MINUTES AND OVERVIEW PLAN
CIBMTR WORKING COMMITTEE FOR GRAFT SOURCES & MANIPULATION
Orlando, FL
Thursday, February 20, 2020, 2:45 – 5:15 pm

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1. Introduction

Dr. Brunstein opened the meeting at 2:45 pm by welcoming the working committee members for attending the Graft Sources and Manipulation Working Committee (GSWC) meeting. He disclosed the funding and conflict of interest information for the CIBMTR. He introduced the GSWC's leadership, welcomed the incoming chair Dr. Milano and thanked Dr. Bashey for his contributions to the committee over the years. Dr. Brunstein asked for and received approval of 2019 meeting minutes. He then discussed working committee membership, goals, proposal selection, voting and rules of authors. Dr. Brunstein described the differences in data sources at the CIBMTR, trends in donor types in the United States, and the Advisory Committee metrics. Dr. Brunstein invited Dr. Bashey to the podium.

2. Published/ submitted papers and studies in progress

a. Dr. Bashey invited Dr. Fatobene to present GS18-03: *Comparison of outcomes of reduced intensity transplantation in lymphoma patients using haploidentical related donors vs unrelated cord blood* (*Journal of Clinical Oncology.* In Press). Dr. Bashey then invited Dr. Grunwald to present GS18-04: *Comparison of Outcomes with Haploidentical and Matched Unrelated Donors for Hematopoietic Stem Cell Transplantation in Myelodysplastic Syndromes* (Poster at ASH 2019, manuscript preparation). Dr. Bashey recommended committee members stop by the Graft Sources Poster Session on Saturday evening to see the poster for GS19-01: *Comparison of myeloablative haploidentical or umbilical cord blood transplantation for pediatric and adult patients with acute leukemia*. Dr. Bashey invited Dr. McNiece to introduce proposals.

3. Future/proposed studies

a. **PROP 1910-10** This proposal was seeking to compare outcomes between bone marrow and peripheral blood grafts and cell dose in myelofibrosis cases in matched related donors and matched unrelated donors. Dr. Salas presented the proposal.
The CIBMTR identified 621 cases of adults with myelofibrosis who received a peripheral blood transplant from a matched related or unrelated donor between 2008 and 2018. There was CD3+ infusion information available for 511 of these cases.
The primary objective of this proposal is to compare efficacy of graft sources. Due to low numbers of bone marrow grafts available and the proposal aimed to include a descriptive analysis of these cases only. The secondary aim of this study is to explore the optimal cell dose in each graft source. This became the primary aim as the proposal was limited to peripheral blood cases.
There was discussion on the importance of splenectomy and spleen size in outcomes of myelofibrosis cases. There was a recommendation to include the CD3 and TNC dose. There was a comment that pre-transplant management, specifically the Jakafi inhibitor and maintenance would be an important factor to consider and if we collect this information. Andrew informed the committee that we collect splenectomy and Jakafi inhibitor information. Dr. Bashey recommended we remove donor types with small numbers if the proposal is accepted to decrease heterogeneity in the study population.

b. **PROP 1911-06** This proposal was seeking to create primary graft failure (PGF) scoring systems for UCB and haploidentical with PTCY for adults with hematologic malignancies. Dr. Nathan presented the proposal.
The CIBMTR identified 1753 cases first allo transplants for adults with a hematologic malignancy (n=1435 haploidentical with PT-Cy, n=61 UCB, and n=257 dUCB) between 2014 and 2019.
The primary aim of the study is to create scoring systems for PGF for each graft source. The secondary aims are to predict PGF following transplant of Haploidentical with PT-Cy and UCB.
There was some discussion of donor specific antibodies. There was discussion if it would be important to add secondary graft failure to the study and the differences in determinants of primary and secondary graft failure. There was a question about how PGF was defined and Dr. Nathan responded that PGF is achieving counts greater than 500 for three consecutive days and by donor chimerism decreasing after initial engraftment. Dr. Brunstein asked if this study would be helpful if chimerism was not available. Andrew St. Martin commented that chimerism data is not consistent by cell type or time point. Dr. Bashey commented specific cell types. There was discussion on how many graft scoring systems would be necessary in this proposal, by graft source or donor type. There was a comment that chimerism is essential to the study and it does not have to be consistent information to be valid.

