year 2018-2019.

MM16-01b: Revised-International staging system is independently predictive and prognostic for early relapse after upfront autologous hematopoietic cell transplantation (AHCT) for Newly Diagnosed Multiple Myeloma (S Kumar/E Scott). Manuscript is underway and we plan to submit paper by April 2018. Hours to completion: 30 hours. 30 statistical hours were allocated for submission, 0 hours corresponding to fiscal year 2018-2019.

MM16-02: Alternative donor allogeneic hematopoietic transplantation strategies for multiple myeloma in adult patients: Haploidentical related donor transplantation. EBMT collaborative study (A Kanate/N Shah/Q Bashir/S Ciurea). The goal of the study is to submit paper by July 2018. Hours to completion: 70 hours. 70 statistical hours were allocated for submission, 0 hours corresponding to fiscal year 2018-2019.

MM17-01: Hematopoietic Cell Transplantation for Primary Plasma Cell Leukemia in the Era of Novel Agents (Saulius Girnius/Sagar Patel/Lohith Bachegowda/Binod Dhakal) The goal of the study is to have data file ready for analysis by July 2018. We anticipate to finalize analysis and manuscript preparation by June 2019. Hours to completion: 250 hours. 250 statistical hours were allocated, 200 hours corresponding to fiscal year 2018-2019.

MM17-02: The impact of bortezomib-based induction therapy vs no induction therapy on outcomes for light chain amyloidosis (Robert Cornell/ Luciano Costa/ Stacey Goodman) The goal of the study is to finalize protocol and move to data file preparation by July 2018. We anticipate to finalize analysis and manuscript preparation by

June 2019. Hours to completion: 280 hours. 280 statistical hours were allocated, 250 hours corresponding to fiscal year 2018-2019.

MM18-01: Racial Discrepancy in Clinical Outcomes of Multiple Myeloma Patients Harboring t(11;14) Genetic Abnormality (Dharshan Sivaraj/Amrita Krishnan/Cristina Gasparetto) Protocol development is underway. The goal of the study is to complete analysis by July 2018 and submit an abstract to ASH. Hours to completion: 310 hours. 240 statistical hours were allocated to finalize analysis by July 2018 and 70 hours for submission by July 2019, 70 hours corresponding to fiscal year 2018-2019.

MM18-02: Prognostic Scoring System of Outcomes in Patients Undergoing Autologous Stem Cell Transplantation for Multiple Myeloma (Dhakal Binod/Chhabra Saurabh/Natalie Callander/ Aric Hall/ Zhubin Gahvari). We anticipate developing the study protocol after July 2018. Hours to completion: 310. 240 hours were allocated to finalize data file preparation and analysis by June 2019, all hours corresponding to fiscal year 2018-2019.

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 (Pashna Munshi/ Artur Jurczyszyn/ Jan Maciej Zaucha/ David Vesole) We anticipate developing the study protocol after July 2018. Hours to completion: 310. 240 hours were allocated to finalize data file preparation and analysis by June 2019, all hours corresponding to fiscal year 2018-2019.

Oversight Assignments for Working Committee Leadership (March 2017)

Tomer Mark:	**MM14-01:** High dose chemotherapy and auto HCT for germ cell tumors
	MM16-01a: Validation of R-ISS in MM population
	MM16-01b: R-ISS in early relapsers
Shaji Kumar:	**MM16-02:** Haplo HCT for MM
	MM17-01: HCT for primary plasma cell leukemia
	MM17-02: Bortezomib induction therapy for light chain amyloidosis
Nina Shah:	**MM18-01:** Racial discrepancy in MM patients with t(11;14)
	MM18-02: Prognostic score system
	MM18-03: Compare young vs. old MM patients

Accrual Summary for the Plasma Cell Disorders and Adult Solid Tumor Working Committee

Recipients of first autologous transplant for **Plasma Cell Disorders** registered to the CIBMTR, 1990-2018

Characteristics	TED	CRF
Number of patients	80342	14725
Number of centers	465	308
Age at transplant, median (range), years	60 (18-85)	59 (20-83)
Disease		
Multiple Myeloma	75726 (94)	13047 (89)
Amyloidosis	2460 (3)	1299 (9)
Plasma cell leukemia	689 (<1)	146 (<1)
Solitary plasmacytoma	348 (<1)	48 (<1)
Waldenstrom macroglobulinemia[a]	305 (<1)	43 (<1)
POEMS Syndrome	413 (<1)	60 (<1)
Multiple Plasmacytomas	48 (<1)	4 (<1)
LCDD	267 (<1)	67 (<1)
Others[b]	86 (<1)	11 (<1)
Graft type		
BM	366 (<1)	82 (<1)
PB	78549 (98)	14498 (98)
CB	10 (<1)	2 (<1)
Missing	1417 (2)	143 (<1)
Year of transplant		
1990-1991	207 (<1)	44 (<1)
1992-1993	322 (<1)	70 (<1)
1994-1995	630 (<1)	243 (2)
1996-1997	1326 (2)	475 (3)
1998-1999	2335 (3)	697 (5)
2000-2001	3504 (4)	930 (6)
2002-2003	4632 (6)	850 (6)
2004-2005	4932 (6)	1491 (10)
2006-2007	5225 (7)	1387 (9)
2008-2009	6317 (8)	1526 (10)
2010-2011	9967 (12)	677 (5)
2012-2013	10859 (14)	1186 (8)
2014-2015	11686 (15)	1894 (13)
2016-2017	13894 (17)	2016 (14)
2018[c]	4506 (6)	1239 (8)
Median follow-up of survivors (range), months	49 (<1-297)	64 (<1-248)

[a] Small lymphoplasmacytic lymphoma cases were not included.

[b] Other include: other plasmacytoma (n=36), MGUS (n=17); plasmablastic (n=14), Scleromyexdema (n=13), EPS (n=2), plasma cell dyscrasia (n=10), plasmacytosis (n=5),

[c] Cases continue to be reported.

Abbreviations: TED=Transplant essential data, CRF=Comprehensive report form.

Recipients of first allogeneic transplant for **Plasma Cell Disorders** registered to the CIBMTR, 1990-2018

Characteristics	TED	CRF
Number of patients	**4908**	**2026**
Number of centers	334	262
Age at transplant, median (range), years	50 (1-78)	50 (10-79)
Disease		
Multiple Myeloma	4441 (90)	1814 (90)
Amyloidosis	30 (<1)	7 (<1)
Plasma cell leukemia	226 (5)	115 (6)
Solitary plasmacytoma	40 (<1)	5 (<1)
Waldenstrom macroglobulinemia[a]	112 (2)	70 (3)
POEMS Syndrome	1 (<1)	0
Multiple Plasmacytomas	1 (<1)	1 (<1)
Others[b]	57 (1)	14 (<1)
Graft type		
BM	1160 (24)	622 (31)
PB	3629 (74)	1361 (67)
CB	26 (<1)	39 (2)
Missing	93 (2)	4 (<1)
Donor		
HLA-identical sibling	3196 (65)	1289 (64)
Monozygotic twin	138 (3)	131 (6)
Other relative	318 (6)	89 (4)
Unrelated donor	1165 (24)	497 (25)
Missing	91 (2)	20 (<1)
Prior Auto transplant		
No	2252 (46)	1178 (58)
Yes	2656 (54)	848 (42)
Year of transplant		
1990-1991	71 (1)	95 (5)
1992-1993	171 (3)	141 (7)
1994-1995	282 (6)	146 (7)
1996-1997	339 (7)	144 (7)
1998-1999	311 (6)	128 (6)
2000-2001	460 (9)	248 (12)
2002-2003	567 (12)	208 (10)
2004-2005	458 (9)	255 (13)
2006-2007	345 (7)	204 (10)
2008-2009	404 (8)	134 (7)
2010-2011	431 (9)	59 (3)
2012-2013	387 (8)	49 (2)
2014-2015	359 (7)	86 (4)
2016-2017	287 (6)	85 (4)
2018[c]	36 (<1)	44 (2)
Median follow-up of survivors (range), months[c]	60 (<1-323)	108 (<1-264)

[a] Small lymphoplasmacytic lymphoma cases were not included.

[b] Other include: LCDD (n=1), Other plasmacytoma (n=9), not specified (n=61).

[c] Cases continue to be reported.

Abbreviations: TED=Transplant essential data, CRF=Comprehensive report form.

First adult autologous transplant for **Sarcoma** registered to the CIBMTR, 1990-2018

	Bone Sarcoma		Other Sarcoma	
	TED	CRF	TED	CRF
Characteristics	N (%)	N (%)	N (%)	N (%)
Number of patients	**496**	**150**	**219**	**82**
Number of centers	161	76	103	49
Age at transplant, years, median (range)	23 (18-61)	23 (18-59)	28 (18-64)	28 (18-61)
Disease				
Bone sarcoma (exc. Ewing)	124 (25)	35 (23)	0	0
Ewing sarcoma	372 (75)	115 (77)	0	0
Soft tissue sarcoma	0	0	168 (77)	68 (83)
Sarcoma unspecified	0	0	51 (23)	14 (17)
Gender				
Male	343 (69)	98 (65)	137 (63)	38 (46)
Female	153 (31)	52 (35)	82 (37)	44 (54)
Graft type				
BM	37 (7)	17 (11)	30 (14)	10 (12)
PB	445 (90)	133 (89)	177 (81)	72 (88)
Missing	14 (3)	0	12 (5)	0
Year of transplant				
1990-1991	18 (4)	8 (5)	23 (11)	6 (7)
1992-1993	28 (6)	14 (9)	27 (12)	4 (5)
1994-1995	22 (4)	12 (8)	23 (11)	8 (10)
1996-1997	28 (6)	33 (22)	20 (9)	20 (24)
1998-1999	50 (10)	37 (25)	28 (13)	21 (26)
2000-2001	57 (11)	15 (10)	17 (8)	9 (11)
2002-2003	52 (10)	2 (1)	28 (13)	3 (4)
2004-2005	44 (9)	3 (2)	9 (4)	3 (4)
2006-2007	34 (7)	12 (8)	13 (6)	2 (2)
2008-2009	47 (9)	10 (7)	6 (3)	3 (4)
2010-2011	39 (8)	1 (<1)	11 (5)	0
2012-2013	31 (6)	3 (2)	4 (2)	0
2014-2015	25 (5)	0	3 (1)	2 (2)
2016-2017	17 (3)	0	6 (3)	1 (1)
2018 [a]	4 (<1)	0	1 (<1)	0
Follow-up of survivors, months, median (range)	63 (<1-314)	107 (3-193)	65 (<1-181)	121 (15-145)

[a] Cases continue to be reported in this interval.

Abbreviations: TED=Transplant essential data, CRF=Comprehensive report form.

First adult autologous transplant for **Neuroblastoma, Medulloblastoma & Wilm's Tumor** registered to the CIBMTR, 1990-2018

	Neuroblastoma		Medulloblastoma		Wilm's Tumor
	TED	CRF	TED	CRF	TED
Characteristics	N (%)	N (%)	N (%)	N (%)	N (%)
Number of patients	**126**	**27**	**173**	**29**	**35**
Number of centers	75	24	87	24	31
Age at transplant, years, median (range)	24 (18-62)	22 (18-39)	27 (18-66)	28 (19-49)	25 (18-53)
Disease					
Neuroblastoma	126	27	0	0	0
Medulloblastoma	0	0	173	29	0
Wilm's Tumor	0	0	0	0	35
Gender					
Male	70 (56)	14 (52)	111 (64)	17 (59)	20 (57)
Female	56 (44)	13 (48)	62 (36)	12 (41)	15 (43)
Graft type					
BM	8 (6)	3 (11)	11 (6)	3 (10)	4 (11)
PB	115 (91)	23 (85)	159 (92)	26 (90)	30 (86)
Missing	3 (2)	1 (4)	3 (2)	0	1 (3)
Year of transplant					
1990-1991	7 (6)	2 (7)	0	1 (3)	1 (3)
1992-1993	9 (7)	2 (7)	1 (<1)	1 (3)	1 (3)
1994-1995	5 (4)	4 (15)	2 (1)	1 (3)	2 (6)
1996-1997	3 (2)	5 (19)	6 (3)	1 (3)	2 (6)
1998-1999	7 (6)	4 (15)	13 (8)	8 (28)	1 (3)
2000-2001	4 (3)	2 (7)	16 (9)	1 (3)	4 (11)
2002-2003	6 (5)	1 (4)	13 (8)	1 (3)	3 (9)
2004-2005	10 (8)	2 (7)	22 (13)	3 (10)	5 (14)
2006-2007	6 (5)	1 (4)	9 (5)	5 (17)	3 (9)
2008-2009	12 (10)	0	20 (12)	5 (17)	1 (3)
2010-2011	15 (12)	0	20 (12)	0	4 (11)
2012-2013	14 (11)	0	11 (6)	2 (7)	2 (6)
2014-2015	16 (13)	1 (4)	19 (11)	0	4 (11)
2016-2017	9 (7)	2 (7)	12 (7)	0	1 (3)
2018[a]	3 (2)	1 (4)	9 (5)	0	1 (3)
Follow-up of survivors, months, median (range)	60 (1-183)	86 (9-86)	60 (<1-315)	95 (1-232)	44 (<1-241)

[a] Cases continue to be reported in this interval.

