MINUTES AND OVERVIEW PLAN
CIBMTR WORKING COMMITTEE FOR HEALTH SERVICES AND INTERNATIONAL STUDIES
Orlando, FL
Friday, February 17, 2023, 12:00 – 2:00 pm

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1. Introduction

The Health Services and International Studies Working Committee (HSWC) met on Friday, February 17, 2023, at 12:00 p.m. The chairs, scientific directors, and statisticians were all present at the meeting. Attendees were asked to have their name badges scanned at the front door to register physical attendance while those members attending the meeting virtually were counted as part of the committee membership roster.
As chair of the HSWC, Dr. Shahrukh Hashmi welcomed the attendees on behalf of the working committee leadership and started the welcome presentation by introducing each member of the working committee leadership, acknowledging Dr. Saber for his contributions as the outgoing scientific director and introducing Dr. Yusuf as the new scientific director. Dr. Hashmi then explained how to enroll and maintain membership, the goals, and expectations of the working committee. Subsequently, Dr. Saber acknowledged and thanked Dr. Shahrukh for all his efforts and contributions as an outgoing co-chair and introduced Dr. Minoo Battiwalla as the newly appointed Chair for the Working Committee starting March 1, 2023.

Dr. Hashmi introduced the committee goals and expectations to the audience, then emphasized the scoring process and scoring guide. Dr. Hashmi discussed the rules of authorship and location of the publicly available datasets for secondary analysis on the CIBMTR webpage. He encouraged attendees to attend the Collaborative Study Proposal Session, where two proposals submitted to the Working Committee were selected for presentation. He then reviewed presentations, publications and submitted papers in 2022, and gave updates on the status of ongoing studies and their goals for 2023. Dr. Hashmi emphasized the productivity and engagement from the committee. He discussed important details about how the committee works, CIBMTR study development cycle, and explained the different sources of CIBMTR data collection. In addition, he discussed future priorities of the committee and clarified the voting process for submitted proposals to the audience and explained the PI's rule of conduct on the study cycle: timely completion of abstract, slides, and manuscript after the analysis is completed. If the PI does not write the first draft of the manuscript, after 3 requests, writing of the paper will be reassigned and the

investigator/member of the writing committee who writes the first draft will become the first author. The CIBMTR statistical resource was clarified to the audience. The average time to complete a study is 2-3 years dependent upon statistical hours allocation and other competing projects.

2. Accrual summary

The accrual summary was referenced by Dr. Hashmi for review but not formally presented due to a full agenda. The link to the full accrual summary was available online as part of the attachments. The accrual summary provides information about the number of patients available in the registration level (TED) and research level (CRF) for potential studies. Research level patients are subset of registration level. As of December 2022, 2,468,578 transplant cases were reported at the TED level only and 46,263 cases at the research level to the CIBMTR for first autologous transplant. For first allogeneic transplants, these numbers are 255,199 cases and 107,880 cases respectively.

3. Presentations, Published or Submitted Papers

Dr. Hashmi went through the abstracts presented at various conferences, mentioning that it was a very productive year. At the time three abstracts were presented or accepted for presentation.
These include:

a. HS16-03 Karen K. Ballen, Tao Wang, Naya He, Shahrukh Hashmi, Leslie E. Lehmann, William A. Wood, Hemalatha G. Rangarajan, Wael Saber. Does Race/Ethnicity Impact Umbilical Cord Blood Transplant Outcomes in a Contemporary Era? ***Oral presentation, ASH 2022 and Poster Presentation, 2023 Tandem Meetings***.
b. HS18-01 Yasuyuki Arai, Yoshiko Atsuta, Ruta Brazauskas, Naya He, Shahrukh Hashmi, Leslie E. Lehmann, William A. Wood, Hemalatha G. Rangarajan, Shingo Yano, Shinichi Kako, Masamitsu Yanada, Yukiyasu Ozawa, Noriko Doki, Yoshinobu Kanda, Takahiro Fukuda, Yuta Katayama, Tatsuo Ichinohe18, Junji Tanaka, Junya Kanda, Takanori Teshima, Shinichiro Okamoto, Wael Saber; International Collaborative Study to Compare the Prognosis for Acute Leukemia Patients Transplanted with Intensified Myeloablative Regimens. ***Poster presentation, ASH 2022.***
c. HS16-01 Nandita Khera, Megan Herr, Ruta Brazauskas, Jinalben Patel, Benjamin Jacobs, Naya He, Leslie Lehmann, Shahrukh Hashmi, Hemalatha Rangarajan, Sikander Ailawadhi, Wael Saber, Theresa Hahn; Trends in Utilization and Outcomes of Autologous and Allogeneic Hematopoietic cell Transplantation in Racial and Ethnic Minorities. ***Poster Presentation, 2023 Tandem Meetings.***

