Not for publication or presentation

MINUTES AND OVERVIEW PLAN
CIBMTR WORKING COMMITTEE FOR GRAFT-VERSUS-HOST DISEASE
San Antonio, TX
Friday, February 23, 2024 1:00 – 3:00 PM CT

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1. Introduction

The CIBMTR Working Committee for Graft-Versus-Host Disease met on Friday, February 23rd, 2024 at 1:00pm. Dr. MacMillan welcomed the attendees and introduced the working committee leadership. Dr. MacMillan was thanked for her contributions to the working committee during his acting time as a chair, and Dr. Nosha Farhadfar was welcomed as the incoming chair. Dr. Najla El Jurdi was welcomed as the WCTL program participant. Dr. MacMillan discussed the committee's goals, expectations, and limitations, the proposal scoring process, and rules of authorship. Two opportunities were shared: (1) WCTL program to include younger physicians in leadership, (2) CIBMTR's new Patient-Reported Outcomes (PRO) Protocol and data collection. Attendees were also encouraged to attend the Collaborative Session on Saturday February 24th 1pm-3pm. Lastly, Dr. MacMillan brought up the CIBMTR publicly available datasets, their use cases, and the required citations if used for research. Dr. Najla El Jurdi reviewed the Tandem scoring process.

2. Accrual Summary

The accrual tables were included in the meeting materials but were not reviewed in the interest of time.

3. Presentations, published or submitted papers

Updates on the committee's presentations, published or submitted papers were included in the meeting materials but were not discussed at the meeting.

a. **GV18-01b** Lee CJ, Wang T, Chen K, Arora M, Brazauskas R, Spellman SR, Kitko C, MacMillan ML, Pidala JA, Badawy SM, Bhatt N, Bhatt VR, DeFilipp Z, Diaz MA, Farhadfar N, Gadalla S, Hashmi S, Hematti P, Hossain NM, Inamoto Y, Lekakis LJ, Sharma A, Solomon S, Lee SJ, Couriel DR. Severity of chronic graft-versus-host disease and late effects following allogeneic hematopoietic cell transplantation for adults with hematologic malignancy. ***Transplantation and Cellular Therapy. 2024 Jan 1; 30(1):97.e1-97.e14. doi:10.1016/j.jtct.2023.10.010. Epub 2023 Oct 14.***

b. **GV18-02** Wallis W, Gulbis AM, Wang T, Lee CJ, Sharma A, Williams KM, Nishihori T, Prestidge T, Gowda L, Byrne M, Krem M, MacMillan ML, Kitko C, Pidala J, Spellman SR, Lee SJ, Alousi AM.
Incidence of Bacterial Blood Stream Infections in Patients with Acute GVHD. ***Submitted.***

c. **GV19-01** Gillis N, Padron E, Wang T, Chen K, DeVos JD, Spellman SR, Lee SJ, Kitko CL, MacMillan ML, West J, Tang YH, Teng M, McNulty S, Druley TE, Pidala JA, Lazaryan A. Pilot study of donor-engrafted clonal hematopoiesis evolution and clinical outcomes in allogeneic hematopoietic cell transplantation recipients using a national registry. ***Transplantation and Cellular Therapy. 2023 Oct 1; 29(10):640.e1-640.e8. doi:10.1016/j.jtct.2023.07.021. Epub 2023 Jul 28. PMC10592088.***

d. **GV20-02** Sandhu KS, Altin J, Wang T, DeVos JD, Askar M, Phillip Z, Gendzekhadze K, Kitko CL, Lee SJ, MacMillan ML, Spellman SR, Nakamura R. Prediction of Graft-versus-Host Disease (GVHD) in Recipients of Hematopoietic Cell Transplant (alloHCT) from a Single Mismatched Unrelated Donor Using a Highly Multiplexed Proteomics Assay: MHC-PepSeq. ***Poster Presentation, ASH 2023.***

e. **GV22-01/22-03** Farhadfar N, Rashid N, DeVos JD, Wang T, Ballen K, Beitinjaneh A, Bhatt VR, Hamilton B, Hematti P, Gadalla S, Solomon SR, Jurdi NE, Lee CJ, MacMillan ML, Rangarajan H, Schoemans H, Sharma A, Spellman SR, Wingard JR, Lee SJ. Racial, Ethnic, and Socioeconomic Diversity and Outcomes of Patients with Graft-versus-Host Disease: A CIBMTR Analysis. ***Submitted.***