Abbreviations: TED=Transplant essential data, CRF=Comprehensive report form.

First adult autologous transplant for **Ovarian/Testicular Cancer & Germ Cell Tumor** registered to the CIBMTR, 1990-2018

	Ovarian/Testicular cancer		Germ Cell Tumor	
	TED	CRF	TED	CRF
Characteristics	N (%)	N (%)	N (%)	N (%)
Number of patients	**2968**	**1145**	**1022**	**119**
Number of centers	262	170	205	70
Age at transplant, years, median (range)	37 (18-73)	43 (18-76)	31 (18-69)	31 (19-58)
Disease				
Ovarian (epithelial)	1084 (37)	605 (53)	0	0
Testicular	1884 (63)	540 (47)	0	0
Germ cell tumor, extragonadal	0	0	1022	119
Gender				
Male	1888 (64)	538 (47)	890 (87)	98 (82)
Female	1080 (36)	607 (53)	132 (13)	21 (18)
Graft type				
BM	188 (6)	195 (17)	29 (3)	9 (8)
PB	2641 (89)	941 (82)	981 (96)	109 (92)
Missing	139 (5)	9 (<1)	12 (1)	1 (<1)
Year of transplant				
1990-1991	188 (6)	195 (17)	29 (3)	9 (8)
1992-1993	2641 (89)	941 (82)	981 (96)	109 (92)
1994-1995	139 (5)	9 (<1)	12 (1)	1 (<1)
1996-1997	188 (6)	195 (17)	29 (3)	9 (8)
1998-1999	2641 (89)	941 (82)	981 (96)	109 (92)
2000-2001	139 (5)	9 (<1)	12 (1)	1 (<1)
2002-2003	188 (6)	195 (17)	29 (3)	9 (8)
2004-2005	2641 (89)	941 (82)	981 (96)	109 (92)
2006-2007	139 (5)	9 (<1)	12 (1)	1 (<1)
2008-2009	188 (6)	195 (17)	29 (3)	9 (8)
2010-2011	2641 (89)	941 (82)	981 (96)	109 (92)
2012-2013	139 (5)	9 (<1)	12 (1)	1 (<1)
2014-2015	188 (6)	195 (17)	29 (3)	9 (8)
2016-2017	2641 (89)	941 (82)	981 (96)	109 (92)
2018 [a]	139 (5)	9 (<1)	12 (1)	1 (<1)
Follow-up of survivors, months, median (range)	60 (<1-315)	95 (1-232)	44 (<1-241)	54 (2-183)

[a] Cases continue to be reported in this interval.

Abbreviations: TED=Transplant essential data, CRF=Comprehensive report form.

First adult autologous transplant for **Breast Cancer, Lung Cancer & CNS Tumor**[a] registered to the CIBMTR, 1990-2018

	Breast Cancer		Lung Cancer		CNS Tumor	
	TED	CRF	TED	CRF	TED	CRF
Characteristics	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Number of patients	**17012**	**5647**	**87**	**119**	**573**	**105**
Number of centers	276	199	42	26	127	45
Age at transplant, years, median (range)	46 (19-73)	46 (19-72)	50 (21-74)	50 (30-66)	33 (18-69)	34 (18-62)
Disease						
Breast cancer, NOS	14705 (86)	4983 (88)	0	0	0	0
BC, inflammatory	431 (3)	87 (2)	0	0	0	0
BC, non-inflammatory	1876 (11)	577 (10)	0	0	0	0
Lung, small cell	0	0	58 (67)	114 (96)	0	0
Lung, non-small cell	0	0	22 (25)	5 (4)	0	0
Lung, not specified	0	0	7 (8)	0	0	0
CNS tumor, including CNS PNET	0	0	0	0	573	105
Gender						
Male	134 (<1)	27 (<1)	47 (54)	64 (54)	370 (65)	64 (61)
Female	16878 (99)	5620	40 (46)	55 (46)	203 (35)	41 (39)
Graft type						
BM	1802 (11)	820 (15)	7 (8)	15 (13)	43 (8)	21 (20)
PB	13811 (81)	4822 (85)	73 (84)	104 (87)	488 (85)	84 (80)
Missing	1399 (8)	5 (<1)	7 (8)	0	42 (7)	0
Year of transplant						
1990-1991	619 (4)	495 (9)	13 (15)	16 (13)	40 (7)	6 (6)
1992-1993	1852 (11)	930 (16)	8 (9)	30 (25)	37 (6)	7 (7)
1994-1995	3477 (20)	1269 (22)	19 (22)	28 (24)	38 (7)	12 (11)
1996-1997	5373 (32)	1473 (26)	13 (15)	34 (29)	71 (12)	13 (12)
1998-1999	4596 (27)	1273 (23)	16 (18)	11 (9)	81 (14)	17 (16)
2000-2001	755 (4)	181 (3)	11 (13)	0	45 (8)	12 (11)
2002-2003	150 (<1)	19 (<1)	1 (1)	0	33 (6)	4 (4)
2004-2005	78 (<1)	5 (<1)	2 (2)	0	49 (9)	4 (4)
2006-2007	17 (<1)	0	0	0	22 (4)	6 (6)
2008-2009	43 (<1)	2 (<1)	3 (3)	0	27 (5)	17 (16)
2010-2011	39 (<1)	0	0	0	36 (6)	0
2012-2013	13 (<1)	0	0	0	31 (5)	4 (4)
2014-2015	0	0	0	0	32 (6)	2 (2)
2016-2017	0	0	1 (1)	0	19 (3)	1 (<1)
2018[b]	0	0	0	0	12 (2)	0
Follow-up of survivors, months, median (range)	134 (<1-318)	114 (<1-258)	46 (<1-216)	58 (4-193)	56 (<1-263)	84 (2-216)

[a] Includes CNS PNET.

[b] Cases continue to be reported in this interval.

Abbreviations: BC=Breast cancer, CNS=Central nervous system, PNET=Primitive neuroectodermal tumor, TED=Transplant essential data, CRF=Comprehensive report form.

Recipients of first adult allogeneic transplant for **Adult Solid Tumor** registered to the CIBMTR, 1990-2018

	Hepatobiliary		Renal carcinoma/kidney		Ovarian cancer		Breast cancer	
	TED	CRF	TED	CRF	TED	CRF	TED	CRF
Characteristics	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Number of patients	**13**	**12**	**267**	**210**	**15**	**9**	**93**	**89**
Year of transplant								
1990-1991	0	0	0	0	1 (7)	0	2 (2)	2 (2)
1992-1993	0	0	0	0	0	0	2 (2)	3 (3)
1994-1995	0	0	0	0	1 (7)	0	3 (3)	12 (13)
1996-1997	0	2 (17)	1 (<1)	0	0	0	11 (12)	24 (27)
1998-1999	0	2 (17)	19 (7)	2 (<1)	2 (13)	2 (22)	14 (15)	23 (26)
2000-2001	1 (8)	3 (25)	102 (38)	121 (58)	2 (13)	0	22 (24)	12 (13)
2002-2003	6 (46)	3 (25)	114 (43)	55 (26)	4 (27)	2 (22)	17 (18)	5 (6)
2004-2005	3 (23)	2 (17)	19 (7)	21 (10)	2 (13)	5 (56)	13 (14)	7 (8)
2006-2007	3 (23)	0	2 (<1)	5 (2)	0	0	6 (6)	1 (1)
2008-2009	0	0	4 (1)	6 (3)	1 (7)	0	2 (2)	0
2010-2011	0	0	6 (2)	0	1 (7)	0	1 (1)	0
2014-2015	0	0	0	0	1 (7)	0	0	0
2016-2017	0	0	0	0	0	0	0	0
2018	0	0	0	0	0	0	0	0

Characteristics	TED N (%)	CRF N (%)
Other disease	**172**	**79**
Other malignant, unknown	78 (45)	26 (33)
Head and neck	1 (<1)	1 (1)
Lung cancer, small cell	3 (2)	1 (1)
Lung cancer, non-small cell	6 (4)	0
Pancreas	7 (4)	6 (8)
Prostate	8 (5)	2 (3)
Testis	6 (3)	6 (8)
Cervical	0	1 (1)
Sarcoma unspecified	10 (6)	3 (4)
Bone sarcoma (exc. Ewing)	9 (5)	6 (8)
CNS tumors	1 (<1)	4 (5)

(continued on next column)

	TED N (%)	CRF N (%)
(continued)		
Wilm tumor	1 (<1)	1 (1)
Ewing sarcoma	18 (11)	14 (18)
Germ cell tumor	7 (5)	3 (4)
Medulloblastoma	2 (<1)	1 (1)
PNET	0	1 (1)
Gastric malignancy	1 (<1)	0
Thymoma	1 (<1)	1 (1)
Rhabdomyasarcoma	9 (5)	2 (3)
Leiomyosarcoma	1 (<1)	0
Fibrosarcoma	2 (1)	0
Synovial sarcoma	1 (<1)	0

Abbreviations: CNS=Central nervous system, PNET=Primitive neuroectodermal tumor, TED=Transplant essential data, CRF=Comprehensive report form.

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

	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Number of patients	**766**	**228**	**108**
Source of data			
CRF	347 (45)	88 (39)	46 (43)
TED	419 (55)	140 (61)	62 (57)
Number of centers	113	66	58
Disease at transplant			
Plasma Cell Disorders, MM	766 (100)	228 (100)	108 (100)
Recipient age at transplant			
10-19 years	3 (<1)	0	1 (1)
20-29 years	5 (1)	4 (2)	1 (1)
30-39 years	65 (8)	22 (10)	10 (9)
40-49 years	221 (29)	61 (27)	24 (22)
50-59 years	336 (44)	105 (46)	49 (45)
60-69 years	134 (17)	35 (15)	23 (21)
70+ years	2 (<1)	1 (<1)	0
Median (Range)	53 (10-71)	53 (22-72)	54 (18-69)
Recipient race/ethnicity			
Caucasian, non-Hispanic	653 (86)	194 (86)	86 (90)
African-American, non-Hispanic	50 (7)	17 (8)	3 (3)
Asian, non-Hispanic	13 (2)	6 (3)	2 (2)
Pacific islander, non-Hispanic	1 (<1)	1 (<1)	0
Native American, non-Hispanic	2 (<1)	1 (<1)	0
Hispanic	38 (5)	7 (3)	5 (5)
Unknown	9 (N/A)	2 (N/A)	12 (N/A)
Recipient sex			
Male	471 (61)	149 (65)	74 (69)
Female	295 (39)	79 (35)	34 (31)
Karnofsky score			
10-80	302 (39)	104 (46)	46 (43)
90-100	433 (57)	118 (52)	57 (53)
Missing	31 (4)	6 (3)	5 (5)
HLA-A B DRB1 groups - low resolution			
5/6	94 (13)	23 (12)	7 (7)
6/6	656 (87)	167 (88)	95 (93)
Unknown	16 (N/A)	38 (N/A)	6 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	7 (1)	0	0
6/8	25 (4)	1 (1)	3 (4)
7/8	122 (17)	22 (15)	14 (18)
8/8	544 (78)	126 (85)	59 (78)
Unknown	68 (N/A)	79 (N/A)	32 (N/A)

