Not for publication or presentation

A G E N D A
CIBMTR WORKING COMMITTEE FOR HEALTH SERVICES AND INTERNATIONAL STUDIES
Salt Lake City, UT
Saturday, April 23, 2022, 12:15 PM - 1:45 PM

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1. **Introduction**
   a. Minutes from February 2021 meeting (Attachment 1)
   b. Instructions for sign-in and voting

2. **Accrual summary** (Attachment 2)

3. **Presentations, published or submitted papers**
   a. **HS16-01** Nandita Khera, Theresa E. Hahn, Ruta Brazauskas, Benjamin Jacobs, Leslie E. Lehmann, Hashmi Shahrukh, William A. Wood, Sikander Ailawadhi, Wael Saber; Trends in Use and Outcomes of Autologous and Allogeneic Hematopoietic Cell Transplantation in Racial/Ethnic Minorities. ***Blood 2021; 138 (Supplement 1): 427. doi: https://doi.org/10.1182/blood-2021-146967. Oral presentation, ASH 2021.***
   b. **HS18-02** Brandon J. Blue, Ruta Brazauskas, Karen Chen, Shahrukh Hashmi, Leslie E. Lehmann, William A. Wood, Navneet S. Majhail, Wael Saber; Racial and Socioeconomic Disparities in Long-Term Outcomes in ≥ 1 Year Allogeneic Hematopoietic Cell Transplantation Survivors: A CIBMTR Analysis. ***Blood, 2021; 138 (Supplement 1): 3929. doi: https://doi.org/10.1182/blood-2021-153357. Poster presentation, ASH 2021.***

4. **Studies in progress** (Attachment 3)
   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)
   Analysis

b. **HS16-03** Relationship of Race/Ethnicity and Survival after Single and Double Umbilical Cord Blood Transplantation (K Ballen) **Analysis**

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) **Analysis**

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) **Data file preparation**

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**

h. **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) **Data file preparation**

i. **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) **Protocol development**

5. Future/proposed studies

a. **PROP 2109-18** Health Care Utilization and costs of haploidentical allogeneic stem cell transplants in a contemporary cohort of pediatric patients with acute leukemia and myelodysplastic syndrome (H Rangarajan/ P Satwani) (Attachment 4)

b. **PROP 2110-28** Utilization of chimeric antigen receptor (CAR) T-cells differs by race and ethnicity compared to autologous hematopoietic cell transplant (autoHCT) (M Herr/ C Ho) (Attachment 5)

c. **PROP 2110-164** Changes in international Hematopoietic Cell Transplantation (HCT) Practices since publication of "Choosing Wisely BMT" (M Seftel) (Attachment 6)

d. **PROP 2110-229** The impact of ethnicity, race, and socio-economic status (SES) in mismatched unrelated donor (MMUD) allogeneic hematopoietic cell transplantation (HCT) (T Wang; A Jimenez) (Attachment 7)

6. *Proposed studies; not accepted for consideration at this time*

a. **PROP 2110-41** Association of Racial and ethnic disparities and outcomes of acute leukemia patients receiving a haploidentical stem cell transplant. *Dropped-overlap with recent study.*

b. **PROP 2110-140** Trend in Survival in Patients Undergoing Allogeneic Hematopoietic Stem Cell Transplantation. *Dropped overlap with recent study.*

c. **PROP 2110-226** Comparing demographic characteristics of pediatric and young adult patients receiving cellular therapy versus hematopoietic stem cell transplantation for relapsed/refractory acute lymphoblastic leukemia. Dropped-low scientific impact.

d. **PROP 2110-247** Characterizing Changes in the Transplant and Cellular Therapy Workforce and Associations with Race-Ethnic Treatment Equity *Dropped-supplemental data needed.*

e. **PROP 2110-297** Evaluation of Allogeneic Hematopoietic Cell Transplantation Outcomes in Underrepresented Minorities in the Era of Haploidentical Donor Transplant with Post-Transplant Cyclophosphamide. *Dropped-overlap with recent study.*

