Not for publication or presentation

MINUTES AND OVERVIEW PLAN
CIBMTR WORKING COMMITTEE FOR GRAFT-VERSUS-HOST DISEASE
Salt Lake City, UT
Saturday, April 23, 2022 12:15 PM - 1:45 PM MDT

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1. **Introduction**
   Dr. Joseph Pidala called the meeting to order and introduced the current GVWC leadership members. Dr. Pidala discussed the goals, expectations, and limitations of the GVWC and criteria that must be met to be considered for authorship on a manuscript. Details on publicly available datasets on the CIBMTR website were discussed. Dr. Margaret MacMillan explained the proposal scoring process and guidelines.

2. **Accrual Summary**
   The accrual summary was not presented, but was made available to attendees as an attachment.

3. **Presentations, published or submitted papers**
   Details regarding presentations and publications were not presented, but were made available to attendees as an attachment.

4. **Studies in progress**
   Details regarding the studies in progress were not presented, but were made available to attendees as an attachment.

5. **Future/proposed studies**
   Drs. MacMillan and Carrie Kitko led this session, which is where the committee chose to devote its available time. Presenters were reminded to limit their presentations to 5 minutes to ensure time for discussion (5 minutes).

a. **PROP 2108-02/2109-19/2110-72:** Post-Transplant Cyclophosphamide vs *in vivo* T-Cell Depletion with Anti-Thymocyte Globulin or Alemtuzumab in Patients with Acute Leukemia or Myelodysplastic Syndrome undergoing Unrelated Donor Hematopoietic Cell Transplant (A Jimenez/L Arcuri/A Marinos/K Komanduri/N Hamerschlak/P Lulla)

Dr. Alejandro Marinos presented the proposal. The main objective of the proposed study is to compare post-transplant clinical outcomes between patients who received post-transplant cyclophosphamide (PT-Cy) with those who received anti-thymocyte globulin (ATG) or alemtuzumab. A total of 2684 patients aged 18 and older underwent first unrelated donor allo-HCT for AML, ALL, or MDS in 2010-2020, with 548 receiving PT-Cy and 2136 receiving ATG or alemtuzumab.

Questions were asked about the availability of ATG dosing and timing. Suggestions were made to do separate analyses for ATG and alemtuzumab patients, to exclude patients who received both ATG and alemtuzumab, and to consider evaluating viral infections and PTLD as outcomes.

b. **PROP 2110-193/2110-278:** Comparative analysis of the incidence of graft versus host disease by age group in pediatric hematopoietic stem cell transplant recipients and impact on non-relapse mortality (M Nishitani/C Duncan/R Graham/M Qayed)

Dr. Miki Nishitani presented the proposal. The main objective of the proposed study is to compare the incidence, severity, and risk factors for acute and chronic GVHD in patients aged 0-17 years who underwent HCT in 2002-2011 with those who underwent HCT in 2012-2020. A total of 14,234 patients aged 17 years or younger received first allo-HCT in 2002-2020, with 8437 in 2002-2011 and 5797 in 2012-2020.

Attendees suggested grouping adolescents based on sex in addition to age and adding a cohort of patients aged 18-30. Concerns were raised about the heterogeneity of the population due to the inclusion of all disease types and changes in HLA typing technology over the span of years included in the study.

c. **PROP 2108-04:** 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)

Dr. Annie Im presented the proposal. The main objectives of the proposed study are to develop a risk score based on clinical factors to predict the likelihood of developing moderate to severe chronic GVHD and to validate the risk score using the CIBMTR dataset. A total of 25,457 patients who underwent first allo-HCT in 2010-2019 met the criteria for this study.