	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
HLA-DPB1 Match			
Double allele mismatch	103 (28)	11 (24)	3 (21)
Single allele mismatch	212 (57)	22 (48)	7 (50)
Full allele matched	54 (15)	13 (28)	4 (29)
Unknown	397 (N/A)	182 (N/A)	94 (N/A)
High resolution release score			
No	3 (1)	2 (67)	3 (60)
Yes	324 (99)	1 (33)	2 (40)
Unknown	439 (N/A)	225 (N/A)	103 (N/A)
KIR typing available			
No	698 (91)	228 (100)	108 (100)
Yes	68 (9)	0	0
Graft type			
Marrow	135 (18)	29 (13)	18 (17)
PBSC	629 (82)	199 (87)	90 (83)
BM+PBSC	1 (<1)	0	0
PBSC+UCB	1 (<1)	0	0
Number of cord units			
1	1 (100)	0	0
Conditioning regimen			
Myeloablative	282 (37)	98 (43)	49 (45)
RIC/Nonmyeloablative	476 (62)	126 (55)	57 (53)
TBD	8 (1)	4 (2)	2 (2)
Donor age at donation			
To Be Determined/NA	8 (1)	34 (15)	1 (1)
10-19 years	16 (2)	10 (4)	0
20-29 years	326 (43)	87 (38)	44 (41)
30-39 years	207 (27)	61 (27)	34 (31)
40-49 years	148 (19)	24 (11)	23 (21)
50+ years	61 (8)	12 (5)	6 (6)
Median (Range)	32 (18-61)	30 (18-58)	33 (20-57)
Donor/Recipient CMV serostatus			
+/+	176 (23)	57 (26)	26 (25)
+/-	78 (10)	33 (15)	9 (9)
-/+	231 (30)	61 (28)	31 (30)
-/-	274 (36)	70 (32)	38 (37)
Unknown	7 (N/A)	7 (N/A)	4 (N/A)
GvHD Prophylaxis			
Ex vivo T-cell depletion	13 (2)	8 (4)	2 (2)
CD34 selection	49 (6)	24 (11)	6 (6)
Tacrolimus + MMF +- others	137 (18)	21 (9)	14 (13)
Tacrolimus + MTX +- others (except MMF)	275 (36)	101 (44)	27 (25)
Tacrolimus + others (except MTX, MMF)	40 (5)	11 (5)	5 (5)
Tacrolimus alone	23 (3)	5 (2)	4 (4)
CSA + MMF +- others (except Tacrolimus)	124 (16)	24 (11)	23 (21)
CSA + MTX +- others (except Tacrolimus, MMF)	43 (6)	15 (7)	13 (12)
CSA + others (except Tacrolimus, MTX, MMF)	5 (1)	2 (1)	4 (4)
CSA alone	8 (1)	4 (2)	2 (2)
Other GVHD prophylaxis	21 (3)	8 (4)	3 (3)
Missing	28 (4)	5 (2)	5 (5)

	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Donor/Recipient sex match			
Male-Male	331 (44)	90 (41)	47 (44)
Male-Female	182 (24)	48 (22)	21 (20)
Female-Male	135 (18)	54 (25)	25 (24)
Female-Female	109 (14)	28 (13)	13 (12)
CB - recipient M	1 (<1)	0	0
Unknown	8 (N/A)	8 (N/A)	2 (N/A)
Year of transplant			
1986-1990	1 (<1)	0	0
1991-1995	15 (2)	4 (2)	5 (5)
1996-2000	46 (6)	16 (7)	8 (7)
2001-2005	107 (14)	14 (6)	17 (16)
2006-2010	251 (33)	44 (19)	30 (28)
2011-2015	257 (34)	87 (38)	38 (35)
2016-2019	89 (12)	63 (28)	10 (9)
Follow-up among survivors, Months			
N Eval	196	79	30
Median (Range)	48 (2-264)	30 (0-194)	42 (3-195)

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

	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Number of patients	**34**	**10**	**5**
Source of data			
CRF	26 (76)	6 (60)	2 (40)
TED	8 (24)	4 (40)	3 (60)
Number of centers	18	8	3
Disease at transplant			
Plasma Cell Disorders, MM	34 (100)	10 (100)	5 (100)
Recipient age at transplant			
20-29 years	1 (3)	0	0
30-39 years	2 (6)	0	0
40-49 years	9 (26)	1 (10)	2 (40)
50-59 years	20 (59)	6 (60)	2 (40)
60-69 years	2 (6)	3 (30)	1 (20)
Median (Range)	51 (22-64)	57 (48-67)	53 (46-65)
Recipient race/ethnicity			
Caucasian, non-Hispanic	18 (58)	5 (56)	2 (50)
African-American, non-Hispanic	8 (26)	3 (33)	1 (25)
Asian, non-Hispanic	1 (3)	0	1 (25)
Hispanic	4 (13)	1 (11)	0
Unknown	3 (N/A)	1 (N/A)	1 (N/A)
Recipient sex			
Male	19 (56)	7 (70)	1 (20)
Female	15 (44)	3 (30)	4 (80)
Karnofsky score			
10-80	11 (32)	3 (30)	3 (60)
90-100	23 (68)	5 (50)	2 (40)
Missing	0	2 (20)	0
HLA-A B DRB1 groups - low resolution			
4/6	19 (61)	3 (43)	4 (80)
5/6	12 (39)	3 (43)	1 (20)
6/6	0	1 (14)	0
Unknown	3 (N/A)	3 (N/A)	0 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	19 (79)	3 (75)	3 (100)
6/8	3 (13)	1 (25)	0
7/8	2 (8)	0	0
Unknown	10 (N/A)	6 (N/A)	2 (N/A)
HLA-DPB1 Match			
Double allele mismatch	1 (14)	0	1 (50)
Single allele mismatch	5 (71)	0	1 (50)
Full allele matched	1 (14)	0	0
Unknown	27 (N/A)	10 (N/A)	3 (N/A)

	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
High resolution release score			
Yes	3 (100)	0	0
Unknown	31 (N/A)	10 (N/A)	5 (N/A)
KIR typing available			
No	31 (91)	10 (100)	5 (100)
Yes	3 (9)	0	0
Cord blood number of units			
1	19 (56)	0	3 (60)
2	15 (44)	0	2 (40)
Unknown	0 (N/A)	10 (N/A)	0 (N/A)
Graft type			
UCB	32 (94)	10 (100)	3 (60)
PBSC+UCB	2 (6)	0	2 (40)
Conditioning regimen			
Myeloablative	11 (32)	4 (40)	2 (40)
RIC/Nonmyeloablative	22 (65)	5 (50)	3 (60)
TBD	1 (3)	1 (10)	0
Donor age at donation			
To Be Determined/NA	2 (6)	1 (10)	0
0-9 years	32 (94)	9 (90)	3 (60)
10-19 years	0	0	1 (20)
50+ years	0	0	1 (20)
Median (Range)	3 (1-9)	2 (1-10)	7 (2-63)
Donor/Recipient CMV serostatus			
+/+	7 (21)	3 (30)	1 (20)
+/-	4 (12)	2 (20)	1 (20)
-/+	5 (15)	1 (10)	1 (20)
-/-	2 (6)	2 (20)	0
CB - recipient +	10 (29)	0	1 (20)
CB - recipient -	6 (18)	0	1 (20)
CB - recipient CMV unknown	0	2 (20)	0
GvHD Prophylaxis			
CD34 selection	1 (3)	0	0
Tacrolimus + MMF +- others	10 (29)	3 (30)	0
Tacrolimus + MTX +- others (except MMF)	1 (3)	0	2 (40)
Tacrolimus + others (except MTX, MMF)	1 (3)	0	0
Tacrolimus alone	0	2 (20)	0
CSA + MMF +- others (except Tacrolimus)	14 (41)	4 (40)	1 (20)
CSA + MTX +- others (except Tacrolimus, MMF)	0	1 (10)	0
CSA alone	0	0	2 (40)
Other GVHD prophylaxis	6 (18)	0	0
Missing	1 (3)	0	0
Donor/Recipient sex match			
CB - recipient M	19 (56)	7 (70)	1 (20)
CB - recipient F	15 (44)	3 (30)	4 (80)
Year of transplant			
2006-2010	6 (18)	4 (40)	2 (40)
2011-2015	25 (74)	4 (40)	3 (60)
2016-2019	3 (9)	2 (20)	0

	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Follow-up among survivors, Months			
N Eval	6	2	0
Median (Range)	24 (12-61)	68 (64-72)	. (.-.)

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

	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Number of patients	**182**	**30**	**15**
Source of data			
CRF	61 (34)	5 (17)	6 (40)
TED	121 (66)	25 (83)	9 (60)
Number of centers	28	11	5
Disease at transplant			
Plasma Cell Disorders, MM	182 (100)	30 (100)	15 (100)
Recipient age at transplant			
20-29 years	2 (1)	0	0
30-39 years	8 (4)	1 (3)	0
40-49 years	49 (27)	9 (30)	3 (20)
50-59 years	78 (43)	12 (40)	7 (47)
60-69 years	43 (24)	8 (27)	5 (33)
70+ years	2 (1)	0	0
Median (Range)	55 (26-75)	55 (35-69)	55 (43-65)
Recipient race/ethnicity			
Caucasian, non-Hispanic	121 (67)	18 (60)	10 (67)
African-American, non-Hispanic	14 (8)	6 (20)	3 (20)
Asian, non-Hispanic	10 (6)	1 (3)	1 (7)
Pacific islander, non-Hispanic	2 (1)	0	0
Hispanic	34 (19)	5 (17)	1 (7)
Unknown	1 (N/A)	0 (N/A)	0 (N/A)
Recipient sex			
Male	107 (59)	23 (77)	9 (60)
Female	75 (41)	7 (23)	6 (40)
Karnofsky score			
10-80	64 (35)	12 (40)	6 (40)
90-100	115 (63)	18 (60)	9 (60)
Missing	3 (2)	0	0
Graft type			
Marrow	15 (8)	0	3 (20)
PBSC	167 (92)	30 (100)	10 (67)
PBSC+UCB	0	0	2 (13)
Conditioning regimen			
Myeloablative	67 (37)	14 (47)	5 (33)
RIC/Nonmyeloablative	115 (63)	16 (53)	10 (67)
Donor age at donation			
To Be Determined/NA	0	0	1 (7)
0-9 years	1 (1)	0	0
10-19 years	2 (1)	0	1 (7)
20-29 years	14 (8)	0	1 (7)
30-39 years	14 (8)	3 (10)	4 (27)
40-49 years	45 (25)	9 (30)	0
50+ years	106 (58)	18 (60)	8 (53)

	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Median (Range)	52 (0-76)	53 (34-69)	55 (17-63)
Donor/Recipient CMV serostatus			
+/+	73 (40)	11 (37)	5 (33)
+/-	18 (10)	3 (10)	3 (20)
-/+	41 (23)	4 (13)	4 (27)
-/-	50 (27)	12 (40)	3 (20)
GvHD Prophylaxis			
Ex-vivo T-cell depletion	1 (1)	0	0
CD34 selection	0	1 (3)	0
Post-CY + other(s)	22 (12)	3 (10)	3 (20)
TAC + MMF +- other(s) (except post-CY)	24 (13)	2 (7)	1 (7)
TAC + MTX +- other(s) (except MMF, post-CY)	82 (45)	16 (53)	9 (60)
TAC + other(s) (except MMF, MTX, post-CY)	8 (4)	3 (10)	1 (7)
TAC alone	1 (1)	1 (3)	0
CSA + MMF +- other(s) (except post-CY)	5 (3)	0	0
CSA + MTX +- other(s) (except MMF, post-CY)	4 (2)	0	0
CSA + other(s) (except MMF, MTX, post-CY)	1 (1)	1 (3)	0
CSA alone	1 (1)	0	0
Other(s)	15 (8)	0	0
Missing	18 (10)	3 (10)	1 (7)
Donor/Recipient sex match			
Male-Male	65 (36)	14 (47)	7 (47)
Male-Female	36 (20)	3 (10)	2 (13)
Female-Male	42 (23)	9 (30)	1 (7)
Female-Female	39 (21)	4 (13)	3 (20)
CB - recipient M	0	0	1 (7)
CB - recipient F	0	0	1 (7)
Year of transplant			
2006-2010	22 (12)	5 (17)	4 (27)
2011-2015	97 (53)	16 (53)	6 (40)
2016-2019	63 (35)	9 (30)	5 (33)
Follow-up among survivors, Months			
N Eval	95	13	8
Median (Range)	26 (3-99)	24 (3-121)	15 (6-97)

