Not for publication or presentation

MINUTES AND OVERVIEW PLAN
CIBMTR WORKING COMMITTEE FOR GRAFT SOURCES & MANIPULATION
Orlando, FL
Friday, February 17, 2022, 12:00 p.m. – 2:00 p.m. (EST)

Co-Chair:	**Claudio Brunstein, MD, PhD, Cleveland Clinic Foundation, Cleveland, OH; Telephone: 216-444-9310; E-mail: brunst@ccf.org**
Co-Chair:	**Filippo Milano, MD, PhD, Fred Hutchinson Cancer Center, Seattle, WA; Email: fmilano@fredhutch.org; Phone: 206-667-5925**
Co-Chair	**Cara Benjamin, PhD, University of Miami, Miami, FL; Email: c.benjamin3@miami.edu; Phone: (305) 243-5534**
Scientific Director:	**Stephen Spellman, MBS, CIBMTR/NMDP, Minneapolis, MN; Telephone: 763-406-8334; E-mail: sspellma@nmdp.org**
Statistical Director:	**Mei-Jie Zhang, PhD, CIBMTR Statistical Center, Milwaukee, WI; Telephone: 414-456-8375; E-mail: meijie@mcw.edu**
Statistician:	**Molly Allbee-Johnson, MPH, CIBMTR Statistical Center, Milwaukee, WI; Telephone: 414-805-2258, E-mail: mallbeejohnson@mcw.edu**

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1. Introduction

Mr. Spellman opened the meeting at 12:05 by welcoming the working committee members to the Graft Sources and Manipulation Working Committee (GSWC) meeting. He thanked Dr. Brunstein for his contributions to the working committee and welcomed Dr. Mehta to the committee leadership. Mr. Spellman invited Dr. Brunstein to the podium. Dr. Brunstein reviewed the membership rules, goals, expectations, and limitations of the working committee. He discussed the rules of authorship for studies and current data sources. Dr. Brunstein highlighted the publicly available datasets, new Patient Reported Outcomes (PRO) data collection, and the upcoming collaborative working committee session. He invited Dr. Benjamin to the podium. Dr. Benjamin discussed scoring process and prioritization of studies. Dr. Benjamin invited Dr. Milano to introduce the first proposal.

2. Proposals

Future/proposed studies

a. **PROP 2210-84/ PROP 2210-286:** This combined proposal seeks to compare outcomes for haploidentical hematopoietic stem cell transplants (HCT) using post-transplant cyclophosphamide (ptcy) using a first-degree or non-first-degree relative.

The CIBMTR identified n=5,587 cases of adults with malignant disease who received their first allogeneic (allo) transplant with a bone marrow or peripheral blood graft between 2008 and 2019. There were n=154 non-first degree relatives, n=4,603 first-degree relatives and n=830 half-siblings identified.

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 disease-free survival, GVHD-relapse free survival,

chronic GVHD-relapse-free survival, non-relapse mortality, relapse, GVHD, cause of death, graft failure, immune reconstitution and CMV reactivation.

The session was opened for questions. Dr. Milano asked Dr. Munshi if her institution utilizes non-first degree haploidentical relatives for transplant. Dr. Munshi confirmed that if insurance allows them to continue to look at matches, they will.

b. **PROP 2210-121:** This proposal seeks to evaluate the optimal donor selection for second allo HCT in cases with relapsed malignant disease.

The CIBMTR identified n=1,779 cases of second allo transplants for malignant disease after relapse from a previous allo transplant between 2008 and 2019. Of these cases n=405 had the same donor for their second allo transplant as their first.

The primary aim of the proposal is to evaluate the impact of donor selection in second allo transplant on leukemia-free survival in pediatric and adult recipients. Secondary outcomes of interest include overall survival, relapse, non-relapse mortality, graft failure and GVHD for two cohorts; unrelated cord blood grafts (by cell dose) and cases with haploidentical donor (same vs different donors). Additionally, to evaluate GVHD impact on incidence of relapse after second transplant by same or different donor.

The session was opened for questions. Discussion around the design of this study, subgroup analysis for different donor groups in first transplant including sibling transplants. There was discussion regarding the collection and evaluation of chimerism in the first transplant. Time from first transplant to relapse was recommended to be evaluated. Dr. Brunstein discussed use of ATG in cord blood transplants and importance of considering in the analysis.

c. **PROP 2210-228:** This proposal seeks to evaluate the impact of adherence to published cord blood selection guidelines on patient outcomes.