Attendees suggested developing separate risks scores for those who received traditional GVHD prophylaxis and those who received post-transplant cyclophosphamide, including factors that have not been evaluated in existing studies, and including post-HCT measurements collected before GVHD onset. Statistical questions were raised regarding the risk factor weighting and whether relapse will be a competing event for GVHD.

d. **PROP 2110-25/2110-266:** A Risk-Score for Bronchiolitis Obliterans Syndrome after Allogeneic Hematopoietic Cell Transplantation (S Patel/R Mehta/C Ustun/A Alousi)

Dr. Sagar Patel presented the proposal. The main objective of the proposed study is to identify risk factors for developing bronchiolitis obliterans (BOS) following allo-HCT with the goal of creating a risk score. A total of 72,438 patients who underwent first allo-HCT in 1996-2019 met the criteria for this study.

Concerns were raised about the quality of the BOS data due to cases of BOS reported without GVHD diagnosis. It was suggested to compare outcomes between BOS patients with GVHD and without GVHD and to include available data on respiratory viral infections.

e. **PROP 2106-01:** Incidence and Risk Factors for thromboembolism in patients with Chronic Graft-versus-Host Disease (N El Jurdi/M Arora)

Dr. Najla El Jurdi presented the proposal. The main objective of the proposed study is to evaluate the impact of GVHD and ABO mismatch on the incidence and risk factors for thromboembolism (TEE) following allo-HCT. A total of 9650 patients aged 18 years or older who underwent first allo-HCT for AML or ALL in 2008-2019 met the criteria for this study.

Attendees made several suggestions including differentiating between catheter related and spontaneous DVT and adding prior infections and TMA as risk factors. There was also interest in comparing the incidence of TEE in the CIBMTR cohort with that of the general population.

f. **PROP 2110-24:** Does race/ethnicity or socio-economic status impact the outcomes of patients with acute GVHD? (N Rashid/N Farhadfar)

Dr. Nahid Rashid presented the proposal. The main objective of the proposed study is to evaluate the impact of race, ethnicity, and socioeconomic status on long term post-transplant outcomes after onset of acute GVHD. A total of 7038 patients underwent alloHCT for AML, ALL, or MDS in the United States in 2008-2019 and subsequently developed acute GVHD. Within this cohort, 5343 identified as non-Hispanic white, 548 as non-Hispanic black, 706 as Hispanic, 318 as Asian, and 123 as either Native Hawaiian, Pacific Islander, American Indian, Alaskan Native, or multi-racial.

A comment was made that patients with acute GVHD are often admitted, so the study may not find differences in access to care due to factors such as travel distance to transplant center.

Dropped proposed studies

a. **PROP 2109-06:** Risk Factors For Engraftment Syndrome And Its Impact On Clinical Outcomes In Pediatric Allogeneic Stem Cell Transplant Recipients: A Contemporary Analysis. ***Concern about accurate capture of engraftment syndrome; lower scientific impact relative to other proposals.***

b. **PROP 2109-23:** Assessing if multiparous female donors increase the risk of graft vs host disease in HLA-Matched un-related and related allogenic stem cell transplant in the era of post-transplant cyclophosphamide. ***Need for additional data collection; lower scientific impact relative to other proposals.***

c. **PROP 2110-30:** Risk of cardiovascular disease, infections, secondary malignancies, and non-relapse mortality among patients who received sirolimus. ***Concern about study population heterogeneity and ability to isolate effect of sirolimus; unclear feasibility; lower scientific impact relative to***

other proposals.

d. **PROP 2110-70:** Comparing Patterns, Outcomes and Organ Involvement with Acute and Chronic Graft-versus-Host Disease Between Patients with Non-Malignant Diseases Undergoing Haploidentical Transplantation Using Post-Transplantation Cyclophosphamide vs. Matched Unrelated Donor Transplantation Using Calcineurin Inhibitors. ***Overlap with CIBMTR study GV17-03.***

e. **PROP 2110-97:** Is there differential benefit of alternative GVHD prophylaxis strategies among racial and ethnic groups? Graft-versus host disease-free relapse-free survival by race and ethnicity comparing post-transplant cyclophosphamide-based to calcineurin inhibitor plus methotrexate-based GVHD prophylaxis. ***Minority sample size too small; transplant approach confounded by donor availability*.**