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

	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Number of patients	**7**	**3**	**1**
Source of data			
CRF	5 (71)	2 (67)	1 (100)
TED	2 (29)	1 (33)	0
Number of centers	3	3	1
Disease at transplant			
Breast cancer	7 (100)	3 (100)	1 (100)
Recipient age at transplant			
20-29 years	1 (14)	0	0
30-39 years	2 (29)	1 (33)	0
40-49 years	1 (14)	0	0
50-59 years	3 (43)	1 (33)	0
60-69 years	0	1 (33)	1 (100)
Median (Range)	41 (29-58)	51 (35-62)	64 (64-64)
Recipient race/ethnicity			
Caucasian, non-Hispanic	7 (100)	3 (100)	1 (100)
Recipient sex			
Female	7 (100)	3 (100)	1 (100)
Karnofsky score			
10-80	2 (29)	1 (33)	0
90-100	4 (57)	1 (33)	1 (100)
Missing	1 (14)	1 (33)	0
HLA-A B DRB1 groups - low resolution			
6/6	7 (100)	1 (100)	1 (100)
Unknown	0 (N/A)	2 (N/A)	0 (N/A)
High-resolution HLA matches available out of 8			
7/8	3 (50)	0	0
8/8	3 (50)	0	0
Unknown	1 (N/A)	3 (N/A)	1 (N/A)
HLA-DPB1 Match			
Double allele mismatch	2 (50)	0	0
Single allele mismatch	2 (50)	0	0
Unknown	3 (N/A)	3 (N/A)	1 (N/A)
High resolution release score			
Yes	5 (100)	0	0
Unknown	2 (N/A)	3 (N/A)	1 (N/A)
KIR typing available			
No	7 (100)	3 (100)	1 (100)
Graft type			
Marrow	3 (43)	1 (33)	1 (100)
PBSC	4 (57)	2 (67)	0

	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Number of cord units			
Unknown	7 (N/A)	3 (N/A)	1 (N/A)
Conditioning regimen			
Myeloablative	2 (29)	0	0
RIC/Nonmyeloablative	5 (71)	3 (100)	1 (100)
Donor age at donation			
To Be Determined/NA	0	1 (33)	0
20-29 years	2 (29)	1 (33)	1 (100)
30-39 years	2 (29)	1 (33)	0
40-49 years	2 (29)	0	0
50+ years	1 (14)	0	0
Median (Range)	36 (24-52)	27 (22-31)	26 (26-26)
Donor/Recipient CMV serostatus			
+/+	2 (29)	0	0
+/-	1 (14)	0	0
-/+	2 (29)	1 (50)	1 (100)
-/-	2 (29)	1 (50)	0
Unknown	0 (N/A)	1 (N/A)	0 (N/A)
GvHD Prophylaxis			
Tacrolimus + MTX +- others (except MMF)	5 (71)	2 (67)	1 (100)
CSA + MMF +- others (except Tacrolimus)	1 (14)	1 (33)	0
CSA + MTX +- others (except Tacrolimus, MMF)	1 (14)	0	0
Donor/Recipient sex match			
Male-Female	6 (86)	2 (67)	1 (100)
Female-Female	1 (14)	1 (33)	0
Year of transplant			
1991-1995	1 (14)	0	0
2001-2005	4 (57)	1 (33)	1 (100)
2006-2010	2 (29)	2 (67)	0
Follow-up among survivors, Months			
N Eval	0	1	0
Median (Range)		109 (109-109)	. (.-.)

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	Samples Available for Recipient and Donor N (%)
Number of patients	**1**
Source of data	
TED	1 (100)
Number of centers	1
Disease at transplant	
Breast cancer	1 (100)
Recipient age at transplant	
40-49 years	1 (100)
Median (Range)	45 (45-45)
Recipient race/ethnicity	
Hispanic	1 (100)
Recipient sex	
Female	1 (100)
Karnofsky score	
10-80	1 (100)
Graft type	
PBSC	1 (100)
Conditioning regimen	
RIC/Nonmyeloablative	1 (100)
Donor age at donation	
40-49 years	1 (100)
Median (Range)	42 (42-42)
Donor/Recipient CMV serostatus	
-/+	1 (100)
GvHD Prophylaxis	
TAC + MTX +- other(s) (except MMF, post-CY)	1 (100)
Donor/Recipient sex match	
Male-Female	1 (100)
Year of transplant	
2006-2010	1 (100)
Follow-up among survivors, Months	
N Eval	0

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CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH

TO: Plasma Cell Disorders and Adult Solid Tumors Working Committee Members

FROM: Parameswaran Hari, MD, MS; Scientific Director and Anita D'Souza, MD; Assistant Scientific Director for the Plasma Cell Disorders and Adult Solid Tumors Working Committee

RE: Studies in Progress Summary

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.

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.

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.

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.

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.

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.

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.

Proposal: 1811-58

Title:
Outcomes of Autologous Hematopoietic Cell Transplantation for Relapsed/Refractory Germ Cell Tumors in Females

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Navneet Majhail, MD, MS, majhain@ccf.org, Cleveland Clinic - Taussig Cancer Institute

Hypothesis:
We hypothesize that outcomes of autologous hematopoietic cell transplantation (autoHCT) for relapsed/refractory germ cell tumors (GCTs) in females are comparable to those with males with testicular germ cell tumors.

Specific aims:

- The primary aim is to assess overall survival (OS), progression free survival (PFS), relapse mortality (RM), and non-relapse mortality (NRM) in females receiving an autoHCT for GCTs
- To compare the OS, PFS, RM, and NRM in females receiving a single autoHCT versus a tandem autoHCT

Scientific impact:
However, limited data and experience exists with the optimal management of relapsed and/or refractory GCTs, particularly in female patients. While high-dose chemotherapy with autoHCT is often used, much of this data is extrapolated from male GCTs. As such there is an absence of comprehensive studies to know if female patients derive the same benefit as males from standard dose chemotherapy options vs. single autoHCT vs. tandem autoHCT. A recent experience at our institution highlighted delays in obtaining insurance coverage for a female GCT patient needing autoHCT; this study would be the largest study to date and would solidify the available evidence to ensure appropriate access and coverage. As many patients with GCTs are young, examining treatment related toxicity is paramount as well. This study is critically important to address an unmet need of this population and will provide the foundation for future prospective studies.

Scientific justification:
GCTs occur more commonly in males and are usually seen in young adults.[1] They are aggressive neoplasms and usually arise along the midline. Broadly, they can be divided into seminomas and non-seminomas. Prognostic risk stratification is based on a study of metastatic GCT patients receiving cisplatin or carboplatin-containing regimens as initial therapy.[2]
Those patients with localized small seminomas are usually treated initially with radiation, while those with bulky disease or non-localized tumors are treated with etoposide-based and cisplatin-based chemotherapy regimens.[1] Patients with non-seminomatous extragonadal GCTs who relapse after front-line chemotherapy generally have poor prognoses with poor responses to salvage chemotherapy regimens, including autoHCT, which has had success for recurrent testicular cancer.[3] Those with mediastinal non-seminomas have higher risk disease, more likely to be resistant to chemotherapy, and have a greater predisposition to develop hematologic malignancies.[4]
Previously, a randomized trial compared conventional salvage to high-dose chemotherapy with autoHCT in 263 patients with recurrent or refractory GCTs.[5] However, there is a paucity of data on outcomes strictly in female GCT patients, who may have a different disease biology and response to therapy. Previously, a study of 13 females with recurrent primary ovarian GCTs showed that platinum sensitivity

and use of autoHCT as initial salvage provided a higher probability of achieving no evidence of disease.[6] An EBMT study of 60 females with GCTs showed that conditioning with carboplatin in the salvage autoHCT setting was a viable therapeutic option; half received a tandem autoHCT.[7]

Patient eligibility population:
Eligible patients include:

- Females with a disease diagnosis of GCTs (any location)
- Received a first and/or second autologous HCT from 2000-2017
- Peripheral blood, bone marrow grafts only
- All disease stages
- All conditioning regimens
- Patients ≥ 18 years of age

Data requirements:
Data to be analyzed will be from data collected in the CIBMTR Report forms. No supplemental data will be required. Patient, disease and transplant variables to collect as below.

Patient characteristics:

- Age at transplant
- Race
- Karnofsky performance status
- Co-morbidity index (HCT-CI)
- RFI risk category
- Transplant center

Disease characteristics:

- Disease type
- Date of disease diagnosis
- Disease stage
- LDH, AFP, bHCG at diagnosis
- Date of pre-transplant chemotherapy initiation
- Pre-transplant chemotherapy regimen
- Number of cycles of chemotherapy
- Date of pre-transplant chemotherapy completion
- Total number of lines of chemotherapy
- Remission status at transplant
- Seminoma risk group (good, intermediate)
- Non-seminoma risk group (good, intermediate, poor)

Transplant characteristics:

- Bone marrow versus peripheral blood grafts
- Conditioning regimen including agents, dose, and intensity
- Date of transplant
- Donor age
- Donor-recipient gender match
- Planned upfront transplant (Yes vs. No)

- Planned tandem transplant (Yes vs. No)

Outcomes:

- Transplant-related mortality
- Date of relapse
- Overall survival
- Date of last follow up and status
- Date and cause of death

Study design (scientific plan):

This is a retrospective analysis examining outcomes of relapsed/refractory GCTs after autoHCT in females. This analysis will be restricted to the years 1990 to 2017, with a subset analysis of patients in a more contemporary cohort from 2000 to 2017. Outcomes include OS, PFS, RM, and NRM. Post-transplant follow-up data will be assessed at day +100, 6 months, 1 year, 2 years, and > 2 years. OS and PFS will be estimated using the Kaplan-Meier method and prognostic factors will be identified using Cox proportional hazards analysis. All other outcomes will be estimated using cumulative incidence and prognostic factors will be identified using Fine and Gray competing risk regression. Potential prognostic factors include patient-, disease-, and transplant-related characteristics. Variables to be considered in the multivariate analysis include site of disease, age, performance status, disease status, and single vs. tandem autoHCTs.

Data source:

Primary data source will be the CIBMTR Research Database. We will use existing TED forms to provide basic survival data with CRF forms providing more detailed disease, treatment, and transplant information. No external data sources will be utilized.

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Table 1. Characteristics of female patients who underwent 1st autoHCT for Germ Cell Tumor from 2008-2017 and reported with CIBMTR (TED population)

Characteristic	N (%)
Number of patients	98
Number of centers	69
Research level data	13 (13)
Age at transplant, years	
median (range)	17 (<1-56)
< 18	53 (54)
18-39	33 (34)
40-49	6 (6)
50-59	6 (6)
Region	
US	75 (77)
Other	23 (23)
Race	
Caucasian	69 (70)
African-American	9 (9)
Other	11 (11)
Missing	9 (9)
Karnofsky score	
90-100	73 (74)
< 90	22 (22)
Missing	3 (3)
HCT-CI	
0	57 (58)
1	7 (7)
2	10 (10)
≥3	21 (21)
Not reported	3 (3)
Time from diagnosis to transplant	
<6 months	5 (5)
6-12 months	30 (31)
12-18 months	25 (26)
18-24 months	13 (13)
>24 months	25 (26)

Characteristic	N (%)
Year of transplant	
2008	8 (8)
2009	4 (4)
2010	10 (10)
2011	13 (13)
2012	12 (12)
2013	11 (11)
2014	7 (7)
2015	10 (10)
2016	12 (12)
2017	11 (11)
Median follow-up of survivors (range), months	38 (2-97)

Proposal: 1811-168

Title:
Second autologous stem cell transplantation as salvage therapy for relapsed or refractory AL amyloidosis

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Hypothesis:
A 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.

Specific aims:

- To estimate the progression free survival (PFS) and overall survival (OS) at 2 and 5 years after salvage high-dose chemotherapy (HDT) and autologous stem cell transplant (ASCT) in patients with relapsed/refractory (R/R) AL amyloidosis.
    - We will identify patients with relapsed/refractory AL amyloidosis who have received a second course of HDT/ASCT as salvage therapy reported to the CIBMTR. Survival estimates will be computed using the method of Kaplan-Meier.

- To estimate the hematologic and organ response rate associated with a second course of HDT/ASCT.
    - Hematologic and organ response will be assessed according to the Consensus Opinion of the 10th International Symposium on Amyloid and Amyloidosis [1] as detailed in the Amyloidosis Post-HSCT data form. Responses will be assessed at day 100, 6 months, and 1 year after the second ASCT.

- To evaluate the safety and tolerability of a second course of HDT/ASCT in R/R AL amyloidosis.
    - We will assess the treatment-related mortality (TRM) with a second course of HDT/ASCT. TRM will be defined as all causes of death within 100 days after transplantation.