4. Studies in progress

Updates on the committee's studies in progress were included in the meeting materials but were not discussed at the meeting.

a. **GV20-01** Machine learning models and clinical decision support tool for acute and chronic graft-versus-host disease in patients with acute myelogenous leukemia undergoing allogeneic transplants (T Kindwall-Keller/ B Lobo) **Analysis.**

b. **GV20-02** Prediction of graft-versus-host disease in recipients of hematopoietic cell transplant from a single mismatched unrelated donor using a highly-multiplexed proteomics assay: MHC-PepSeq (K Sandhu/ J Altin/ M Askar/ R Nakamura) **Manuscript Preparation.**

c. **GV21-02** Determinants of successful discontinuation of immune suppression following allogeneic hematopoietic cell transplantation: A validation study (J Pidala/ B Logan/ M Martens) **Analysis.**

d. **GV22-01** Acute and chronic graft versus host disease in infants and toddlers following hematopoietic cell transplantation (M Nishitani/ C Duncan/ R Graham/ M Qayed) **Manuscript Preparation.**

e. **GV22-02** Chronic GVHD Risk Index: A clinical risk assessment score for development of moderate-severe chronic graft-versus-host disease after hematopoietic cell transplantation (A Im/ S Pavletic) **Datafile Preparation.**

f. **GV23-01** The effect of calcineurin inhibitor vs post-transplant cyclophosphamide (with or without mycophenolate mofetil) based graft-vs-host disease prophylaxis on HLA matched hematopoietic cell transplantation (R Mehta/ R Nath) **Protocol Development.**

g. **GV23-02** Incidence of chronic graft versus host disease in cryopreserved versus fresh peripheral blood allogeneic hematopoietic stem cell grafts. (K Maurer) **Protocol Development.**

5. Future/proposed studies – Zach DeFilipp and Najla El Jurdi

a. **PROP 2310-175** Independent validation of a data-driven grading system for acute GVHD in HCT patients receiving post-transplant cyclophosphamide (PTCy). (AT Turki)

-The proposal was presented by Dr. Amin Turki. The study hypothesizes that an alternative data driven approach to aGvHD risk scoring is better than the current aGvHD grading practice. Proposal feasibility analysis of CIBMTR data found N=1921 patients with Grade I aGvHD, N=2222 patients with Grade II aGvHD, N=645 patients with Grade III aGvHD, and N=245 patients with Grade IV aGvHD for a total of N=5033 patients. Modified Glucksberg was used for this grading. The population was restricted to patients undergoing a first allogenic HCT from 2015-2022. Additional restrictions included patient age of 18+, MUD or haplo donors, PTCy/TAC or PTCy/MMF GvHD prophylaxis, and data availability for organ-specific aGvHD staging. CIBMTR embargo and consent exclusions were applied.
The following questions and comments were addressed during the Q&A:

i. Was the grading system created in Germany using Max grade staging for aGvHD? (yes) If so wouldn't this cause an issue as clinically when we see the patient we do not know the timepoint of max grade of aGvHD? Do you have any plans to look at initial grade of aGvHD for this validation system as well?

ii. Is initial staging accurately captured in CIBMTR data? What method does CIBMTR use to grade aGvHD and is it the same as the initial data used to create the model?

iii. *Will you have enough power and/or heterogeneity in the dataset in terms for Grade III/IV aGvHD as using PTCy-based GvHD prophylaxis results in lower incidence of higher-grade aGvHD*

b. **PROP 2310-172** Effect of acute graft-versus-host disease (GVHD) on the outcome of hematopoietic cell transplantation (HCT) with post-transplantation cyclophosphamide (PTCy): a CIBMTR analysis (AD Hadjis/ SR McCurdy)

-The proposal was presented by Dr. Ashley Hadjis. The study hypothesizes that recipients who develop grade II aGvHD after HCT with PTCy will have improved RFS and OS when compared to recipients who do not develop aGvHD or who develop grades III-IV aGvHD. Proposal feasibility analysis of CIBMTR data found N=7728 patients with no GvHD, N=2333 patients with Grade I aGvHD, N=2668 patients with Grade II aGvHD, N=1150 patients with grade III/IV aGvHD, and N=2950 patients with GvHD information not reported. The population was restricted to all patients receiving haplo, MSD, or MUD donor HCT with PTCy for acute leukemia, MDS, or lymphoma.
The following questions and comments were addressed during the Q&A:

i. *Consider using Grade I GvHD instead of no GvHD as the baseline comparison. With PTCy there is a rate of failed engraftment that should be considered.*
ii. *Should you potentially want to look at grade I/II GvHD combined as a sub analysis?*
iii. *Why were mismatched unrelated donors not included in the analysis?*
iv. *How will you consider cell dose? Especially for peripheral blood in haplo donors?*
v. *Will patients who received ATG be excluded?*

c. **PROP 2310-155** Post-Transplantation Cyclophosphamide (PTCy)/Sirolimus versus PTCy/Calcineurin-inhibitor (CNI) -based Graft-Versus-Host Disease Prophylaxis (R Mehta/ N Bejanyan)