The CIBMTR identified cases of first allo transplants for AML, ALL or MDS who received a single or double cord blood graft between 2005-2019 (single cord: n=760 total cases; n=257 did not adhere to the cell dose guidelines, n=270 adhered, n=233 did not report information on cell dose; double cord: n=2,832, n=1,287 did not adhere, n=596 adhered, n=949 did not report information on cell dose for some or all measures).

The primary aim is to compare overall survival, treatment related mortality, relapse, and disease-free survival for transplants that adhered to the guidelines to those that did not (including cell dose, HLA matching, conditioning intensity and GVHD prophylaxis regimens). The secondary aims are to compare engraftment, GVHD incidence, GVHD-Relapse-free survival between adherence groups.

The session was opened for questions. There was discussion about the evaluation of grafts that did not adhere to the guidelines regarding any documentation that explained poor collection This information is not collected by the CIBMTR. Dr. Brunstein asked Dr. Zhang to comment on the impact of adjusting for center volume by cord blood transplants done annually. Dr. Zhang stated random center effect would be evaluated and adjusted for in the model. Center effect is the random effect but agreed that center volume can be adjusted in models. High resolution HLA typing was discussed and could be reviewed for subset that has information available. Dr. Scaradavou recommended transplant period be considered as there are improvements over time based on changes in practice and support. Dr. Mehta asked if

pediatric cases were included in the inclusion criteria. Dr. Metheny noted that pediatric cases were included in the population selection.

d. **PROP 2210-272:** This proposal aims to evaluate the impact of ex vivo expanded cord blood grafts on outcomes compared to non-ex-vivo expanded (conventional) cord blood and haploidentical grafts following myeloablative conditioning alloHCT.

The CIBMTR identified n=280 ex vivo expanded cord blood grafts, n=5,555 conventional cord blood grafts and n=6586 haploidentical transplanted for malignant diseases between 2005-2019.

The primary aim is to compare overall survival of ex-vivo expanded and conventional cord blood and haploidentical grafts in the myeloablative transplant population. The secondary aims are to compare progression-free survival, non-relapse mortality, relapse, and engraftment between groups.

The session was opened for questions. The haplo group was noted to be an older patient population that would need to be adjusted for as a comparison group. Dr. Milano discussed that the ex-vivo expanded cord cohort may potentially be highly selected for clinical trial inclusion compared to conventional cord that may or may not be following the guidelines (see PROP2210-228 above). Dr. Mehta recommended comparison of the ex-vivo expanded cord blood to those that met the cord blood selection guidelines to ensure comparable groups. The committee recommended expanding the patient ages to include pediatric cases. Dr. Metheny requested clarification on the diseases included and that there were very few pediatric cases were available and not included here. The audience recommended that haploidentical transplants be restricted to peripheral blood for this comparison.

3. Other Business

Mr. Spellman presented on the current state of stem cell boost collection in the CIBMTR and the challenges of evaluating stem cell boosts. Dr. Soiffer agreed the current collection is inadequate to answer the questions for the community. It was discussed that these events could potentially be captured in the same way as DLIs. Dr. Mehta asked if the coding for insurance is related to the current capture of these data. Indications for boost include chimerism issues, relapse, and consolidation remission after relapse. Discussion that this would be important to explore further. Dr. Brunstein asked about the goal of the infusion, which is captured. Boost is known to be variable in practice across centers. Discussion that data managers might benefit from additional education around these matters.

Mr. Spellman reminded members to vote and closed the meeting at 1:20pm.

Working Committee Overview Plan for 2023-2024		
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 Development	2
GS23-01: Impact of donor source in second allogeneic hematopoietic cell transplant in patients with acute leukemia/MDS who relapsed after prior allograft during the current era (2014-2020).	Protocol pending	4
GS23-02: Impact of adherence to cord blood guidelines.	Protocol pending	3

Oversight Assignments for Working Committee Leadership	
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
Parinda Mehta	**GS23-01:** Impact of donor source in second allogeneic hematopoietic cell transplant in patients with acute leukemia/MDS who relapsed after prior allograft during the current era (2014-2020).
Cara Benjamin	**GS23-02:** Impact of adherence to cord blood guidelines.