- To identify potential prognostic factors that influence the outcomes of a second course of HDT/ASCT in R/R AL amyloidosis.
    - Variables considered will include age at second course of HDT/ASCT, prior therapies, Karnofsky performance status (KPS) before HDT/ASCT (≤80% vs >80%), lines of therapy, organ involvement at any time before the second ASCT, cardiac involvement, conditioning regimen, time from first course of HDT/ASCT to the second course, and year of transplantation.

Scientific impact:
There is a paucity of data regarding the management of R/R AL amyloidosis. Over the past 15 years, there have been significant advances in the diagnosis and management of AL amyloidosis. High-dose melphalan with autologous stem cell transplant has led to significant improvement in the ability to achieve deep hematologic and organ responses as well as improvement in survival [2,3]. However, many patients still relapse and require further lines of therapy. There are currently no studies evaluating the role of a second course of HDT/ASCT in the management of R/R AL amyloidosis. Large centers have

included a few patients who have undergone a second ASCT for relapsed disease in their retrospective studies evaluating the management of R/R AL amyloidosis [4-6]. However, the extent to which this intervention is being utilized and its role in the management of R/R AL amyloidosis at various transplant centers is not well-described. This proposal will be the first study evaluating the efficacy and toxicity associated with a second course of HDT/ASCT in the management of R/R AL amyloidosis. We will also assess for potential prognostic factors to further elucidate which patients may derive benefit from a second ASCT. Results of this study may help better define another line of therapy and change current practice for patients with R/R AL amyloidosis.

Scientific justification:

High-dose melphalan and autologous stem cell transplant in AL amyloidosis was first described in 1993[7]. As first-line therapy, HDT/ASCT has led to significant improvements in hematologic and organ responses as well as survival [2,3]. Studies on HDT/ASCT as initial therapy in AL amyloidosis have reported hematologic CR rates ranging from 16 to 67%, organ response rates between 25% to 45%, and median overall survival between 5 to 10 years [2,8-10]. Although, patients who achieve a hematologic CR in the setting of their first HDT/ASCT have high organ response rates and longer survival[11-13], the majority of patients still develop relapsed or progression of disease. There are various treatment options for the management of R/R AL amyloidosis [14-17]. In multiple myeloma, a second ASCT has been shown to improve relapsed-associated mortality and OS compared to conventional chemotherapy [18-20]. However, the role of a second course of HDT/ASCT in R/R AL amyloidosis has not been studied. We propose to evaluate the safety and outcomes of a second course of HDT/ASCT in the management of R/R AL amyloidosis using the CIBMTR Research Database. In addition, we will identify potential factors that may be predictive of outcomes to determine which patients may derive benefit from a second course of HDT/ASCT.

Patient eligibility population:

Inclusion criteria:

- Patients must have a diagnosis of AL amyloidosis confirmed by laboratory data and tissue biopsy.
- Patients must have had prior line(s) of therapy and evidence of relapsed or refractory AL amyloidosis.
- Patients must have been treated with a second course of HDT/ASCT for their R/R AL amyloidosis.

Exclusion criteria:

- Patients with multiple myeloma or other B-cell lymphoproliferative disorders associated with AL amyloidosis.

Data requirements:

Data will be collected from the CIBMTR Research Database from the following forms:

- Form 2017 Amyloidosis Pre-HSCT Data
- Form 2000 Recipient Baseline Data
- Form 2117 Amyloidosis Post-HSCT Data
- Form 2100 Post-HSCT data/100 day Post-HSCT Data
- Form 2200 Six Months to Two Years Post-HSCT Data
- Form 002-DCI-AMY
- Form 095-AMY
- Form 095-AMYFU

Study Design:
This study will be an observational study of patients identified through the CIBMTR Research Database as diagnosed with AL amyloidosis and having had a second course of HDT/ASCT for R/R AL amyloidosis between 1995 and 2018. We will describe various patient characteristics, including demographics (age and gender), date of diagnosis, type of paraprotein, KPS, organ involvement, date of first ASCT and second ASCT, and transplant conditioning regimen. We will describe prior therapies, pre-transplant bone marrow plasma cell percentage, pre-transplant disease status, post second ASCT disease status/response criteria based on the Consensus Opinion of the 10th International Symposium on Amyloid and Amyloidosis. We will evaluate various outcomes associated with a second course of HDT/ASCT, including PFS and OS. PFS will be calculated from the time of the second course of HDT/ASCT to the date of the first documented relapsed or disease progression or death due to any cause, whichever occurs first. Overall survival after a second ASCT will be calculated from the start of HDT/ASCT to death from any cause. We will assess the treatment-related mortality, defined as all causes of death within 100 days after transplantation, associated with a second course of HDT/ASCT.

Survival estimates will be computed using the method of Kaplan-Meier. Potential prognostic factors that influence outcome will be evaluated in a multivariate analysis using Cox proportional hazards regression.

Data source:
CIBMTR Research Database

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Conflicts of interest:
None

Table 1. Characteristics of adult patients who underwent 2nd HCT for Amyloidosis from 1999-2016 and registered with CIBMTR, (TED population)

Characteristic	N (%)
Number of patients	**90**
Number of centers	48
Research level data	**27 (30)**
Age at transplant, years	
median (range)	58 (33-75)
18-39	4 (4)
40-49	15 (17)
50-59	40 (44)
60-69	27 (30)
70+	4 (4)
Gender	
Male	55 (61)
Female	35 (39)
Region	
US	82 (91)
Other	8 (9)
Race	
Caucasian	76 (84)
African-American	7 (8)
Asian	4 (4)
Not reported	3 (3)

Characteristic	N (%)
Year of transplant	
1999	2 (2)
2000	2 (2)
2001	2 (2)
2002	1 (<1)
2003	7 (7)
2004	5 (5)
2005	9 (8)
2006	11 (10)
2007	4 (4)
2008	9 (8)
2009	2 (2)
2010	13 (12)
2011	2 (2)
2012	10 (9)
2013	4 (4)
2014	11 (10)
2015	6 (6)
2016	6 (6)
Median follow-up of survivors (range), months	68 (3-148)

Proposal 1811-49

Title:
Serum Free light Chain ratio at Day +100 and Day + 180 following Autologous Hematopoietic Cell Transplantation is predictive of outcomes in Multiple Myeloma

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Hypothesis:
Normalization of serum free light chain at day +100 and day +180 following autologous hematopoietic cell transplantation (Auto-HCT) is independently predictive of superior progression free and overall survival in multiple myeloma

Specific aims:

- To compare outcomes of autologous HCT patients at day +100 and day +180 with normalization of serum free light chain ratio compared to those without normalization of of serum free light chain ratio.
- To compare assess prognostic impact of % change in dFLC from baseline and day +100 and day +180 post-Auto-HCT on relapse, PFS and OS
- To analyze disease and patient specific characteristics that are associated with normalization of serum free light chain ratio at day +100 and day +180 post Auto-HCT
- To assess prognostic impact of % change in dFLC from baseline and day +100 and day +180 post Auto-HCT on relapse, PFS and OS

Scientific justification:
Multiple myeloma (MM) is the second most common hematologic malignancy in the world. Despite improvement in outcome, the disease is still incurable for most patients. However, not all myeloma are the same. With the same treatment, some patients can have very long survival whereas others can have very short survival. This suggests that there is underlying heterogeneity in myeloma(1)
Measurements of serum kappa and lambda serum free light chain (*s*FLC) and their ratio are useful makers for diagnosis and monitoring of various plasma cell dyscrasias, including myeloma. FLC assays could be used to follow the disease course in nearly all multiple myeloma patients. In addition, because of their short serum half-life, changes in serum FLC concentrations provide a rapid indication of the response to treatment (2). Recently, normalization of *s*FLCκ/λ ratio and negativity of clonal plasma cells by immunohistochemistry or immunofluorescence were incorporated into the more stringent degree of response, stringent CR (sCR) definition proposed by the International Myeloma Working Group (IMWG)(3,4).
Previous studies have explored the potential role of sFLC monitoring in MM, typically as response to initial therapy , demonstrating favorable prognosis with normalization of sFLC following induction therapy (5–7). There are however, fewer studies reported investigating prognostic value of sFLC normalization following auto-HCT. Kapoor et al was able to demonstrate achieving sCR following auto-HCT, which requires normalization of light chain ratio in addition to CR criteria per IMWG criteria, was correlative with improved outcomes(8).
Gentili et al was able to show in 211 patients that normalization of sFLC ratio on day +90 following Auto-HCT may predict for PFS more accurately than the reduction of M-protein, independent of pre-

transplant reponse(9). A Mayo clinic study reported suppression of involved serum free light chain within 12 months of auto-HCT (defined as clonal or involved FLC reduced below the value of the uninvolved FLC) was associated with improved time to progression and overall survival compared to those who did not have suppression(10). In contrast, a study by Trieu et al showed no significant difference in the PFS of patients with abnormal vs. normal free kappa light chains or FLC ratio following auto-HCT(11).
Given the lack of clarity regarding the role of normalization of FLC ratio following auto-HCT, we propose to utilize the Center for International Blood and Marrow Transplantation Research (CIBMTR) database to investigate the role of normalization of sFLC ratio following auto-HCT on outcomes in MM. The impact of such a study would be that sFLC could be considered a surrogate marker of long term outcomes following auto-HCT independent of assessment of sCR, which would require bone marrow evaluation, potentially creating unnecessary discomfort and distress to patients following auto-HCT.

Patient eligibility population:
Inclusion criteria

- Multiple Myeloma patients >18 years of age, undergoing HDT/ASCT and reported to CIBMTR from 2005-2016
- First transplant only

Exclusion criteria

- MM patients undergoing allogeneic stem cell transplant (allo-HCT)
- Other plasma cell dyscrasias besides MM undergoing with either ASCT or allo-HCT.

Outcomes:

- Progression-free survival (PFS): survival without relapse/progression or death. Relapse or progression of disease and death are events. Those who survive without recurrence or progression are censored at last contact.

- Overall survival (OS): time to death. Death from any cause

- Relapse/Progression: Cumulative incidence of disease relapse/progression at 1, 3, and 5 years, with NRM as competing event.

- Non-relapse mortality (NRM): Cumulative incidence of NRM at day 100 and 1, 3, and 5 years. NRM is defined as death without preceding disease relapse/progression. Relapse/progression are competing events.

Data requirements:
Patient-related

- Age at ASCT, years: 18-29; 30-39; 40-49, 50-59, ≥60 years and continuous
- Sex: male vs. female
- Karnofsky performance score: ≥80% vs. <80%
- Race: White vs. Black vs. Asian/pacific islander vs. Hispanic vs. others
- Hematopoietic cell transplantation co-morbidity index (HCT-CI) (≥3 vs. <3)
- International staging system (ISS)/ Durie Salmon Stage: I vs. II vs. III vs. Revised ISS (R-ISS) (if available)

Disease and pre-HCT treatment related

- Serum free light chain (FLC) at diagnosis

  - Kappa/lambda
  - sFLC ratio at diagnosis (involved/ uninvolved)
  - involved FLC at diagnosis (mg/L)
  - dFLC (dFLC, difference between iFLC and uninvolved FLC)
- Immunochemical subtype: IgG vs. IgA vs. light chain vs. non-secretory/others
- Hemoglobin at transplant, g/dl: continuous
- Creatinine at transplant: <2mg/dl vs. ≥2 mg/dl
- Cytogenetics: High risk vs. standard risk at diagnosis
- Lines of chemotherapy prior to transplant (0 vs 1 vs >1)
- Chemotherapy (doublet versus triplet; IMID containing; PI containing)
- Disease status at HCT (CR vs VGPR vs PR vs SD vs. other)
- Time from diagnosis to transplant (<6 months vs. 6-12 months vs. 12-24 months)

Transplant related:

- Total No. of CD34+ cells infused ($\times 10^6$/kg), continuous
- Melphalan dose, mg/m^2 (200 versus <200)
- Year of transplant, by year

Post-transplant related:

- Serum free light chain (FLC) at day +100 and day +180
  - sFLC ratio (involved/ uninvolved)
  - involved FLC (mg/L)
  - dFLC (dFLC, difference between iFLC and uninvolved FLC)

- Post-ASCT therapy
  - Maintenance therapy (Yes/No, type of maintanence therapy)
  - Consolidation therapy (Yes/No; type of consolidation therapy)
  - Second transplant (tandem)

- Median follow-up of patients from the time of diagnosis, months

Forms required:

- MM pre-hsct (2016)
- MM post-HSCT (form 2116)
- day +100 form (from 2100)
- 6 month-2 year follow up (form 2200)
- Pre-TED (form 2400, 2402)

Study design:

Descriptive tables of patient-, disease-, and transplant-related factors will be prepared. These tables will list median and range for continuous variables and percent of total for categorical variables. The product-limit estimator proposed by Kaplan-Meier will be used to estimate the median and range of the follow-up time. Probability of progression-free survival and overall survival will be calculated using the Kaplan-Meier estimator, with the variance estimated by Greenwood's formula. Values for other endpoints will be generated using cumulative incidence estimates. Comparison of survival curves will be done using the log-rank test.

