Not for publication or presentation

MINUTES AND OVERVIEW PLAN
CIBMTR WORKING COMMITTEE FOR GRAFT SOURCES & MANIPULATION
Salt Lake City, UT
Monday, April 25, 2022, 12:15 pm – 1:45 pm MDT

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1. Introduction

Dr. Brunstein opened the meeting at 12:15 by welcoming the work committee members to the Graft Sources and Manipulation Working Committee (GSWC) meeting. He disclosed the funding and conflict of interest information for the working committee leadership and for the CIBMTR. He introduced the GSWC's leadership and welcomed Dr. Benjamin to the committee. Dr. Brunstein thanked Dr. Eapen (past Scientific Director) and Dr. McNiece for their many contributions over the years. He then discussed the working committee membership, goals, proposal selection, voting and rules of authorship. Dr. Brunstein invited Mr. Spellman to review the current portfolio and presentations.

2. Presentations, published or submitted papers

Mr. Spellman highlighted the committees' recent publications and presentations and invited Dr. Milano to introduce the proposal presenters.

3. Future/proposed studies

a. **PROP 2110-79/PROP 2110-125/PROP 211-284/PROP 2110-300:** This combined proposal seeks to compare outcomes for haploidentical hematopoietic cell transplants (HCT) using post-transplant cyclophosphamide (ptCy) using a first-degree or non-first-degree related donor.

The CIBMTR identified n=3,312 cases of adults with malignant disease who received their first allogeneic transplant with bone marrow or peripheral blood between 2008 and 2019. There were n=152 with non-first degree related donors and n=3,160 cases with first-degree related donors.

The primary objective of this proposal is to compare the impact of relatedness on overall survival. The secondary outcomes of interest in this proposal are progression-free survival, relapse, non-relapse mortality and acute and chronic GVHD.

There was discussion on the opportunity of a third donor group to explore half-siblings (n=323). The overall goal of the study is to assess the potential to expand the related donor pool beyond first degree relatives. Dr. Soiffer asked if there are sufficient numbers to adjust for the age discrepancy where the donor age is younger for first degree related donors. The GSWC Statistical Director, Dr. Zhang,

indicated that if there is little to no overlap we cannot adjust. There was also discussion on the collection of HLA data from donors that are tested for match degree but not used for transplant. Mr. Spellman addressed that this information is not collected at the CIBMTR.

b. **PROP 2110-113/ PROP 2110-248/ PROP 2110-340:** This combined proposal seeks to evaluate the optimal donor selection in second allo HCT in cases with relapsed malignant disease.

The CIBMTR identified n=1232 cases of adult second allo transplants after previous transplant with relapse between 2014 and 2019. Of these cases, n=970 had the same donor in the second transplant.

The primary aim of the proposal is to evaluate impact of donor selection on leukemia-free survival in the pediatric and adult recipients for second allo transplant. Secondary aims include examining the cell dose for second transplant, same or different haplo donor, and GVHD development after first transplant impact on relapse in the second transplant.

There was brief discussion that focused on the lack of prospective data on the choice of an optimal donor for second allo HCT and the potential importance of measurable residual disease (MRD) data for evaluation. As much of the data is CRF level, MRD assessments should be available.

c. **PROP 2110-250:** This proposal seeks to examine the impact of CD34+ cell dose in peripheral blood transplants with matched sibling and unrelated donors.

The CIBMTR identified n=24,757 cases of adults with first allo peripheral blood HCT for malignant disease between 2008 and 2019.

The primary aim of this proposal is to examine CD34+ cell dose impact on overall survival. Secondary aims are to examine impact on engraftment, relapse, non-relapse mortality, and treatment related mortality.

There was a question about the type of cell dose (cryo vs infused dose). It was clarified that infusion dose would be used. Dr. Kanakry brought up the discussion around institutional practices and heterogeneity of doses. The study would examine center effect to adjust for any institutional practice differences. Dr. Brunstein discussed the impact of actual and ideal absolute infused dose.

d. **PROP 2110-301:** This proposal aims to identify the optimal cell dose for haplo peripheral blood HCT with ptCy for GVHD prophylaxis

The CIBMTR identified n= 1729 haploidentical cases transplanted for AML, ALL or MDS reported to the CIBMTR (2014-2019) who received post-transplant cyclophosphamide for GVHD prophylaxis.

The primary aim is to examine progression-free survival with CD34+, CD3+ and TNC to determine impact of the cell dose. Secondary aim is to examine cell dose on OS, relapse, non-relapse mortality, GVHD, engraftment and GVHD-free/relapse-free survival.

Dr. Brunstein asked if it would be important to examine days of collection for the patients and the age of the donor. Dr. Elmariah agreed if that information was available it would be valuable to include in the study. Study leadership does not believe the registry collects the length of product collection. There was also discussion on the inclusion of CRS, the data is available for more recent transplants. Dr. Strouse asked about the urgency of a transplant being a confounding factor. Dr. Elmariah stated this might be a minor issue in the analysis, might be a center related decision with lower cell doses. Dr. Brunstein added the goal is to evaluate certain cell thresholds to help guide practice.

4. Future/proposed studies to be presented at the CIBMTR Collaborative Working Committee Study Proposals Session

a. **PROP 2110-50/PROP 2110-317:** Optimizing HLA Matched Sibling versus Alternative (Well-Matched Unrelated and Haploidentical) Donor Selection: Update Including Donor Age and HLA-DPB1 Match Status in Recipients of Allogeneic Hematopoietic Cell Transplantation (K Nath/ B Shaffer/ H Choe)

5. Other Business

a. **Discussion on Future Research Priorities:** *Dr. Milano facilitated a discussion with the working membership regarding future areas of focus for the GSWC. The role of CD34 boosts was discussed and concerns raised about the completeness of the data reported to CIBMTR. Dr. Milano invited the committee membership to submit proposals for consideration in the next review cycle.*

Mr. Spellman thanked everyone for attending and then closed the session after reminding everyone to vote and attend the collaborative proposal session. The session closed at 1:15pm.

Working Committee Overview Plan for 2022-2023

Study Number and Title	Current Status	Chair Priority
GS19-02: Graft Failure in MDS and Acute Leukemia with PT-Cy	Manuscript preparation	1
GS22-01: HLA Matched Sibling versus Alternative Donor Selection: Allogeneic HCT	Protocol pending	1

Working Assignments for Working Committee Leadership (May 2022)

Claudio Brunstein	**GS19-02:** Graft Failure in MDS and Acute Leukemia with PT-Cy
Filippo Milano	**GS22-01:** HLA Matched Sibling versus Alternative Donor Selection: Allogeneic HCT