4. Studies in Progress

Dr. Hashmi presented the summary of studies in progress.

a. HS16-01 Trends in Utilization and Outcomes of Autologous and Allogeneic Hematopoietic cell Transplantation in Racial and Ethnic Minorities (N Khera/ T Hahn/ S Ailawadhi / W Saber), Manuscript Preparation.
b. HS16-03 Relationship of Race/Ethnicity and Survival after Single and Double Umbilical Cord Blood Transplantation (K Ballen), Manuscript Preparation.
c. HS18-01 International collaborative study to compare the prognosis for acute leukemia patients transplanted with intensified myeloablative regimens (Y Arai/ Y Atsuta/ S Yano), Manuscript Preparation.
d. HS18-02 Racial differences in long term survivor outcomes after allogeneic transplants (B Blue/ N Majhail), Manuscript Preparation.
e. HS19-01 Factors Associated with Clinical Trial Participation among HCT Patients: A CIBMTR Analysis (T F Gray/ A El-Jawahri), Protocol Development.
f. HS19-03 Haploidentical Stem Cell Transplantation for malignant and non-malignant hematological diseases in patients without sibling donor: A multicenter prospective and longitudinal study of the

Brazilian bone marrow transplantation study group (SBTMO) (N Hamerschlak/ M N Kerbauy/ A A F Ribeiro), Data Collection.

g. HS19-04 Outcomes after allogeneic stem cell transplants performed in Brazil from HLA-matched siblings, unrelated and mismatched related donors. Retrospective study on behalf of the Brazilian Bone Marrow Transplantation Society (SBTMO), GEDECo (Brazil-Seattle Transplant-related complications Consortium), Hospital Israelita Albert Einstein (AmigoH), Associação da Medula Óssea do Estado de São Paulo (Ameo), Programa Nacional de Apoio à Atenção Oncológica (Pronon), and CIBMTR (A Seber/ N Hamerschlak/ M E Flowers/ M Pasquini), Analysis.

h. HS20-01 Resource Intensity of End-of-Life Care in Children After Hematopoietic Stem Cell Transplant for Acute Leukemia: Rates and Disparities (E E Johnston/ C W. Elgarten/ L Winestone/ R Aplenc/ K Getz/ V Huang/ Y Li), Datafile Preparation.

5. Future/Proposed Studies/Study Updates

Dr. Shahrukh thanked the investigators whose proposals were submitted but not selected for presentation. This year, we had a record of 10 proposals received. Two were invited for presentation at the individual HSWC meeting and 2 (1 of which was a combination of 4 of the received proposals due to similar/complementary themes) were presented at the Collaborative Session. Dr. Shahrukh emphasized that the remaining were dropped due to overlaps with current studies and data availability issues; and reiterated the voting process. Dr. Leslie Lehmann introduced the presenters for the 2 proposals.

a. **PROP 2209-20**: Impact of Ambient Air Pollution Exposure on Outcomes in Pediatric Bone Marrow Transplantation (Paul George; Staci Arnold)