7. Study Presentation

1. HS16-01 Analysis result update (N Khera)
2. Updates on the CSA research project (A Sharma)

MINUTES
CIBMTR WORKING COMMITTEE SESSION
Thursday, February 11, 2021, 1:00 - 4:00 pm
Co-Chair: Bronwen Shaw, MD, PhD; CIBMTR Statistical Center, Milwaukee, WI; E-mail: beshaw@mcw.edu
Co-Chair: John Wingard, MD; University of Florida, Gainesville, FL; E-mail: wingajr@ufl.edu

INTRODUCTION:

Dr. Wingard opened the virtual meeting at 1:00 pm by welcoming the working committee members and the presenters. He discussed the proposal selection and voting process. Though the pandemic amended the process for proposal selection, 368 working committee proposals were submitted and evaluated altogether by CIBMTR Working Committee Chairs and Scientific Directors. About 61% were screened out, 30% had less-relative scientific merit, and 3% were combined with overlapping proposals with relevant nature. 21 proposals (about 6%), were considered for advancing of further pro-development. The proposals were pre-recorded 5-minutes presentations of the 15 semi-finalists, which were presented by the principal investigators. Each presentation was followed by a 5-minute question and answer session, in which audience was invited to submit questions via live chat. For those not able to attend the live session, a link was posted with the session recording and voting was closed on Monday, February 15, 2021. Audience was also instructed on where to locate the scoring and voting links for the presentations. It was mentioned that over 1,000 Working Committee members voted on the first screening of these proposals. Dr. Shaw led the second part of the meeting starting with presentation #9.

GENERAL REMINDERS:

The following reminders were mentioned and posted via the chat option:

a. Thank you for participating in the CIBMTR Working Committee Session! Please cast your score here: https://mcwisc.co1.qualtrics.com/jfe/form/SV_7QwO1ZvzfPZV1NY to vote on the proposals that were presented during the session.
b. Several presenters provided their email addresses for any future communication.

PRESENTATIONS:

1. **Risk of subsequent neoplasms in patients with post-transplant cyclophosphamide use for graft-versus-host disease prophylaxis.** This proposal was presented by Dr. Ana Alarcon Tomas. The primary objective of this proposal is to describe the incidence rate, risk factors, characteristics, and outcomes of subsequent neoplasms in patients receiving post-transplant cyclophosphamide (PTCy) and compare it with calcineurin inhibitors-based graft-versus-host disease prophylaxis and the general population. The CIBMTR identified 64,935 patients ≥18 years of age who underwent a first allogeneic for a malignant disease between 2008-2017. 5,771 (9%) of these patients developed a subsequent neoplasm. Currently, there are no published studies on the incidence of subsequent neoplasms in patients who received post-transplant cyclophosphamide. The following questions were answered during the Q&A:
    a. How are we going to prove that these secondary neoplasms are related to post-transplant cyclophosphamide or cyclophosphamide in conditioning and not due to "by chance" itself- as in general population? This is a case-controlled study. For example, for each patient received with a post-transplant cyclophosphamide will be matched with at least three patients who didn't receive post-transplant cyclophosphamide. Characteristics including primary disease, HLA complexity, survival, follow up time etc. would be used for matching and reviewing survival will also allow us to see that this is because of PTCy and not by coincidence.

b. What is the median follow up time from transplant and subsequent malignancy in post-transplant cyclophosphamide group? I assume it is much shorter than other cohort? Information is not available for each median follow up time cohort. What is available is the median follow up for all patients and some numbers related to the type of diseases for each group. Dr. Rachel Phelan included in the chat that the median follow-up for the PT-Cy group is 38.2 months, and for the proposed control population is 60.3 months.
c. How is this in comparison with matched unrelated donor and cord transplants? Cord transplants will be excluded from the analysis because we don't think we can match those patients.
d. Do we have adequate follow up to answer this important question? We have follow-up for mantle hematological diseases but less time for solid tumors. However, when we saw the numbers that we have (around 5,000 - 5,700) subsequent neoplasms, the majority of cases occurred after the 1st - 5th year of post- transplant and have a 5-year median follow up. We think we have enough numbers to address this question now and we should not wait because it hasn't been published before. This is a noble study and if we wait for a longer median follow up, we might lose that opportunity to have it published first.

Additional questions and comments posted via the chat but were unanswered due to limited time can be found in Appendix A.