-The proposal was presented by Dr. Rohtesh Mehta. The study hypothesizes that PTCy/Siro-based GvHD prophylaxis will be at least as effective as PTCy/CNI-based GvHD prophylaxis with a reduced toxicity profile. Proposal feasibility analysis of CIBMTR data found N=1616 patients with PTCy/Siro-based GvHD prophylaxis and N=16,320 patients with PTCy/CNI-based GvHD prophylaxis. The population was restricted to first allo HCT for any donor/graft/conditioning/disease with PTCy/Siro or PTCy/CNI-based GvHD prophylaxis from 2014-2022.
The following questions and comments were addressed during the Q&A:
i. *For whom is sirolimus the more ideal treatment? Should look at baseline demographics like conditioning, etc. to subset the population and look at effectiveness.*
ii. *There could be a center-effect for the sirolimus arm due to the reduced number of centers and the learning curve of using sirolimus in a clinical setting.*
iii. *Will you also be analyzing lymphocyte recovery? We found that PTCy/TAC/MMF has significantly delayed lymphocyte recovery compared to PTCy/Siro.*
iv. *There could be some toxicities CIBMTR doesn't collect that Siro is more likely to cause.*
v. *Could look at PTCy/TAC vs. PTCy/cyclosporin?*
vi. *Is it possible to look at the duration of treatment?*
vii. *How many patients had both TAC and sirolimus? How will these patients be handled in the analysis?*

d. **PROP 2310-58** Differences in the characteristics of Acute and Chronic Graft-Versus-Host Disease (GVHD) After Post-Transplantation Cyclophosphamide Versus Conventional Calcineurin Inhibitor-based GVHD Prophylaxis (R Mehta/ RM Saliba)

-The proposal was presented by Dr. Rohtesh Mehta. The study hypothesizes that patterns of organ involvement in aGvHD/cGvHD differ among patients with PTCy-based vs. conventional GvHD prophylaxis. It also hypothesizes that the incidence of de novo and progressive/relapsing cGvHD may differ between PTCy vs conventional groups. The last aim looks at immunosuppression burden after GvHD development and the "response" to treatment. Proposal feasibility analysis of CIBMTR data found N=3883 patients with PTCy-based GvHD prophylaxis and N=14381 patients with CNI-based GvHD prophylaxis. The population was restricted to first allo HCT for malignant disease from 2008-2021 on CRF track with MSD, MUD, or Haplo donors. Additional restrictions included PB or BM graft, MAC, RIC

,or NMA conditioning, PTCY or CNI-based GvHD prophylaxis, embargo, consent, and exclusion of ex-vivo T-cell depletion/CD34 selection.
The following questions and comments were addressed during the Q&A:

i. *Will you remove CNI/MMF patients? Could have 3 comparator arms to analyze*
ii. *Is immunosuppression data available for TED or CRF only?*
iii. *Immunosuppression data was missing for some patients without GvHD, could affect that analysis.*

e. **PROP 2310-178** Quantification of Severe and Highly Morbid Chronic Graft-Versus-Host Disease Forms in Pediatric Hematopoietic Cell Transplantation Patients Since Implementation of the 2014 NIH Consensus Criteria (J Boiko)

-The proposal was presented by Dr. Julie Boiko. The study hypothesizes that a large-scale pediatric cGVHD quantification using 2014 NIH Consensus Criteria-based reporting could show dominant organs' contributions to severe cGVHD and the association of predispositions with severe and/or highly morbid cGVHD forms in children. Proposal feasibility of CIBMTR data found N=1933 patients with no cGVHD and N=479 patients with cGVHD. The population was restricted to first allo HCT in patients under 21 years of age with reported follow-up in terms of both 6-month and greater F2100 follow-up as well as cGVHD data available through 2 years or death after 100 days.
The following questions and comments were addressed during the Q&A:

i. *Will you have the granularity of data available on the forms to properly analyze the question? Will you have the numbers needed to look at specific cGVHD manifestations?*
ii. *If you have small children, are they being properly diagnosed/tested?*
iii. *Will you be able to capture TMA using the CIBMTR forms?*
iv. *Are you collecting data starting at 2017 because of form revisions? Can you capture data going back further?*