Multivariate analyses will be performed using proportional hazards models. These analyses will fit models to determine which risk factors may be related to a given outcome. All variables will first be examined to assure that they comply with the proportional hazards assumption. Factors found to have non-proportional hazards will be adjusted for in subsequent analyses. A stepwise model building approach will then be used to develop models for relapse, treatment-related mortality, progression-free survival and overall survival.

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Table 1. Characteristics of patients who underwent 1st PB melphalan based autoHCT for Multiple Myeloma from 2008-2016 and reported with CIBMTR, (CRF population)

Characteristic	N (%)
Number of patients	4586
Number of centers	149
Age at transplant, years	
median (range)	60 (20-82)
18-39	146 (3)
40-49	620 (14)
50-59	1570 (34)
60-69	1870 (41)
70+	380 (8)
Gender	
Male	2552 (56)
Female	2034 (44)
Region	
US	4387 (96)
Other	199 (4)
Race	
Caucasian	2965 (65)
African-American	1279 (28)
Other	222 (5)
Not reported	120 (3)
Karnofsky score	
≥ 90	2493 (54)
< 90	1971 (43)
Not reported	122 (3)
HCT-CI	
0	1492 (33)
1	686 (15)
2	750 (16)
≥ 3	1619 (35)
Not reported	39 (<1)
Kappa/Lambda light chain ratio available @ dx and 100d	
No	2749 (60)
Yes	1837 (40)

Characteristic	N (%)
Immunochemical subtype	
IgG	2714 (59)
IgA	878 (19)
IgD	31 (<1)
IgE	2 (<1)
IgM	13 (<1)
Light chain	887 (19)
Non-secretory	59 (1)
Unknown Type	2 (<1)
Disease status prior to transplant	
sCR/CR[a]	681 (15)
VGPR	1434 (31)
PR	1978 (43)
SD	315 (7)
PD/Relapse	168 (4)
Not reported	10 (<1)
Time from diagnosis to transplant	
< 6 months	1292 (28)
6 - 12 months	2161 (47)
12 - 24 months	695 (15)
≥ 24 months	438 (10)
Year of transplant	
2008	915 (19)
2009	314 (6)
2010	249 (5)
2011	338 (7)
2012	344 (7)
2013	636 (13)
2014	554 (11)
2015	709 (15)
2016	776 (16)
Median follow-up of survivors (range), months	49 (<1-127)

[a] sCR (n=162); CR (n=519)

Proposal: 1811-108

Title:
Maintenance therapy after second autologous hematopoietic cell transplantation for Multiple Myeloma

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Hypothesis:
There is growing evidence to support the use of post-transplant maintenance therapy in multiple myeloma (MM) after the first autologous hematopoietic cell transplantation (AHCT), however data are lacking regarding the role of maintenance therapy after second AHCT. We hypothesize that maintenance therapy may also prolong progression free survival (PFS) and overall survival (OS) after second AHCT.

Specific aims:
- Examine trends in real-life data regarding maintenance therapy after second AHCT in MM patients.
- Study the effect of maintenance therapy given after second AHCT on PFS and OS of MM patients.

Scientific impact:
The results of this retrospective study may:
- Influence recommendations on the need of maintenance therapy after a second AHCT in MM.
- Justify initiation of a randomized prospective study.

Scientific justification:
Maintenance therapy in MM after 1st AHCT consists of long-term treatment, aimed to maintain the depth of response achieved by induction and consolidation treatment phases, through suppression of residual disease [1]. The existing literature supports maintenance therapy after the first AHCT. The immunomodulatory drugs thalidomide and lenalidomide have both shown efficacy in this setting, with most studies suggesting an improved PFS. A recent meta-analysis has also demonstrated improvement in OS with lenalidomide maintenance after 1st AHCT. The median OS for patients who received lenalidomide maintenance was not reached compared with 82 months in the control group (HR = 0.74; 95% CI, 0.62–0.89; log-rank P = 0.001) and 5-, 6- and 7-year OS rates were higher in the maintenance therapy group (71 vs 66%, 65 vs 58% and 62 vs 50%, respectively) [2].
Bortezomib, a proteasome inhibitor, has been shown to be particularly efficacious as maintenance therapy in high risk MM [3]. Although there is continued debate regarding the optimal regimen and duration of maintenance therapy after 1st AHCT, the robust body of evidence in the literature has led to widespread use of this strategy.
Data regarding maintenance therapy after 2nd AHCT in the setting of relapsed MM are scarce. Gossi et al. conducted a retrospective analysis of 86 relapsed MM patients who underwent a 2nd AHCT. Lenalidomide maintenance after 2nd AHCT was associated with longer PFS (41.0 vs 21.6 months, P = .0034) and better OS (not reached vs 129.6 months, P = .0434) compared with patients without maintenance [4].

Patient eligibility population:

Inclusion criteria:

- Patients with relapsed MM who had a second AHCT between the years 2010 and 2017.
- Existing data on maintenance therapy after second AHCT.

Exclusion criteria:

- No available data on maintenance data after second AHCT.

Data requirements:

- Data will be extracted from the standard forms including: Multiple Myeloma / Plasma Cell Leukemia Pre-HCT Data form, Recipient Baseline Data form, Hematopoietic Stem Cell Transplant (HCT) Infusion form, Multiple Myeloma / Plasma Cell Leukemia Post-HCT Data form, Multiple Myeloma / Plasma Cell Leukemia Post-HCT Data, Post-HSCT Data form.
- Data requirements include patient demographics including age, sex, race; disease characteristics at diagnosis including year of diagnosis, stage, genetics; treatment given before first transplantation, disease status before first transplantation, date of first transplantation, conditioning therapy given at first transplantation, best disease status after first transplantation, maintenance therapy given or not after first transplantation, type of maintenance given after first transplantation; date of disease relapse, disease stage at relapse or progression, treatment given after relapse and before second transplantation; disease status before second transplantation, conditioning therapy given at second transplantation, best disease status after second transplantation; maintenance therapy or not given after second transplantation, type of maintenance therapy given; date of disease relapse or progression after second transplantation, date of last follow up, disease status at last follow up, date of death, cause of death.

Study design:

This is a retrospective registry study on behalf of the Plasma Cell Disorders and Adult Solid Tumors Working Committee of the CIBMTR.

We will include all patients with multiple myeloma who underwent two non-consecutive (not as part of a tandem transplant regimen) AHCT. Currently we do not know to what extent institutional policy, patient characteristics or disease-related variables affect the decision regarding maintenance therapy in this setting. Therefore, we will examine whether certain variables predict the administration of maintenance therapy: age, gender, performance status, pre- and post- transplant disease status, cytogenetics and previous treatments. This will be implemented using logistic regression model with type of post-transplant surveillance (with/without maintenance) as a dependent variable, and the outlined variables as covariates.

Patients will be stratified according to whether or not they received maintenance after the 2nd transplant, and we will compare these two groups in terms of PFS and OS. The probability of PFS and OS will be evaluated with the Kaplan-Mayer estimator and we will use the log-rank test to compare these groups. In addition, in the group of patients who received maintenance we will document the type and duration of treatment and stratify patients based on these variables.

Data source:

CIBMTR Research Database.

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Conflicts of interest:

None

Table 1. Characteristics of patients who underwent 2nd HCT[a] for Multiple Myeloma from 2008-2016 and reported with CIBMTR, (CRF population)

Characteristic	N (%)
Number of patients	500
Number of centers	92
Age at transplant, years	
median (range)	61 (31-79)
18-39	10 (2)
40-49	67 (13)
50-59	146 (29)
60-69	236 (47)
70+	41 (8)
Gender	
Male	287 (57)
Female	213 (43)
Region	
US	488 (98)
Other	12 (2)
Race	
Caucasian	395 (79)
African-American	84 (17)
Other	12 (2)
Not reported	9 (2)
Karnofsky score	
≥ 90	244 (49)
< 90	232 (46)
Not reported	24 (5)
HCT-CI	
0	57 (11)
1	25 (5)
2	32 (6)
>= 3	86 (17)
Need review	300 (60)
Melphalan dose in conditioning regimen, mg/m^2	
MEL 140	192 (38)
MEL 200	307 (61)
Unknown dose	1 (<1)

Characteristic	N (%)
Disease status prior to transplant	
sCR/CR	30 (6)
VGPR	92 (18)
PR	168 (34)
SD	85 (17)
PD/Relapse	123 (25)
Not reported	2 (<1)
Year of transplant	
2008	47 (9)
2009	44 (9)
2010	62 (12)
2011	73 (15)
2012	74 (15)
2013	50 (10)
2014	45 (9)
2015	54 (11)
2016	51 (10)
Post-HCT therapy for this transplant	
VR ± other	24 (5)
VC ± other	6 (1)
V ± other	35 (7)
R ± other	132 (26)
KR ± other	17 (3)
K ± other	19 (4)
Other[b]	56 (11)
No planned rx	207 (41)
Not reported	4 (<1)
Median follow-up of survivors (range), months	62 (3-124)

[a] Tandem HCTs where excluded

[b] Other post-HCt therapy: Thalidomide ± other(n=13); Pomalidomide (n=26); Cy ± other (n=3); Corticosteroid ± other (n=2); other (n=12).

Proposal: 1811-05

Title:
Outcomes for patients with Multiple Myeloma treated with Autologous or Syngeneic Allogenic Stem Cell Transplantation

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Hypothesis:
The role of autologous stem cell transplantation in multiple myeloma has been established with regards to prolonged progression free survival and perhaps attaining an overall survival benefit for patients. There has also been data corroborating the efficacy and superiority of syngeneic transplant when compared to autologous transplant in multiple myeloma. However, in view of the advent of novel therapies for multiple myeloma, this raises the question of validity of this previously established treatment paradigm. We propose that autologous stem cell transplant will still be shown to provide benefit to patients with multiple myeloma. Furthermore, we propose that syngeneic transplantation will be demonstrated to be safe and efficacious as well.

Specific aims:
The aim of this study is to determine the role and outcomes of patients with multiple myeloma, treated with autologous stem cell transplantation (ASCT) compared to syngeneic hematopoietic stem cell transplantation (SCT) from an HLA-identical sibling donor. Study endpoints include:

- Overall survival (OS) and progression free survival (PFS) in patients with multiple myeloma treated with ASCT and SCT
- Response rate (RR) and non-relapse mortality (NRM) in patients treated with ASCT and SCT

Scientific impact:
The ideal management of patients with multiple myeloma is generally to proceed to autologous stem cell transplant after induction therapy if a patient is eligible. However, much of the data supporting this treatment algorithm came before the development of newer and highly effective therapies for multiple myeloma. Previously, CIBMTR data has also shown SCT to be safe and effective with a lower relapse rate than ASCT. This study would help elucidate how ASCT and SCT fit into the treatment paradigm of multiple myeloma in this new era by providing information on response rates, treatment related mortality, overall survival after transplantation, and progression free survival after ASCT or SCT.

Scientific justification:
Prior data has established the role of autologous stem cell transplantation in providing deep clinical remissions and prolonged progression free survival in patients with multiple myeloma. In addition, there has also been data comparing autologous stem cell transplantation to syngeneic stem cell transplants. SCT has been shown to be safe and efficacious with a lower risk of relapse than ASCT. Reasons for the superiority of SCT over ASCT may be attributable to lack of graft contamination or a more robust, immunologically vigilant graft with graft vs. tumor effect. Specifically, prior CIBMTR data analyzing outcomes of patients transplanted between 1988 and 2003 has shown the 5 year cumulative relapse rate with ASCT and SCT to be 71% at 5 years vs. 43%, respectively (1). The 5 year overall survival in ASCT and SCT was demonstrated to be 40% and 60%, respectively (1). In a single center study from MD Anderson, median progression free survival was 98.6 months in the SCT group and 34.5 months in the ASCT group (2).

