1. Introduction

The CIBMTR Plasma cell disorders and adult solid tumors Working Committee was called to order at 12:15PM. Dr. D'Souza introduced the committee leadership and welcomed the committee participants. Dr. D'Souza introduced Dr. Shaji Kumar as the newly appointed Chair for the Working Committee starting March 1, 2017. Drs. D'Souza and Parameswaran Hari acknowledged Dr. Amrita Krishnan for all of her efforts during the past years as Co-Chair. Dr. D'Souza welcomed guest Dr. Laurent Garderet from the EBMT Myeloma Working Party. Dr. D’Souza introduced the committee goal and expectations to the audience and reviewed previous meeting presentations, published/submitted papers in 2016. Dr. Hari discussed important details about how the committee works and discussed future priorities of the committee: eg. POEMS syndrome, more studies with cytogenetics information and consolidation/maintenance of data. 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**

The accrual summary provides information about the number of patients available in the registration level and research level for potential studies. As of December 2016, 65,659 plasma cell disorder cases were reported at the registration level and 12,131 cases at the research level to the CIBMTR for (first) autologous transplant. For first allogeneic transplants, these numbers are 4,674 cases and 1,921 cases respectively.

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

The following publications and presentations came from the committee’s work during this year.


k. **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. *Oral presentation at BMT Tandem in Orlando, Feb 2017.*

4. **Studies in progress**

Dr. D’Souza introduced the following studies in progress and goal by July 2017:

**MM14-03:** Trends in survival outcomes among patients relapsing early after autologous stem cell transplantation for multiple myeloma (S Kumar/ A Dispenzieri) The study proposed to determine if overall survival from the time of relapse has improved over time among patients relapsing early after autologous stem cell transplantation for multiple myeloma. Manuscript is underway. The goal of the study is to submit manuscript by July 2017.

**MM15-02:** Post-relapse Survival Rates after Tandem Auto-HSCT vs. Auto/Allo-HSCT in Multiple Myeloma (M Sharma/A Krishnan/B Bruno/N Tank) The primary purpose of this study is to compare Tandem Auto-HSCT and AUTO/ALLO HSCT for post-relapse patients and determine TRM, relapse/progression-free survival and overall survival in patients with MM who underwent PB autologous stem cell transplant. The goal of the study is to submit manuscript after 2017 BMT Tandem meeting.

**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. This was a combined study of ST1301 and proposal1311-09. We looked into our
database in Aug 2014 and realized that the newer version of research level disease from (version
2008) needs to be updated among 200 records. The protocol is in progress. The goal of the study is to
work on data file preparation after 2017 BMT Tandem meeting.

MM16-01 Validation of R-ISS in real world population of MM undergoing HDM and evaluate
outcomes of autologous hematopoietic cell transplantation in patients with high risk multiple
myeloma using the international myeloma working group 2014 and 2015 criteria (S Kumar/E Scott).
This study will assess the newly developed R-ISS and 2014 IMWG staging on patients from the
CIBMTR database and validate the prognostic significance (response rate, progression free and overall
survival) of the 2014 IMWG and R-ISS staging systems in patients that received an autologous
hematopoietic cell transplant for multiple myeloma registered with the CIBMTR. Protocol
development is in progress. The goal of the study is to complete analysis by July 2017.

MM16-02 Alternative Donor Allogeneic Hematopoietic Transplantation Strategies for Multiple
Myeloma in Adult Patients: Comparing Umbilical Cord Blood versus Haploidentical Related Donor
Transplantation (A Kanate/N Shah/Q Bashir/S Ciurea) Protocol Development is underway. This study
will compare the post-transplantation outcomes in patients with MM undergoing UCB versus
haploidentical allo-HCT. The goal of the study is to finalize data file by July 2017.

MM16-03 Third Stem Cell Transplant (SCT) for Multiple Myeloma: An analysis from the CIBMTR
database (R Nath). This study hypothesize the evaluation of the frequency, disease and transplant
characteristics and outcomes of patients undergoing third SCT for multiple myeloma will help define
its role in myeloma management in the era of novel agents. Protocol development is in progress. The
goal of the study is to finalize protocol by July 2017.

5. Future/proposed studies
This year, we received 15 proposals, 8 of which were invited to present at the meeting (including 1
merged proposal with similar interest).