It was a pre-recorded presentation by Dr. George on behalf of the group with Dr. Arnold attending in-person. This study hypothesizes that ambient air pollution exposure is a key biologic link between sociodemographic risk factors and poor health outcomes and therefore higher levels of neighborhood air pollution will be associated with worse overall survival and event free survival among pediatric BMT recipients. It further hypothesizes that these associations will be highest amongst socially vulnerable patients, including those living in high-poverty neighborhoods, minority patients, and those without private insurance. The primary exposure of interest will be neighborhood PM2.5 levels (continuous variable), and the primary outcomes of interest will be overall survival and event-free survival (binary variables). Covariates of interest will include age, gender, race, ethnicity, disease (malignant vs. non-malignant), neighborhood poverty, and primary insurance. Interactions between air pollution exposure and key sociodemographic factors will also be investigated as secondary outcomes, as it is hypothesized that air pollution exposure has increased harms amongst patients living in poverty. Time to-event analyses will also be performed as key secondary outcomes.

Comments from the audience: One of the attendees asked why the age is restricted to 21, will it not affect the older population? Dr. George answered that his area of interest is pediatric oncology, so his population of interest is pediatric population. Dr. Arnold added if the committee approves the study and is willing to extend the population and year that would be great. Another question was, how would the investigators tease out if low income/poverty not air pollution is the real cause of the outcomes under consideration? Dr. George commented that they will be accounting on neighborhood poverty data using US census data. And explained their hypothesis that these associations will be highest amongst socially vulnerable patients, including those living in high-poverty neighborhoods, minority patients, and those without private insurance, which would look for poverty. . Dr. Saber asked about hypothesis concerning autologous transplant and he stated it would be more corresponding to allogenic transplant than autologous transplant. Dr. George agreed that pathology under allogenic transplant would have higher impact and, also mentioned that sickle cell disease would have more pathophysiology undergoing transplant. He further explained that air pollution also damages endothelial layer and that was a justification that both auto- and allo-transplant would have overlapping pathophysiologic impact. Also,

he added that with large sample size we would be able to see the impact. Dr. Battiwalla added that other covariates like pulmonary comorbidities should be considered. The audience was concerned about granularity of air pollution. Dr. George replied that it would be used on 1 km to 1 km grade by consolidating as CIBMTR data is zip code level. One of the attendees mentioned that gradient keep changing throughout measurement and what would be the cut point. Dr. George replied that yearly average would be considered. Dr. Rangarajan pointed out along with pre-transplant and ongoing transplant outcomes, the investigators should look for post-transplant outcome along with the lung outcomes.

b. **PROP 2210-93:** Community health status and long-term outcomes in 1-year survivors of autologous and allogeneic hematopoietic cell transplantation in the United States (Betty Hamilton; Sanghee Hong)

   Dr. Hong presented the proposal on behalf of the group. This study hypothesizes that poor community health factors (high community risk), measured using the County Health Rankings and Roadmaps (CHRR) database, (refs 1,2) are associated with inferior long-term outcomes in HCT recipients surviving at least 1 year after transplant. The primary objective of this proposal is to investigate the association between community health status based on patient's residence (Patient Community Score [PCS]) and both continuous and 5-year overall survival (OS) in long-term survivors (≥1 year) of allogeneic and autologous HCT. The secondary objectives are to investigate the association between PCS and the following long-term transplant outcomes: non-relapse mortality (NRM), relapse, and chronic graft-versus-host disease (cGVHD) (measured by incidence and maximum grade, only for allogeneic HCT recipients). Investigate the association between PCS and other late effects of transplant and to identify associations between long-term outcomes (secondary aim 1) or late effects (secondary aim 2) and each of the four PCS subcategories: physical environment, social and economic factors, clinical care, and health behaviors.
   Comments from the audience: Dr. Lehmann asked about poverty, how will it be adjusted for? Dr. Hong answered that one of the measures is socioeconomic status defined at county level will be used to adjust for it. Dr. Khera mentioned that patients might be moving out from the transplant zip code and that would be a limitation of the analysis. Dr. Hong agreed and added that survivors may have moved once, twice as many times as they want, and they could be impacted by the neighborhood they have been living. One of the attendees, mention that distance to transplant center should be considered to see how far they need to travel to get transplant. Dr. Hong mentioned that in a prior study, they did see a difference in late effects but a long-term survivor does not need to visit transplant center that often so that might be not as huge as we look in short term effects. Dr. Saber asked why the investigators were excluding patients who died within 1st year and wanted to know the rationale. Dr. Hong replied that we already know for short term outcome, and we need to know how the community is impacted by long term outcomes. Long term survivors would be more impacted by the infrastructure, set ups and neighborhoods they live in. Dr. Yusuf asked how the study would explain ecologic fallacy of using aggregate data to individual outcome. One of the attendees asked if all the covariates are continuous or categorical variables. Dr. Hong answered that this data is updated annually and some of the variables are updated 2-3 years. How would quality of life would be measured and if any metrics are available? Dr. Hong said they would consider admission rate, death rates, ED rates.