c. **PROP 1911-13** This proposal was seeking to compare all donor types, graft sources, DRI and conditioning regimens to identify the ideal donor for each transplant after identifying the "optimal goal" for each adult patient eligible for transplant for AML/MDS and ALL. Dr. Varma presented the proposal.
The CIBMTR identified 7065 cases who underwent their first allo transplant for AML, ALL, or MDS between 2012 and 2018 (3832 MAC, 3233 RIC/NMA).
The primary aim of the study was to look at non-relapse mortality, relapse, disease-free survival, overall survival, secondary malignancy at 5 years and GRFS. The secondary aim was to stratify the above outcomes by conditioning intensity for each donor type.
A comment was made about the nuance of donor selection, conditioning, GVHD prophylaxis and that it may need to be further stratified by conditioning regimen. A comment was made about other factors of importance, in order to individualize selection a large cohort would be necessary. A comment was made regarding the importance of mMUD and identifying PT-Cy cases as a separate group entirely. There was a question regarding the feasibility of the study and commented on the need to account for all factors. Dr. Varma responded that it is important to start somewhere, to identify donors and stratify by HCT-CI and conditioning.

d. **PROP 1911-170** This proposal was seeking to compare outcomes after a primary graft failure and associated salvage transplant for adults with hematologic malignancies. Dr. Ali presented the proposal.
The CIBMTR identified 631 adults with AML, ALL or MDS with primary graft failure after the first allogeneic transplant between 2008 and 2019, 147 of these cases went on to a second transplant.
The primary aim of this proposal was to examine 100-day and 1-year overall survival following salvage transplant by graft source. Secondary aims were to compare time to second transplant, relapse, and non-relapse mortality after primary graft failure and conditioning regimens for salvage transplant.
There was discussion about the inclusion of non-malignant diseases and myelofibrosis cases in the study. There was a comment that inclusion of non-malignant cases would introduce more heterogeneity to the study and the primary outcomes are related to relapse. A comment was made regarding the evaluation of early deaths which are not considered graft failure. Dr. Bashey commented on the second more cases being necessary. With 147 cases of salvage transplant, would there be sufficient cases to adjust for donor types and graft sources. There was a question regarding descriptive analysis instead of multivariate analysis. Additionally, the inclusion of lymphoid cases might be important although the disease matters. There was a recommendation to use EBMT and European cases to support the study.

e. **PROP 1911-20** The proposal seeks to compare outcomes of dUCB and HLA-Mismatched unrelated donors with PT-Cy for adults with hematologic malignancies. Dr. Farhadfar presented the proposal.
The CIBMTR identified 402 cases of adults with malignant disease (72 mMUD with PT-Cy, 15 dUCB 6/6 HLA match, 110 dUCB 5/6 HLA match, 205 dUCB ≤4/6 HLA match) transplanted between 2016-2018).
The primary aim of the study is to compare overall survival. The secondary aims include relapse free survival, transplant related mortality, time to engraftment, acute and chronic GVHD, and rates of early infections.
Dr. Soiffer commented that there was a small and heterogeneous population with short follow-up. Dr. Farhadfar recommended the years be increased. There was a comment that Hopkins has a large study ongoing and that the TED level might be an appropriate change. There was a comment on the low median follow-up of mMUD and noted a similar study was accepted 2 years ago. There was also a comment that PT-Cy and mMUD is a recent phenomenon and that may limit the available years.