2. **Outcomes of chimeric antigen receptor-T cell therapy for patients with antecedent chronic lymphocytic leukemia (Richter's Syndrome)**. This proposal was presented by Dr. Farrukh Awan. The objective of this proposal is to assess outcomes in adult patients with chronic lymphocytic leukemia undergoing transformation to diffuse large B-cell lymphoma (Richter's Syndrome) and undergoing CAR-T therapy. The CIBMTR identified 36 patients underwent CAR-T for Richter's Syndrome from 2015-2019. The following questions were answered during the Q&A:
   a. I know that in the Ohio State paper have many patients that used concurrent Bruton Tyrosine Kinase (BTK) inhibitors. Will you be able to collect data on concurrent BTK inhibitors for these patients? Yes, this information is available through the CIBMTR dataset.
   b. Are you looking at diffuse large B-cell lymphoma derived Richter's Syndrome or chronic lymphocytic leukemia derived Richter's Syndrome? Yes, but it is difficult to determine a clonality between related and unrelated Richter's syndrome. Any studies that show similarities versus dissimilarities in the clone would be very helpful but unfortunately, previous studies have shown that this has been consistently difficult.
   c. You mentioned the opportunity of comparing to other treatment groups. Can you talk about that a little more? We can compare to patients with de novo diffuse large B-cell lymphoma. There are multiple approved and ongoing studies within CIBMTR of diffuse large B-cell lymphoma patients, who do undergo CAR-T therapy and look at toxicity outcomes and infectious outcomes, for example. There are efforts in place to look at outcomes of transplantation for patients with Richter's Syndrome, which can improve the impact of this project and be a competitor to those other ongoing studies.
   d. How many pts do we have? 36 patients
   e. How do you plan to deal with the very low patient numbers (n=36) to make meaningful conclusion? I agree that it is a small number, but it is substantial. Despite the small numbers, if the right competitors are used, such as those mentioned previously, this study can still provide an impactful dataset.

   Additional questions and comments posted via the chat but were unanswered due to limited time can be found in Appendix B.

3. **Impact of graft versus host disease following allogeneic hematopoietic cell transplantation on leukemia free survival in hematologic malignancies**. This proposal was presented by Dr. Andrea Bauchat. The objectives of this proposal is to determine the impact of development of grade I-II acute graft versus host disease on relapse and leukemia-free survival, to assess the impact of development of grade III-IV acute graft versus host disease on relapse and leukemia-free survival, and to determine whether the impact of graft versus host disease on

relapse and leukemia-free survival is influenced by disease risk prior to HCT. The CIBMTR identified 1,345 children <18 years who received first HCT for acute lymphoblastic leukemia and acute myeloid leukemia receiving first allogeneic transplantation between 2008 - 2017. The following questions were answered during the Q&A:

a. What is the sample size of each sub-group: disease-risk index (DRI)-low, -intermediate, -high? Exact sample size not available but the high-risk group was less in comparison to others.
b. How will you factor in occurrence of chronic graft versus host disease in your analysis? Our main focus is on acute graft versus host disease because it will have more impact on our clinical practice. However, we will collect the data for the interactions of chronic graft versus host disease alone, and if the patient had a history of acute.
c. What is the biological basis for focusing this study on a pediatric population? The interest from our perspective is looking at the pediatric population compared to the adults. The literature on pediatric is severely lacking in comparison to adults and we need to expand on that for the patient population that we care for.
d. Are you going to separate acute myeloid leukemia and acute lymphoblastic leukemia numbers at DRI level? Yes, they are already divided from DRI protocol. Our acute lymphoblastic leukemia patients are about 1,300 and the acute myeloid leukemia are about 1,200.
e. Is the analysis going to be time dependent or landmark? Landmark
f. Do you have the date of this max acute graft versus host disease grade to take into account the time to event aspect of the effect? No
g. Do you have a plan to include/account for the various GVHD prophylaxis regimen "strengths?" We are taking into consideration of what GVHD prophylaxis regimen the patient uses. This data, which is already categorized, will show us the differences between trends.
h. What is the clinical benefit besides prognostic? This will help define a better foundation of which patients will benefit more from a little bit of graft versus host disease. If we can come up with a patient category that we see is beneficial to have exposure to a little bit of graft versus host disease, it can go forward with clinical trials and GVHD prophylaxis adjustment or manipulation to improve their Leukemia-free survival.