Dr. Hemalatha Rangarajan introduced the presenters for the 2 study updates.

a. **HS16-01:** Trends in Utilization and Outcomes of Autologous and Allogeneic Hematopoietic cell Transplantation in Racial and Ethnic Minorities (N Khera/ T Hahn/ S Ailawadhi / W Saber)

   Dr. Khera presented the study updates on behalf of the group. The main objectives of the study are to describe changes in the volume and rate of auto and alloHCT in different racial/ethnic groups from 2009

to 2018 and to examine trends in survival after auto and alloHCT within each racial/ethnic group from 2009 to 2018 (paper 1). AlloHCT in adult & pediatric patients (Acute Leukemias, Lymphoma and MDS/MPN) and autoHCT in adults (NHL, Hodgkin's lymphoma, and Multiple Myeloma). To examine trends in utilization of autoHCT for MM and Lymphomas and alloHCT for Acute Leukemias and MDS within each racial/ethnic group from 2009 to 2018, comparing two different methodologies (paper 2). Conclusion from the analysis was differences in the magnitude of rates though direction usually similar with the two methods. Significant increases in utilization of alloHCT, but not in autoHCT (except for Hispanics with MM) from 2009 to 2018 and disparities remain for alloHCT for most diseases for AAs.

Comments from the audience: Attendees appreciated the work and its affirmative to work on two methods and suggested to include sensitive analysis in the manuscript. Dr. Lehmann added that it is an amazing work no research to date has compared different methodologies. One of the attendees had concerns if there were any pattern for missing zip code data. Dr. Saber mentioned that CIBMTR started collecting data later so there was lag in reporting and till we get complete data.

b. **HS19-01:** Factors Associated with Clinical Trial Participation among HCT Patients: A CIBMTR Analysis (T F Gray/ A El-Jawahri)

It was a pre-recorded study update presented by Dr. Gray on behalf of the group. This study hypothesizes that patients undergoing allogeneic HCT are more likely to participate in a clinical trial compared to those who undergo autologous HCT. Patients who are White, unmarried, younger, and those with private health insurance are more likely to participate in clinical trials. Patients with higher education and those with higher income are more likely to participate in clinical trials. Clinical trial participation will be associated with better OS and lower NRM among autologous and allogeneic HCT recipients. The specific aims of this study are to describe rates of clinical trial participation based on HCT type. To explore factors that are associated with clinical trial participation in patients with undergoing HCT. To assess the impact of clinical trial participation on overall survival (OS) and non-relapse mortality (NRM) in autologous and allogeneic HCT recipients.

Comments from the audience: Dr. Khera raised the question if there is data of those centers who never have clinical trials and will these centers be excluded. Dr. Gray agreed that we are going to look for that moving forward. One of the attendees mentioned that center effect would play a role as some centers are more motivated and active and get lots of patients' enrollment. Also, PI should look for number of open studies during the period and compare expected vs actual participation. Dr. Lehmann asked how the question is interpreted by the individual, is this question only for interventional study?
PI mentioned that it would be a limitation of study, how the question is interpreted by the person.