6. Dropped proposed studies

f. **PROP 2308-02** A comparison of post transplant cyclophosphamide with MTX and CNI for GVHD prophylaxis in myeloablative conditioning regimens with PBSC graft source with HLA matched donors related and unrelated. *Overlap with CIBMTR study GV23-01.*

g. **PROP 2309-13** Abatacept in Combination with a Calcineurin Inhibitor and Methotrexate Following Allogeneic Hematopoietic Stem Cell Transplantation using FluBu2: Analysis of the Center for International Blood and Marrow Transplant Research Database. *Insufficient sample size.*

h. **PROP 2309-17** Incidence of Genital cGVHD in recipients of Allogeneic Stem Cell Transplantation. *Insufficient data collection.*

i. **PROP 2310-07** Mismatched (7/8) unrelated donor transplantation versus haploidentical transplantation using PTCy: Analysis of the Center for International Blood and Marrow Transplant Research Database. *Overlap with IB23-02.*

j. **PROP 2310-08** Post-transplant cyclophosphamide for Graft versus Host Disease Prophylaxis in patients undergoing allogeneic transplantation using Myeloablative conditioning: Analysis of the Center for International Blood and Marrow Transplant Research Database. *Overlap with GV23-01.*

k. **PROP 2310-101** Post-transplant cyclophosphamide versus abatacept for GVHD prevention in recipients of unrelated donor Allo-HCT. *Insufficient sample size.*

l. **PROP 2310-107** Comparing outcomes between HLA-haploidentical and mismatched unrelated donor transplantation among patients receiving reduced intensity conditioning with posttransplant cyclophosphamide-based graft versus host disease prophylaxis. *Overlap with IB23-02.*

m. **PROP 2310-138** The Impact of Organ Function on GVHD Prophylaxis Outcomes. *Insufficient data collection.*

n. **PROP 2310-171** Outcomes of Non-First Degree Relative Haploidentical Blood or Marrow Transplantation Using Post-Transplant Cyclophosphamide. *Insufficient sample size.*

o. **PROP 2310-179** Haploidentical vs HLA-matched Donor Allogenic Stem Cell Transplantation with Post-Transplant Cyclophosphamide in Acute Myeloid Leukemia with Measurable Residual Disease. Alloreactivity vs. disease kinetics. *Overlap with LK21-01.*

p. **PROP 2310-228** Post-transplant Cyclophosphamide vs Abatacept for GVHD prophylaxis in Mismatched Unrelated Donor Transplant. *Insufficient sample size.*

q. **PROP 2310-239** Dose optimization for post-transplantation cyclophosphamide as GVHD prophylaxis after allogeneic hematopoietic stem cell transplantation. *Insufficient data collection.*

r. **PROP 2310-243** Outcome of renal impairment on outcomes after post-transplantation cyclophosphamide as GVHD prophylaxis. *Insufficient data collection.*

s. **PROP 2310-260** Outcomes for Haploidentical Transplantation with First and Second Degree Relatives. *Insufficient sample size.*

t. **PROP 2310-32** Impact of graft-versus-host disease on salvage treatment selection and outcomes of patients with myeloid neoplasms relapsing following allogeneic HCT. *Insufficient data collection.*

u. **PROP 2310-63** Risk of Relapse for Pediatric Patients with Hematologic Malignancies Undergoing Allogeneic Hematopoietic Cell Transplantation with Post-Transplant Cyclophosphamide as GvHD Prophylaxis vs Other GvHD Prophylaxis Regimens. *Dropped by PI.*

v. **PROP 2310-96** Outcomes in Pediatric Patients with Hematologic Malignancies Undergoing Allogeneic Hematopoietic Cell Transplantation with Post-Transplant Cyclophosphamide Based GVHD Prophylaxis vs Other GVHD Prophylaxis Regimens. *Insufficient sample size.*

7. Concluding Notes

a. The meeting adjourned at about 2:30 PM.

b. After the new proposals were presented, each participant in the meeting had an opportunity to score each proposal electronically using the Tandem app or website. Based on the voting results, current scientific merit, available number of relevant cases, and the impact of the study on the field, the following proposals were accepted to move forward to be added to the committee's active studies:

> ***PROP 2310-155*** *Post-Transplantation Cyclophosphamide (PTCy)/Sirolimus versus PTCy/Calcineurin-inhibitor (CNI) -based Graft-Versus-Host Disease Prophylaxis (R Mehta/ N Bejanyan)*

PROP 2310-172 *Effect of acute graft-versus-host disease (GVHD) on the outcome of hematopoietic cell transplantation (HCT) with post-transplantation cyclophosphamide (PTCy): a CIBMTR analysis (AD Hadjis/ SR McCurdy)*

PROP 2310-58 *Differences in the characteristics of Acute and Chronic Graft-Versus-Host Disease (GVHD) After Post-Transplantation Cyclophosphamide Versus Conventional Calcineurin Inhibitor-based GVHD Prophylaxis (R Mehta/ RM Saliba)*

Working Committee Overview Plan for 2024-2025		
Study Number and Title	**Current Status**	**Priority**
GV18-02 Comparison of bacterial blood stream infection incidence in allogeneic stem cell transplantation patients with and without acute graft vs host disease	Submitted	**1**
GV20-01 Machine learning models and clinical decision support tool for acute and chronic graft-versus-host disease in patients with acute myelogenous leukemia undergoing allogeneic transplants	Analysis	**3**
GV20-02 Prediction of graft-versus-host disease in recipients of hematopoietic cell transplant from a single mismatched unrelated donor using a highly-multiplexed proteomics assay: MHC-PepSeq	Manuscript Preparation	**1**
GV21-01/GV22-03 Racial, ethnicity and socioeconomic disparity in outcome of patients with graft versus host disease	Submitted	**2**
GV21-02 Determinants of successful discontinuation of immune suppression following allogeneic hematopoietic cell transplantation: A validation study	Analysis	**1**
GV22-01 Acute and chronic graft versus host disease in infants and toddlers following hematopoietic cell transplantation	Manuscript Preparation	**1**
GV22-02 Chronic GVHD Risk Index: A clinical risk assessment score for development of moderate-severe chronic graft- versus-host disease after hematopoietic cell transplantation	Datafile Preparation	**1**
GV23-01 The effect of calcineurin inhibitor vs post transplant cyclophosphamide (with or without mycophenolate mofetil) based graft-vs-host disease prophylaxis on HLA matched hematopoietic cell transplantation	Protocol Received	**3**
GV23-02 Incidence of chronic graft versus host disease in cryopreserved versus fresh peripheral blood allogeneic hematopoietic stem cell grafts	Protocol Development	**2**
GV24-01 Post-transplantation cyclophosphamide (PTCy)/sirolimus versus PTCy/calcineurin-inhibitor (CNI) -based graft-versus-host disease prophylaxis	Protocol Pending	**3**
GV24-02 Effect of acute graft-versus-host disease (GVHD) on the outcome of hematopoietic cell transplantation (HCT) with post-transplantation cyclophosphamide (PTCy): a CIBMTR analysis	Protocol Pending	**2**

GV24-03 Differences in the characteristics of acute and chronic graft-versus-host disease (GVHD) after post-transplantation cyclophosphamide versus conventional calcineurin inhibitor-based GVHD prophylaxis	Protocol Pending	**1**

Working Assignments for Working Committee Leadership (March 2024)	
Carrie Kitko	**GV20-01** Machine learning models and clinical decision support tool for acute and chronic graft-versus-host disease in patients with acute myelogenous leukemia undergoing allogeneic transplants **GV22-01** Acute and chronic graft versus host disease in infants and toddlers following hematopoietic cell transplantation **GV23-01** The effect of calcineurin inhibitor vs post transplant cyclophosphamide (with or without mycophenolate mofetil) based graft-vs-host disease prophylaxis on HLA matched hematopoietic cell transplantation
Zachariah DeFilipp	**GV22-02** Chronic GVHD Risk Index: A clinical risk assessment score for development of moderate-severe chronic graft- versus-host disease after hematopoietic cell transplantation **GV23-02** Incidence of chronic graft versus host disease in cryopreserved versus fresh peripheral blood allogeneic hematopoietic stem cell grafts
Nosha Farhadfar	**GV20-02** Prediction of graft-versus-host disease in recipients of hematopoietic cell transplant from a single mismatched unrelated donor using a highly-multiplexed proteomics assay: MHC-PepSeq **GV21-02** Determinants of successful discontinuation of immune suppression following allogeneic hematopoietic cell transplantation: A validation study