f. **PROP 2110-122:** Determining the optimal anti-thymocyte globulin dosing in patients with hematologic malignancies. ***Data on ATG timing not available.***

g. **PROP 2110-169:** Comparison of survival and graft versus host disease outcomes in alternate mismatched graft sources. ***Overlap with published CIBMTR study GV16-01a.***

h. **PROP 2110-215:** Effect of Graft-Versus-Host Disease Prophylaxis on Survival after Reduced Intensity Conditioning Hematopoietic cell transplantation for Older Adults: a CIBMTR analysis. ***Overlap with CIBMTR study GV17-03.***

i. **PROP 2110-218:** To compare CD3+ T-Cell Dose for Patients Receiving Allogeneic Peripheral Blood Stem Cell Transplants from Matched Related Donors using a propensity-matched study. ***The primary single center study population is very small; lower scientific impact relative to other proposals.***

j. **PROP 2110-279:** One Year Graft vs. Host Disease Relapse Free Survival in Acute Lymphoblastic Leukemia patients undertaking Matched Related or Matched Unrelated Allogeneic Stem Cell Transplant Using Post Transplant Cytoxan compared to conventional Graft vs Host Disease prophylaxis. ***Limited sample size; overlap with published CIBMTR study GV16-01a.***

k. **PROP 2110-285:** Sirolimus versus Tacrolimus in combination with post-transplant cyclophosphamide and MMF as a GVHD prophylaxis after allogeneic hematopoietic cell transplantation in patients with hematologic malignancies. ***Limited sample size.***

l. **PROP 2110-324:** Explore the optimal dose and length of post allogeneic hematopoietic stem cell transplant prophylactic immunosuppressant use. ***Data on dosing and timing not available.***

m. **PROP 2110-329:** Immunosuppression discontinuation after allogeneic hematopoietic stem cell transplantation. ***Concern about reliability of late infection data; immunosuppression discontinuation not clearly defined at 1 and 2 years in CIBMTR database.***

6. Other Business

After the proposals were presented, meeting participants had the opportunity to rate each proposal via the Tandem mobile app. Based on the voting results, current scientific merit, available number of relevant

cases, and the impact of the study on the field, the following studies will move forward in the committee's research portfolio for the upcoming year:

- **PROP 2110-193/2110-278:** Comparative analysis of the incidence of graft versus host disease by age group in pediatric hematopoietic stem cell transplant recipients and impact on non-relapse mortality

- **PROP 2108-04:** Chronic GVHD Risk Index: A clinical risk assessment score for development of moderate-severe chronic graft-versus host disease after hematopoietic cell transplantation

- **PROP 2110-24:** Does race/ethnicity or socio-economic status impact the outcomes of patients with acute GVHD?

Working Committee Overview Plan for 2022-2023

Study Number and Title	Current Status	Chairs Priority
GV17-03: Alterations in the characteristics and outcomes of acute and chronic graft-versus-host disease following post-transplant high dose cytoxan prophylaxis for haploidentical transplantation and in patients over 60 at high risk for graft-versus-host disease	Submitted	3
GV18-01a: Comparison of late effects among pediatric allogeneic hematopoietic cell transplantation survivors with and without chronic graft-versus-host disease	Submitted	1
GV18-01b: Comparison of late effects among adult allogeneic hematopoietic cell transplantation survivors with and without chronic graft-versus-host disease	Manuscript Preparation	1
GV18-02: Comparison of bacterial blood stream infection incidence in allogeneic stem cell transplantation patients with and without acute graft vs host disease	Manuscript Preparation	2
GV19-01: Exploring the link between donor-engrafted clonal hematopoiesis and adverse outcomes in allogeneic transplants recipients	Manuscript Preparation	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	Protocol Development	3
GV21-01: Racial, ethnicity and socioeconomic disparity in outcome of patients with chronic graft versus host disease	Analysis	1
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	Protocol Pending	3

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	Protocol Pending	1
GV22-03: Does race/ethnicity or socio-economic status impact the outcomes of patients with acute GVHD?	Protocol Pending	2