Three additional proposals were submitted but not presented as listed below:

a. **PROP 2210-85:** Outcomes of allogeneic hematopoietic stem cell transplantation based on access to care. Dropped-low scientific impact.
b. **PROP 2210-162:** Socioeconomic Disparities Impacting Access to BCMA directed Chimeric Antigen Receptor T cell therapy and Clinical Outcomes. Dropped-supplemental data needed.
c. **PROP 2210-258:** Geographic and Racial Disparities in Access to Chimeric Antigen Receptor-T Cells and Bispecific Antibodies. Dropped-low scientific impact.

The meeting was adjourned at **1:35** p.m. Dr. Saber asked the audience to give an applause and thanked them for actively participating in the meeting.

6. Other Business

The chairs of the working committee, scientific directors, and statisticians had a post-WC meeting afterwards. After the new proposals were presented, each attendee had the opportunity to vote for the proposals using the provided voting sheets. Based on the voting results, current scientific merit, and impact of the studies on the field, the following studies were decided to move forward as the committee's research portfolio for the upcoming year:

a. **PROP 2210-93:** Community health status and long-term outcomes in 1-year survivors of autologous and allogeneic hematopoietic cell transplantation in the United States (Betty Hamilton; Sanghee Hong)

Working Committee Overview Plan for 2023-2024		
Study number and title	**Current status**	**Chairs Priority**
HS16-01 Trends in utilization and outcomes of autologous and allogeneic hematopoietic cell transplantation in racial and ethnic minorities.	Manuscript Preparation	1
HS16-03 Relationship of Race/Ethnicity and Survival after Single and Double Umbilical Cord Blood Transplantation	Manuscript Preparation	2
HS18-01 International collaborative study to compare the prognosis for acute leukemia patients transplanted with intensified myeloablative regimens	Manuscript Preparation	3
HS18-02 Racial differences in long term survivor outcomes after Allogeneic hematopoietic cell transplantation	Manuscript Preparation	2
HS18-03 Racial/ethnic disparities in receipt of hematopoietic cell transplantation and subsequent resource utilization in children with acute leukemia	Protocol Development	4
HS19-01 Factors associated with clinical trial participation among hematopoietic stem cell transplant patients: A CIBMTR analysis.	Data File Preparation	5
HS20-01 Resource Intensity of end-of-life care in children after hematopoietic stem cell transplant for acute leukemia: Rates and disparities.	Protocol Development	6
HS22-01 Health care utilization and costs of haploidentical allogeneic stem cell transplants in a contemporary cohort of	Protocol Development	7

pediatric patients with acute leukemia and myelodysplastic syndrome.		
HS23-01 Community health status and long-term outcomes in 1-year survivors of autologous and allogeneic hematopoietic cell transplantation in the United States.	Protocol Development	8

Oversight Assignments for Working Committee Leadership (March 2023)	
Leslie Lehmann	**HS16-01** Trends in utilization and outcomes of autologous and allogeneic hematopoietic cell transplantation in racial and ethnic minorities
	HS20-01 Resource Intensity of end-of-life care in children after hematopoietic stem cell transplant for acute leukemia: Rates and disparities
	HS22-01 Health care utilization and costs of haploidentical allogeneic stem cell transplants in a contemporary cohort of pediatric patients with acute leukemia and myelodysplastic syndrome.
Hemalatha Rangarajan	**HS16-03** Relationship of race/ethnicity and survival after single and double umbilical cord blood transplantation
	HS19-01 Factors associated with clinical trial participation among HSCT patients: a CIBMTR Analysis
Minoo Battiwalla	**HS18-01** International collaborative study to compare the prognosis for acute leukemia patients transplanted with intensified myeloablative regimens
	HS18-02 Racial differences in long term survivor outcomes after Allogeneic hematopoietic cell transplantation
	HS18-03 Racial/ethnic disparities in receipt of hematopoietic cell transplantation and subsequent resource utilization in children with acute leukemia
	HS23-01 Community health status and long-term outcomes in 1-year survivors of autologous and allogeneic hematopoietic cell transplantation in the United States.