However, the number of effective therapies available for treatment of multiple myeloma has grown significantly over the last few years. With the advent of newer therapies such as monoclonal antibodies, next generation IMIDs and proteasome inhibitors, the benefit of syngeneic stem cell transplantation in myeloma needs to be re-examined.

Patient eligibility population:
Eligible patients would include those with Multiple Myeloma treated with ASCT or SCT from 2003-2018 as reported to the CIBMTR.

Population to be studied

- Age: 18-80
- Disease: Patients with Multiple Myeloma
- Disease Stage: Any
- Year of Transplant: 2003-2018
- Graft and Donor types: Any
- Prior Treatments: Any
- Specific Transplant Regimens: Any

Data requirements:
Data Collection Forms to be utilized include Recipient Baseline Data, Multiple Myeloma / Plasma Cell Leukemia Pre-HCT data, and Multiple Myeloma / Plasma Cell Leukemia Post-HCT data.

From Recipient Baseline Data

- Race
- Age at transplantation
- Karnofsky Performance Status
- Gender

From Multiple Myeloma / Plasma Cell Leukemia Pre-Transplantation data

- Secretory or non-secretory
- Immunoglobulin heavy chain: IgG, IgD, IgA, IgM, or light chain only
- Immunoglobulin light chain: kappa or lambda
- Number of lines of prior therapy
- Types of prior therapies: IMID, proteasome inhibitor, melphalan, elotuzumab, daratumumab, venetoclax, cyclophosphamide, and/or other therapies
- Number of times radiation therapy given in past
- Best Response to previous therapy: sCR, CR, VGPR, PR, MR/SD, or Progressive Disease
- Plasma cells in bone marrow prior to Preparative Regimen
- Cytogenetics if known
- Disease status at last evaluation prior to preparative regimen: sCR, CR, VGPR, PR, MR/SD, or Progressive Disease/Relapse
- Preparative Regimen Chosen: Melphalan, BEAM, or other
- Previous transplantation: yes or no
- Type of previous transplantation: ASCT or SCT

Additional Pre-transplantation Data in those undergoing SCT

- Donor-recipient gender match: MM, MF, FM, or FF
- Donor-recipient CMV status- +/+, +/-, -/+, or -/-
- TBI containing regimen: yes or no

- Stem cell source: bone marrow, peripheral blood

Post-ASCT data and outcomes

- Response rate at day 100 and one year
- Relapse: defined as increase in M-protein >25% from lowest value
- Non relapse Mortality: defined as death without relapse/recurrence within 100 days of transplant
- Progression-free Survival: events are relapse or NRM
- Overall Survival: events are death from any cause

Post-SCT data and outcomes

- Response rate at 100 days and one year
- Relapse: defined as increase in M-protein >25% from lowest value
- Non-relapse Mortality: defined as death without relapse/recurrence within 100 days of transplant
- Progression-free Survival: events are relapse or TRM
- Overall Survival: events are death from any cause
- Incidence of acute and chronic graft versus host disease (GVHD): the number of patients that experienced grade II-IV acute GVHD, limited chronic GVHD, or extensive chronic GVHD after SCT

Study design:

This is a retrospective study of patients with Multiple Myeloma that underwent ASCT or SCT, utilizing data from 2003-2018 in the CIBMTR database. Descriptive tables of baseline patient and disease characteristics will be made. Tables will list median and range values for continuous variables and total percent for categorical variables.

Kaplan-Meier analysis will be used for OS and PFS. Ninety five percent confidence intervals at fixed time points will be reported. We plan to analyze outcomes of all evaluable recipients of genetically-identical twin transplants for multiple myeloma reported to the Center for International Blood and Marrow Transplant Research (CIBMTR) between 2003 and 2018 and compare these to outcomes in a similar population receiving autologous HCT during the same period. To adjust for potential imbalance of risk factors between the cohorts, each twin transplant recipient will be matched with up to four autologous transplant recipients

Data source:

The only source would be the CIBMTR Research Database. No external data will be linked.

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Conflicts of interest:
None

Table 1. Characteristics of patients who underwent 1st PB Autologous or Syngeneic Allogenic HCT for Multiple Myeloma from 2008-2016 and reported with CIBMTR, CRF

Characteristic	Syngeneic	Autologous
Number of patients	55	4624
Number of centers	29	149
Age at transplant, years		
median (range)	58 (37-77)	60 (20-82)
18-39	3 (5)	148 (3)
40-49	7 (13)	621 (13)
50-59	23 (42)	1581 (34)
60-69	18 (33)	1889 (41)
70+	4 (7)	385 (8)
Gender		
Male	25 (45)	2572 (56)
Female	30 (55)	2052 (44)
Region		
US	54 (98)	4413 (95)
Other	1 (2)	211 (5)
Race		
Caucasian	49 (89)	2996 (65)
African-American	5 (9)	1285 (28)
Other	1 (2)	222 (5)
Not reported	0	121 (3)
Karnofsky score		
90-100	37 (67)	2513 (54)
< 90	18 (33)	1988 (43)
Not reported	0	123 (3)
HCT-CI		
0	23 (42)	1508 (33)
1	8 (15)	691 (15)
2	5 (9)	754 (16)
≥3	19 (35)	1627 (35)
Not reported	0	44 (<1)
Conditioning regimen		
Mel alone	52 (95)	4624
Mel/other[a]	3 (5)	0
Melphalan dose in conditioning regimen, mg/m^2		
MEL 140	10 (18)	1337 (29)
MEL 200	45 (82)	3287 (71)

Characteristic	Syngeneic	Autologous
Donor/recipient sex match		
M-M	25 (45)	NA
F-F	30 (55)	
Donor/recipient CMV serostatus		
+/+	15 (27)	NA
+/-	6 (11)	
-/+	11 (20)	
-/-	20 (36)	
Nor reported	3 (5)	
Disease status prior to transplant		
sCR/CR	12 (22)	692 (15)
VGPR	15 (27)	1441 (31)
PR	20 (36)	1996 (43)
SD	7 (13)	317 (7)
PD/Relapse	1 (2)	168 (4)
Not reported	0	10 (<1)
Time from diagnosis to transplant		
< 6 months	13 (24)	1300 (28)
6 - 12 months	31 (56)	2178 (47)
12 - 24 months	7 (13)	706 (15)
>= 24 months	4 (7)	440 (10)
Year of transplant		
2008	5 (9)	888 (19)
2009	6 (11)	303 (7)
2010	3 (5)	234 (5)
2011	9 (16)	332 (7)
2012	8 (15)	318 (7)
2013	6 (11)	604 (13)
2014	6 (11)	529 (11)
2015	6 (11)	670 (14)
2016	6 (11)	746 (16)
Median follow-up of survivors (range), months	60 (7-108)	49 (<1-127)

[a] Mel + other: cy (n=1); nitro + bcnu (n=1); not specified (n=1)

Proposal: 1810-06/1811-117/1811-153

Title:
Comparison of real-world experience of maintenance strategies in multiple myeloma patients after autologous stem cell transplantation

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Hypothesis:
Lenalidomide based maintenance is superior to non-lenalidomide based maintenance; however, the durability of remission with lenalidomide maintenance is shorter than what has been reported in previous phase III studies

Specific aims:
- To evaluate progression free survival (PFS) and overall survival (OS) of lenalidomide and non-lenalidomide based therapy in multiple myeloma patients after autologous stem cell transplantation
- To compare results of real-world maintenance with previously published phase 3 studies.
- To the identify the subgroups of patients that benefit from certain maintenance strategy

Scientific impact:
Upon completion, this study will improve our understanding of the role of lenalidomide and other maintenance strategies in multiple myeloma patients after stem cell transplantation. The study also helps identify patients that may benefit from certain maintenance strategies, and thus will be helpful in guiding clinical decisions.

Scientific justification:
Multiple myeloma (MM) is a heterogeneous disease with survival ranging from few months to years (1). Despite the unprecedented response rates associated with novel agents, high dose therapy and autologous stem cell transplant (HDT/ASCT) remains the preferred strategy for transplant eligible patients. In the novel agent era, four large randomized trials have been conducted to establish the role of ASCT—the results of the trials showed deeper responses, superior progression free survival (PFS) and even overall survival in few studies (2-4). Maintenance after HDT/ASCT is well recognized and has been associated with consistent progression free survival benefit (5,6,7). McCarthy et al. reported on a multi-center, randomized trial comparing continuous treatment with lenalidomide to placebo. The trial was unblinded around 18 months into treatment, at which point crossover was allowed. Maintenance treatment was impressively effective with longer time to progression (57.3 vs. 28.9 months); moreover, despite allowing crossover, maintenance approach granted better overall survival

(113 vs. 84.1 months) (5). The IFM2005-02 trial reported similar results with PFS favoring maintenance approach (41 vs. 23 months) with a median duration of maintenance around two years (6). Lastly, Palumbo et al. used lenalidomide with a slightly different regimen with three weeks on/one week-off regimen and results were in favor of maintenance therapy (54.7 vs. 37.4 months) (7). A meta-analysis of all three randomized trials was performed-- with an average follow-up of 79.5 months; maintenance approach was associated with better survival outcomes (not reached vs. 86.0 months) and better progression-free survival (52.8 vs. 23.5 months) (8). There are several well-known factors known to affect outcome such as baseline prognostic features like International Staging System (ISS) and chromosomal abnormalities, and direct comparisons in these subsets are not available. In a sub-group analysis, lenalidomide maintenance favored OS in all subgroups except those with ISS stage III, high-risk cytogenetics and low creatinine clearance (8).

Bortezomib as a potential long-term maintenance especially in high risk MM is of interest in recent studies (9-13). In a meta-analysis by Liu et al (14), use of bortezomib maintenance resulted in 27% decreased risk of progression while median PFS of 36.5 months was reported by Sivaraj et.al (13). There is a paucity of data comparing bortezomib to lenalidomide-based regimens (9,15). In a study by Huang et al (15) the bortezomib has nearly equal PFS benefit to lenalidomide with decreased risk of secondary malignancies (3% vs. 5.4% in lenalidomide group). Further, recent results showed that use of ixazomib maintenance resulted in improved progression free survival when compared to placebo (HR 0.72; 95% CI; 0.58, 0.89; $p<0.001$), and is being explore in other clinical trials as well (16,17).

Hence it is important to tailor the maintenance strategies based on baseline prognostic factors to derive maximal benefit. In this study, we seek to use data from CIBMTR registry to compare several maintenance strategies in MM patients after HDT/ASCT and aim to identify sub-groups that may benefit from a particular strategy.

Study population:

Inclusion criteria:

- Multiple Myeloma patients >18 years of age, undergoing HDT/ASCT and reported to CIBMTR from 2005-2017

Exclusion criteria:

- MM patients undergoing allogeneic stem cell transplant (allo-HCT)
- Other plasma cell dyscrasias besides MM undergoing with either ASCT or allo-HCT.

Outcomes:

- Non-relapse mortality (NRM): Cumulative incidence of NRM at 1 year, 3 years, and 5 years. NRM is defined as death without preceding disease relapse/progression. Relapse/progression are competing events.
- Relapse/Progression: Cumulative incidence of disease relapse/progression at 1, 3, and 5 years, with NRM as competing event.
- Progression-free survival (PFS): survival without relapse/progression or death. Relapse or progression of disease and death are events. Those who survive without recurrence or progression are censored at last contact.
- Overall survival (OS): time to death. Death from any cause will be considered an event. Surviving patients will be censored at time of last follow-up.
- Disease response: Defined as per the International Myeloma Working Group Criteria.