Additional questions and comments posted via the chat but were unanswered due to limited time can be found in Appendix C.

4. **Effect of HLA evolutionary divergence on survival and relapse following allogeneic hematopoietic cell transplant**. This proposal was presented by Dr. Christine Camacho-Bydume. The primary objective of this proposal is to determine if HLA evolutionary divergence (HED) of HLA class I alleles of HLA-A, -B, -C and HLA class II alleles of HLA-DR is associated with overall survival and relapse. The objective is to also evaluate association of HED with acute and chronic GVHD and treatment-related mortality (TRM). The CIBMTR identified pediatric and adult patients with acute myeloid leukemia, myelodysplastic syndromes, acute lymphoblastic leukemia, chronic myeloid leukemia, or lymphoma (non-Hodgkin or Hodgkin's lymphoma), who have received initial allogeneic 8/8 HLA-matched (HLA-A, -B, -C, -DR) transplant between 2008 - 2018. The following questions were answered during the Q&A:

   a. Could HLA diversity simply be a surrogate for race? How would you account for race in the study? Great question given there are particular HLA alleles that are more common in certain ethnic groups. We do think that evaluation of HED lows and highs within these different ethnicities can help to tease this out more, with potential to adjust for race more in this analysis. We think some of these differences in peptide binding grooves can help us to understand better the different peptides and how antigens are presented to T-cells.
   b. Extrapolating HLA data from solid tumors and checkpoint inhibitors and their antigen presentation is slightly challenging in context of allo donor T-cell interaction with antigen presented for bone marrow origin cancers. Yes, have to consider there could be some differences. Was a small previous study that

looked at this question, saw some signals there, larger population and different types of cancers, may be able to explore that more.

c. Leukemia (both lymphoblastic and myeloid) have low mutational burden as compared to melanoma and lung. Will the HED algorithm still work? Yes, we do expect to see differences in mutational burdens, and we do plan to look at the cohort at large to look at the disease subgroups to see more or less of this phenomenon in these groups. Do you have preliminary data in leukemias? There was a small study in Germany that looked at AML, to my knowledge only one that looked at leukemias. Mutational burden did see some differences, so we do expect it and also, besides the overall cohort, also plan to look at disease subgroups.
d. Given HED implications for infection surveillance, are you going to look at infectious sequelae differences? No, at the moment we have initially requested information in terms of tumor control, relapse, overall survival, graft versus host disease, and TRM. Not sure of availability of the other information but would be interesting to look at if available.
e. Would you please discuss the confounding effects of HLA mismatching for HLA-DRB3, 4, 5, DQ, and DP? Not known off the top of my head the percentages of mismatching differences in this cohort. For DR at least they will be matched, 8/8 matched, in terms of DP, don't have that info but if available it is something that can be looked at.

Additional questions and comments posted via the chat but were unanswered due to limited time can be found in Appendix D.

5. **Impact of IDH1 and IDH2 mutations on outcomes of acute myeloid leukemia patients undergoing allogeneic hematopoietic cell transplantation**. This proposal was presented by Dr. Evan C. Chen. The primary objective of this proposal is to identify differences in survival outcomes between mutIDH1/2 and wtIDH1/2 acute myeloid leukemia patients and to assess the prognostic significance of disease features in mutIDH1/2 and wtIDH1/2 acute myeloid leukemia patients. The CIBMTR identified patients ≥ 18 years old with a diagnosis of normal karyotype acute myeloid leukemia, receiving first allogeneic HCT during CR1 in 2013 - 2019. The following questions were answered during the Q&A:
   a. Is there any concern that patients with IDH1/2 mutated acute myeloid leukemia would have received more intensive conditioning / therapy than IDH1/2 wild-type? Yes, and it's important to look at how conditioning intensity can be an important covariant, which is a variable captured in CIBMTR.
   b. Will you have registry information on the type and duration of use of IDH inhibitors before/after HCT? It's currently not available with CIBMTR.
   c. IDH mutations are usually seen in older subjects. How will you a priori adjust for this known association? Age will certainly be a covariant in our multi-variant analysis.
   d. How reliable are the wild-type patients as some may just not be tested for IDH mutations? It is double checked. There is a datapoint in the forms that indicate whether or not testing has been done, versus if testing was done and IDH was found to be absent.
   e. Do you have information what the numbers will be like when you divide your patient groups with concomitant mutations such FLT3 or p53 that may have an impact on outcomes? Yes, the numbers are about 20-40 for co-mutated for ITD and NPM1 patients. p53 not provided.
   f. Is there data in CIBMTR forms that collect use of IDH inhibitors pre transplant? Will you be able to study their impact on the transplant? I'm not aware of this data point being available in the forms but it is something that we should follow up on.
   g. How do you analyze its (or ITS?) with multiple mutations? With regards to double-mutated patients, IDH1, and IDH2 patients, which are generally rarely reported, we would look at the CIBMTR forms to ensure accurate data entry. In regard to analyzing IDH with other co-mutations, we would include co-mutations as a co-variant in a multi-variant analysis, should the sample size permit.