Multiple Myeloma:

   a. PROP 1611-50 Outcomes of patients with t(11;14) genetic abnormalities in multiple myeloma
      (Liana Nikolaenko/Amrita Krishnan)

   Dr. Nikolaenko introduced the rationale and specific aims of the proposal. The primary aim of
   this proposal is to investigate the true impact of t(11;14) genetic abnormality in MM and
   possibly re-stratify disease risk with this translocation. The estimated eligible number of
   patients for this proposal is 345. There were some concerns about the data that is captured by
   CIBMTR forms and the accuracy of reported cytogenetic abnormality. One of the members
   suggested that FISH and chromosomal test methods should be separated for the cytogenetic
   results. Dr. Hari mentioned that since 2013 we have established auditing process to the
cytogenetic results. Another member suggested that disease status should be considered in
both prior and post-transplant. There was concern about possible confounding results between
patients with t(11;14) abnormality only vs. t(11;14) + other abnormalities. Also the median
follow up time for the patients (27 months) was said to be too low to prove the proposal’s
hypothesis. Due to the concerns mentioned, this proposal did not receive a high enough
priority score for acceptance and was not accepted.
b. **PROP 1611-106** Prevalence of cytogenetic abnormalities by patient race in multiple myeloma and outcomes after stem cell transplant (Sikander Ailwadhi/Shaaji Kumar/Parmeswaran Hari)

Dr. Ailwadhi presented the proposal on behalf of the team. The purpose of the study is to evaluate the prevalence of various cytogenetic abnormalities in patients with multiple myeloma belonging to different racial subgroups and compare the outcomes of patients with different cytogenetic myeloma risk categories from various races after an autologous stem cell transplant. There was some concern about possible confounding between covariates other than race that may account for the difference in outcomes (ex. socioeconomic factors). One of the members noticed that the definition for high risk cytogenetics did not comply with IMWG specifications. Another member wanted to know if it was possible not to limit the study to US patients but to do it internationally, but Dr. Hari said that different countries collect the data in different ways, and, especially with cytogenetics, it will be too messy to work with. The number of patients in the Hispanic group was felt to be too small to do any meaningful analysis. This proposal did not receive a high enough priority score for acceptance and was not accepted.

c. **PROP 1611-34** Exploring the transplant center volume outcomes relationship in MM (Saurabh Chhabra/Binod Dhakal)

Dr. Chhabra presented the proposal on behalf of the team. The purpose of the study is to evaluate overall survival and progression free survival in myeloma patients receiving autologous transplantation as a function of the volume of the transplant center. Although the members agreed that there is evidence of volume and outcome relationship, there was some concern about other possible confounding variables that could explain the difference in outcomes other than the volume of transplants (ex. socioeconomic factors, etc.). It was also mentioned that post-transplant therapy would be an important variable to consider since this will affect the outcomes of the patients and might have a strong effect on the result of the study. Some members proposed that transplant-related mortality as opposed to PFS/OS were better markers of transplant center effect on outcomes but the concern was that TRM after myeloma autotransplant is small to start with. This proposal did not receive a high enough priority score for acceptance and was not accepted.

**Plasma Cell Leukemia:**

**d. Proposal 1609-02/1611-40/1611-53/1611-133** Hematopoietic Cell Transplantation for Primary Plasma Cell Leukemia in the Era of Novel Agents (Saulius Girnius/Sagar Patel/Lohith Bachegowda/Binod Dhakal)

Dr. Girnius presented the proposal on behalf of the team. The purpose of the study is to evaluate transplant outcomes of adult patients (≥ 18 years) with primary plasma cell leukemia (pPCL) who underwent autologous HCT or allogeneic. The primary aim is to determine the overall survival, progression free survival, relapse, and non-relapse mortality in patients with pPCL after HCT. The proposal hypothesize that in the era of novel agents and improved supportive care, overall survival has improved in those treated with hematopoietic cell transplantation for primary plasma cell leukemia. One of the concerns for this proposal is that there is an ongoing EBMT study analysing the same hypothesis and it was presented in ASH last year (2016) as an oral. It was clarified that the purpose of the study was to compare outcomes of pPCL patients Auto vs. Allo, not between pPCL patients vs. non-pPCL patients. Another
concern was that there were very few CRF patients. This proposal received the highest vote and was therefore accepted by the committee members and leadership. One of the major concerns about this proposal was that in order to have a meaningful study, we would need to obtain supplemental data from the centers (i.e. cytogenetic, extramedullary disease at diagnosis, induction regimen, number of cycles), which would add at least a year to gather the information needed.

Amyloidosis:

e. PROP 1611-153 The impact of bortezomib-based induction therapy vs no induction therapy on outcomes for light chain amyloidosis (Robert Cornell/ Luciano Costa/ Stacey Goodman)

Dr. Cornell presented the proposal on behalf of the team. The purpose of the study is to compare pre-transplant bortezomib-based induction therapy with no induction therapy prior to autologous hematopoietic cell transplantation and determine pre-transplant disease status, mortality rates, day-100 post-transplant disease status, TRM, hematopoietic recovery rates, relapse/progression progression-free survival and overall survival in patients with light chain (AL) amyloidosis. There was some concern about the follow up of patients, considering the median was 13 months for patients with bortezomib and 25 month for patients with no bortezomib. It was suggested that for a more robust study it would be better to have longer period of follow up time. There were also suggestions to compare melphalan doses, and to divide patients in groups by time from diagnosis to transplant (short time vs. long time). This proposal received the second highest vote. The WC leadership felt that if the PCL study would be delayed by a year owing to gathering of supplemental data, this study should also be accepted.