Variables to be analyzed:

Patient-related:

- Age at ASCT, years: 18-29; 30-39; 40-49, 50-59, ≥60 years and continuous
- Sex: male vs. female
- Karnofsky performance score: ≥80% vs. <80%
- Race: White vs. Black vs. Asian/pacific islander vs. Hispanic vs. others
- Hematopoietic cell transplantation co-morbidity index (HCT-CI) (≥3 vs. <3)

Disease-related:

- Immunochemical subtype: IgG vs. IgA vs. light chain vs. non-secretory/others
- Hemoglobin at transplant, g/dl: continuous
- Creatinine at transplant: <2mg/dl vs. ≥2 mg/dl, Creatinine clearance: CrCl ml/minute (>60 vs 60-46 vs. 45-31 vs. <30)
- Cytogenetics
- Gene expression profiling
- International staging system (ISS) I vs. II vs. III vs. Revised ISS (R-ISS) (if available)

Transplant-related:

- First line induction chemotherapy: PI+ Imid, Imid vs. others
- If available response to first induction
- Prior lines of therapy before transplant: (1 vs. 2 vs. > 2)
- Dose of lenalidomide used in induction therapy (if available)
- Melphalan Dose: 140-180 mg/m^2 vs. 200 mg/m^2
- Disease status at transplant: CR vs. VGPR vs. PR vs. SD vs. REL/PD
- % of change in M spike (after induction and transplant)
- % Change in dFLC (after induction and transplant)
- Disease status post-transplant D+60: CR vs. VGPR vs. PR vs. NR vs. Relapse/Progression
- Time from diagnosis to HCT: <6 months vs. 6-12 months vs. 12-18 months
- Maintenance: Lenalidomide vs. lenalidomide + bortezomib vs. others
- Dose of lenalidomide dose during maintenance (5mg vs. 10 mg vs. 15 mg.; days 1-21/28 days vs continuous)
- Progression free survival measured from transplantation
- Overall survival measured from transplantation

Study design:

The primary objective of the study is. Patients >18 years of age who underwent HDT/ASCT for MM from 2005-2017 and reported to CIBMTR will be included. After meeting the selection criteria, patient-, disease- and transplant- related variables will be compared between three maintenance groups: Imid versus ImiD +PI versus others using chi-square or Wilcoxon rank sum test when appropriate. Estimates of outcomes of interest will be reported as probabilities with 95% confidence intervals (95% CI). The probability of OS and PFS will be calculated with the Kaplan-Meier estimator. Multivariable analysis will be performed using the Cox proportional hazards regression. Maintenance will be considered the main effect in the multivariable analysis. The assumption of proportional hazards will be tested for each variable, and factors violating the proportionality assumption adjusted by stratification. A stepwise model building approach will be used to develop models for OS, PFS and relapse/progression. Forward selection

and backward elimination procedures will be used to confirm the significant co-variates. Results will be compared with previously published data from phase 3 trials. Response will be categorized based on different myeloma subgroups risk factors to identify myeloma features that entertain most durable response to lenalidomide maintenance

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Table 1. Characteristics of patients who underwent 1st HCT for Multiple Myeloma from 2008-2016 and reported with CIBMTR, CRF

Characteristic	N (%)
Number of patients	4834
Number of centers	150
Age at transplant, years	
median (range)	60 (20-82)
18-39	150 (3)
40-49	643 (13)
50-59	1655 (34)
60-69	1984 (41)
70+	402 (8)
Gender	
Male	2698 (56)
Female	2136 (44)
Region	
US	4625 (96)
Other	209 (4)
Race	
Caucasian	3142 (65)
African-American	1333 (28)
Other	233 (5)
Not reported	126 (3)
Karnofsky score	
≥ 90	2618 (54)
< 90	2088 (43)
Missing	128 (3)
HCT-CI	
0	1585 (33)
1	722 (15)
2	795 (16)
≥ 3	1693 (35)
Not reported	39 (<1)

Characteristic	N (%)
Immunochemical subtype	
IgG	2859 (59)
IgA	928 (19)
IgD	34 (<1)
IgE	2 (<1)
IgM	16 (<1)
Light chain	931 (19)
Non-secretory	61 (1)
Unknown Type	3 (<1)
ISS stage at diagnosis	
Stage I	1434 (30)
Stage II	1323 (27)
Stage III	1008 (21)
Not reported	1069 (22)
Disease status prior to transplant	
sCR/CR	714 (15)
VGPR	1490 (31)
PR	2102 (43)
SD	343 (7)
PD/Relapse	175 (4)
Not reported	10 (<1)
Time from diagnosis to transplant	
< 6 months	1356 (28)
6 - 12 months	2269 (47)
12 - 24 months	727 (15)
≥ 24 months	482 (10)
Year of transplant	
2008	915 (19)
2009	314 (6)
2010	249 (5)
2011	338 (7)
2012	344 (7)
2013	636 (13)
2014	554 (11)
2015	708 (15)
2016	776 (16)

Characteristic	**N (%)**
Post-HCT therapy (for current transplant)	
VR ± other	548 (11)
VC ± other	29 (<1)
V ± other	270 (6)
R ± other	1846 (38)
KR ± other	117 (2)
K ± other	70 (1)
Other	295(6)
No planned therapy	1630 (34)
Not reported	29 (<1)
Median follow-up of survivors (range), months	49 (<1-127)

Proposal 1812-07

Title:
Impact of Induction Therapy with VRD vs. VCD on Outcomes in Patients with Multiple Myeloma Undergoing Stem Cell Transplantation

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Hypothesis:
We hypothesize that patients with newly diagnosed multiple myeloma receiving bortezomib-cyclophosphamide-dexemethasone (VCD) based chemotherapy prior to autologous stem cell transplant have similar progression free survival compared to those receiving bortezomib-lenalidomide-dexamethasone (VRD) based induction, after adjusting for other prognostic factors.

Specific aims:
- To evaluate hematologic response rates using IMWG criteria[1,2] before transplant and best response with first line therapy in patients with newly diagnosed multiple myeloma receiving VCD induction therapy compared to those receiving VRD induction therapy prior to transplant.
- To evaluate progression free survival (PFS) in patients with newly diagnosed multiple myeloma receiving VCD induction therapy compared to those receiving VRD induction therapy prior to transplant, after adjusting for other baseline prognostic factors and post-transplant maintenance.
- To evaluate overall survival (OS) in patients with newly diagnosed multiple myeloma receiving VCD induction therapy compared to those receiving VRD induction therapy prior to transplant, after adjusting for other baseline prognostic factors and post-transplant maintenance.

Scientific impact:
Bortezomib-cyclophosphamide-dexemethasone (VCD) is a commonly used induction regimen in the United States for patients with multiple myeloma, especially those who present with renal impairment. Data from the randomized phase II EVOLUTION trial [3] and a retrospective study[4] show that response rates and survival with VCD are similar to patients receiving VRD. On the other hand, higher response rates were observed when another immunomodulatory drug (IMiD) based regimen VTD (bortezomib-thalidomide-dexamethasone) was compared to VCD in the IFM 2013-14 trial.[5]
Given the variable results from different studies, no definitive conclusion can be made regarding efficacy of the two regimens and their impact on outcomes. The goal of our study is to evaluate outcomes (response rates, PFS and OS) in a large cohort of patients receiving VCD prior to transplant compared to those receiving VRD after accounting for renal failure and maintenance therapy. Our results will be extremely informative for the routine management of newly diagnosed patients with MM.

Scientific justification:
VCD and VRD are the two most common induction regimens used for patients with newly diagnosed multiple myeloma prior to transplant. VCD is often used in patients with renal failure, given challenges with use of lenalidomide in this population. Data comparing VCD to VRD induction show variable results. The IFM 2013-14 trial[5] comparing VCD to another IMiD based regimen, VTD raised some concern, as patients in the VCD arm had lower response rates. However, the VCD regimen used in the study was

different from that is commonly used in the United States. The phase II randomized EVOLUTION trial[3] demonstrated similar response rates, PFS and OS with VRD and VCD. A retrospective study of 176 patients demonstrated that VCD was non-inferior to VRD, in terms of response rates, PFS and OS.[4] A recent study from our institution showed similar PFS and OS rates at 5 years with both regimens, though there was some suggestion that patients receiving VRD may have superior OS after controlling for baseline prognostic factors.[6]

Therefore, a larger study is needed to compare the two regimens and clarify if there is any difference in outcomes with these two regimens. Moreover, factors such as renal failure and post-transplant maintenance/consolidation need to be accounted for as they can impact survival outcomes.[7-9] The use of the CIBMTR database will allow these regimens to be compared in a large cohort of patients.

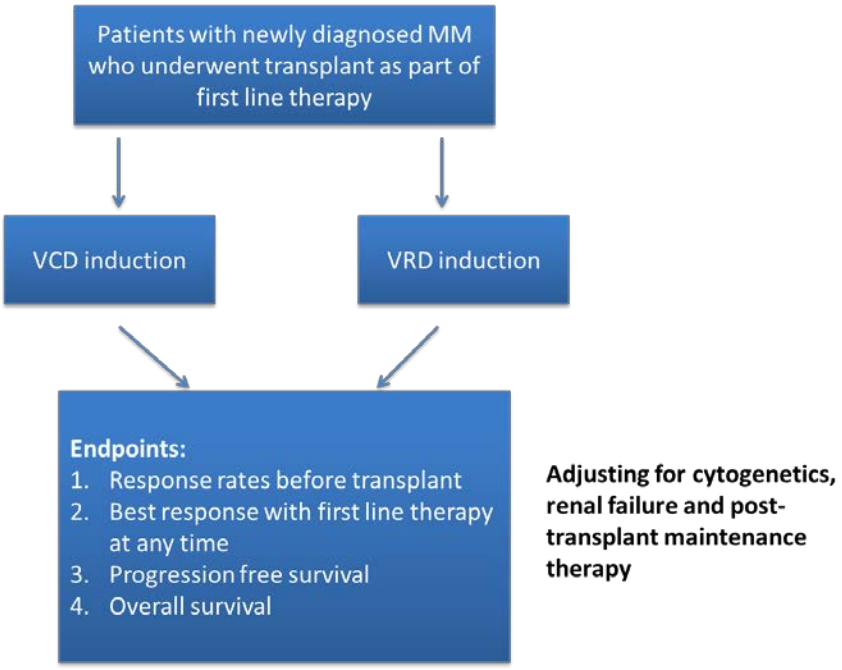
Patient eligibility population:

- Newly diagnosed patients with multiple myeloma who received VCD or VRD induction prior to undergoing transplant
- Study period: January 1st, 2010 to December 31st, 2016
- Time from diagnosis to transplant <=8 months

Data Requirements:

- Baseline demographics and diagnosis data
- Data for risk stratification: Baseline labs (hemoglobin, creatinine, calcium, albumin, beta-2-microglobulin, LDH, monoclonal protein levels and type, light chain level (if available), marker of measurable disease, bone marrow plasma cell percentage, FISH (fluorescence in-situ hybridization) data
- First line chemotherapy details: drugs with start and stop dates
- Date of transplant
- Best hematologic response before transplant
- Best response at any time before progression
- Treatment after transplant: consolidation or maintenance, with start and stop dates
- Date of progression
- Date of death or last follow-up

Study Design:



Abbreviations: VCD: bortezomib-cyclophosphamide-dexemethasone; VRD: bortezomib-lenalidomide-dexamethasone

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Table 1. Characteristics of adult patients who underwent 1st PB MEL 200 HCT for Multiple Myeloma from 2010-2016 and reported with CIBMTR

Characteristic	VRD	VCD
Number of patients	796	291
Number of centers	103	79
Age at transplant, years		
median (range)	58 (28-82)	59 (24-77)
18-39	35 (4)	19 (7)
40-49	145 (18)	27 (9)
50-59	302 (38)	111 (38)
60-69	279 (35)	125 (43)
70+	35 (4)	9 (3)
Gender		
Male	469 (59)	162 (56)
Female	327 (41)	129 (44)
Region		
US	793	260 (89)
Other	3 (<1)	31 (11)
Race		
Caucasian	524 (66)	184 (63)
African-American	227 (29)	60 (21)
Other	36 (5)	32 (11)
Missing	9 (1)	15 (5)
Karnofsky score		
>= 90	442 (56)	205 (70)
< 90	343 (43)	83 (29)
Missing	11 (1)	3 (1)
HCT-CI		
0	291 (37)	108 (37)
1	112 (14)	38 (13)
2	152 (19)	47 (16)
=>3	240 (30)	98 (34)
Missing	1 (<1)	0

Characteristic	VRD	VCD
Disease status prior to transplant		
SCR/CR	152 (19)	45 (15)
VGPR	321 (40)	111 (38)
PR	290 (36)	115 (40)
SD	22 (3)	17 (6)
PD/Relapse	8 (1)	2 (<1)
Missing	3 (<1)	1 (<1)
Time from diagnosis to transplant		
<4 months	43 (5)	12 (4)
4-8 months	753 (95)	279 (96)
Year of transplant		
2010	53 (7)	6 (2)
2011	95 (12)	12 (4)
2012	91 (11)	26 (9)
2013	142 (18)	60 (21)
2014	102 (13)	54 (19)
2015	136 (17)	67 (23)
2016	177 (22)	66 (23)
Median follow-up of survivors (range), months	44 (2-100)	36 (1-78)