f. **PROP 1911-39** This proposal seeks to compare outcomes from the CTN 1101 clinical trial cohort to a contemporaneous CIBMTR registry cohort. Dr. Brunstein presented this proposal.
The CIBMTR identified 875 adults transplanted for AML (CR 1), ALL (CR1), Non-Hodgkin Lymphoma or Hodgkin Lymphoma with TBI/Cy/Flu conditioning regimen (319 BM, 409 PBSC, 147 dUCB) between 6/19/2012 and 6/30/2018.
The primary aim of this study is to compare overall survival at 2 years post-transplant. Secondary aims include hematopoietic recovery, graft failure, acute and chronic GVHD, relapse, non-relapse mortality and progression-free survival.
There was discussion on the importance of including cord blood as it is less used. Dr. Brunstein recommended inclusion in the study as it was the contemporaneous nature of the registry cohort. There was a comment questioning the bias and graft type preference of centers.

g. **PROP 1911-19 / PROP 1911-210** This proposal seeks to compare the impact of cell dose for adults with hematologic malignancies who received a peripheral blood graft from a haploidentical donor. Dr. Farhadfar presented this proposal.
The CIBMTR identified 742 cases of adults who received a haploidentical transplant with PT-Cy with a peripheral blood graft for lymphoma/leukemia between 2013 and 2018.
The primary aim was to examine overall survival. The secondary aims include time to engraftment, acute and chronic GVHD, non-relapse mortality and relapse-free survival.
Dr. Bashey commented that there may be center issues when examining cell dose and haploidentical transplants as many centers may cap/limit the dose infused. A comment was made that all CIBMTR studies check for a center effect. A comment was made regarding the collection of CRS which is not

collected at this time. A comment was made on the importance of the CD3 dose and the conditioning intensity. A comment was made that high cell dose has issues as does low cell dose- different issues potentially.

Meeting adjourned at 4:45 pm.

Working Committee Overview Plan for 2020-2021							
Study number and title	**Current status**	**Goal with date**	**Total hours to complete**	**Total hours to goal - July 2021**	**Hours allocated to 6/30/2020**	**Hours allocated 7/1/2020-6/30/2021**	**Total Hours allocated**
GS18-01: Comparison of outcomes after HCT from haploidentical donor with PT-Cy, MUD with PT-Cy, and MUD with CNI	Datafile prep	Manuscript prep – June 2020 Submitted – July 2021	160	160	90	70	160
GS18-02: Impact of race on relapse after haploidentical with PT-Cy vs cord blood	Submitted	Submitted – April 2020 Published – July 2021	0	0	0	0	0
GS18-04: Haploidentical donor with PT-Cy vs MUD for MDS	Manuscript preparation	Published – July 2021	10	20	10	10	20
GS19-01: Comparison of myeloablative haplo or CB in Acute Leukemia	Manuscript preparation	Published – July 2021	10	20	10	10	20
GS19-02: Graft Failure in MDS and Acute Leukemia with PT-Cy	Protocol pending	Data file preparation – July 2020	330	260	100	160	260

		Analysis- October 2020 Manuscript prep – July 2021					
GS19-03: Impact of G-CSF on in-vivo T-cell depleted Allogeneic Hematopoietic Cell Transplantation	Data file preparation	Manuscript preparation – July 2020 Submit – October 2020	170	170	100	70	170
GS20-01: RIC dUCB and haplo CTN 1101 cohort compared to CIBMTR contemporaneous registry cohort	Protocol pending	Protocol development preparation – July 2020 Manuscript prep – July 2021	330	260	0	260	260

Oversight Assignments for Working Committee Leadership (March 2020)	
Ian McNiece	**GS18-01:** Comparison of outcomes after HCT from haploidentical donor with PT-Cy, MUD with PT-Cy, and MUD with CNI.
Ian McNiece	**GS18-04:** Haploidentical donor with PT-Cy vs MUD for MDS.
Claudio Brunstein	**GS19-01:** Comparison of myeloablative haplo or CB in Acute Leukemia
Claudio Brunstein	**GS19-02:** Graft Failure in MDS and Acute Leukemia with PT-Cy
Ian McNiece	**GS19-03:** Impact of G-CSF on in-vivo T-cell depleted Allogeneic Hematopoietic Cell Transplantation
Filippo Milano	**GS20-01:** RIC dUCB and haplo CTN 1101 cohort compared to CIBMTR contemporaneous registry cohort