The working committee meeting ended at 2:12PM. The committee leadership met with members of the committee and answer questions.

A total of 700 hours of MS biostatistician time was allocated to our WC for the 2017-2018 academic year. Thus, we will be able to accept 2 new studies.
## Working Committee Overview Plan for 2017 - 2018

<table>
<thead>
<tr>
<th>Project Code</th>
<th>Description</th>
<th>Status</th>
<th>Goal</th>
<th>Completion Hours</th>
<th>Statistical Hours</th>
<th>Fiscal Year Correspondence</th>
</tr>
</thead>
<tbody>
<tr>
<td>MM14-01</td>
<td>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)</td>
<td>In protocol development</td>
<td>Complete analysis by July 2017</td>
<td>310</td>
<td>310</td>
<td>2017-2018</td>
</tr>
<tr>
<td>MM14-02</td>
<td>Autologous hematopoietic cell transplantation in patients with renal insufficiency (A Mahindra)</td>
<td>Manuscript preparation</td>
<td>Submit manuscript by July 2017</td>
<td>10</td>
<td>10</td>
<td>2017-2018</td>
</tr>
<tr>
<td>MM14-03</td>
<td>Trends in survival outcomes among patients relapsing early after autologous stem cell transplantation for multiple myeloma (S Kumar/ A Dispenzieri)</td>
<td>Manuscript preparation</td>
<td>Submit manuscript by July 2017</td>
<td>30</td>
<td>30</td>
<td>2017-2018</td>
</tr>
<tr>
<td>MM15-02</td>
<td>Post-relapse Survival Rate after Tandem Auto-HSCT vs. Auto/Allo-HSCT in Multiple Myeloma (M Sharma/A Krishnan/B Bruno/N Tank)</td>
<td>Manuscript preparation</td>
<td>Submit manuscript by July 2017</td>
<td>10</td>
<td>10</td>
<td>2017-2018</td>
</tr>
<tr>
<td>MM16-01</td>
<td>Validation of R-ISS in real world population of MM undergoing HDM and evaluate outcomes of autologous hematopoietic cell transplantation in patients with high risk multiple myeloma using the international myeloma working group 2014 and 2015 criteria (S Kumar/E Scott)</td>
<td>Finalize analysis by July 2017</td>
<td>Submit abstract to ASH</td>
<td>150</td>
<td>150</td>
<td>2017-2018</td>
</tr>
<tr>
<td>MM16-03</td>
<td>Third Stem Cell Transplant (SCT) for Multiple Myeloma: An analysis from the CIBMTR database (R Nath)</td>
<td>Finalize proposal and present at statistical meeting</td>
<td>Submit proposal</td>
<td>210</td>
<td>210</td>
<td>2017-2018</td>
</tr>
<tr>
<td>MM17-01</td>
<td>Hematopoietic Cell Transplantation for Primary Plasma Cell Leukemia in the Era of Novel Agents (Saulius Girnius/Sagar Patel/Lohith Bachegowda/Binod Dhakal)</td>
<td>Supplemental data and finalize data collection by July 2018</td>
<td>Data file completion</td>
<td>310</td>
<td>60</td>
<td>2017-2018</td>
</tr>
<tr>
<td>MM17-02</td>
<td>The impact of bortezomib-based induction therapy vs no induction therapy on outcomes for light chain amyloidosis (Robert Cornell/ Luciano Costa/ Stacey Goodman)</td>
<td>Data file completion by July 2018</td>
<td>Data file completion</td>
<td>210</td>
<td>240</td>
<td>2017-2018</td>
</tr>
</tbody>
</table>
Oversight Assignments for Working Committee Leadership (March 2017)

Amrita Krishnan: MM14-03: Outcomes after early relapse autoHCT for MM
Tomer Mark: MM16-01: Validation of R-ISS in real world population of MM
Cristina MM14-02: Serum creatinine <2g/dl vs. >2g/dl for autoHCT MM
Gasperetto: MM15-02: Post-relapse Survival on Tandem Auto vs. Auto/Allo tx in MM
MM16-03: Third HCT for MM
Yago Nieto: MM14-01: High dose chemotherapy and autoHCT for germ cell tumors
MM16-02: CB vs haplo HCT for MM
Shaji Kumar: MM17-01: HCT for primary plasma cell leukemia
MM17-02: Bortezomib induction therapy for light chain amyloidosis