h. What about other mutations in Wild type IDH? We focus on NPM1 and FLT3-ITD because they are prevalent in the cytogenetic risk population. We will look at the other mutations to see if they have any relevance at all.
i. Do the data forms reliably collect information on use of IDH inhibitors pretransplant? Data point is not available.

Additional questions and comments posted via the chat but were unanswered due to limited time can be found in Appendix E.

6. **Characteristics and outcomes of adolescent and young adults with multiple myeloma treated with autologous hematopoietic cell transplant**. This proposal was presented by Dr. Christin B. DeStefano. The primary objective of this proposal is to describe patient and disease related characteristics of adolescent and young adults (AYAs) with multiple myeloma treated with early high dose melphalan and AutoHCT and to characterize response to AutoHCT, survival outcomes, SPMs, and infections of AYA multiple myeloma patients and AutoHCT. The CIBMTR identified 1,142 AYA multiple myeloma patients who underwent autologous hematopoietic cell transplant) between 2008 -2018. The following questions were answered during the Q&A:
   a. What will differentiate this study from MM18-03 "To compare the outcomes in young patients with multiple myeloma at diagnosis undergoing upfront autologous hematopoietic stem cell transplant with older patients in the US: progression-free and overall survival"? There appears to be substantial population overlap. The Scientific Director clarified via the chat function that MM18-03 included the years 2013-2017 and excluded patients less than 40 years from the outcome analysis owing to small numbers.
   b. How do you plan to control for differences between your AYA group and older control group which would be attributable to age? In total, there are about 1,700 TED and CRF cases. We can adjust the critical variables of these cases, such as stage, treatment rendered, and cytogenetics, for example, to control for differences.
   c. Will results be stratified according to different induction regimens? Yes, we will adjust those critical variables amongst the CRF cases where this information is available.
   d. A cohort going back to 1995 seems too outdated. What was the N for a more recent group (since 2010)? There were 1,142 AYA cases between 2008-2018.
   e. This is a long cohort 1995-2019 with lots of changes in induction treatment, novel agents and time to bone marrow transplant. How will this be controlled for? We are going to study induction regimens, post-transplant treatment, use of tandem transplants in our analysis.
   f. Will you be also studying the effect of post-transplant maintenance therapy? Also, any effect of extramedullary plasmacytomas in this AYA group? We will for cases where this information is available. Extramedullary plasmacytomas are a good focus, as AYA patients may have a more aggressive presentation of myeloma.
   g. Are plasma cell leukemias included in this analysis? No

   Additional questions and comments posted via the chat but were unanswered due to limited time can be found in Appendix F.

7. **Impact of measurable residual disease status on outcomes of AML in patients 18-65 years old in CR1 undergoing Allo-HCT**. This proposal was presented by Dr. Firas El Chaer. The objectives of this proposal is to determine if acute myeloid leukemia measurable residual disease (MRD) analysis as currently performed has prognostic value when measured prior to AlloHCT, to explore factors that may modify the risk associated with detectable acute myeloid leukemia MRD pre-AlloHCT, and identification, using MRD combined with other clinical factors, of patients most at risk of post-AlloHCT relapse. The CIBMTR identified 753 MRD positive and 1986 MRD negative adult patients receiving first AlloHCT for de-novo AML in CR1 in 2007-2018. The following questions were answered during the Q&A:

a. What kind of MRD data is collected? Depending on the individual participating centers, the methodology uses molecular or immunotherapy? MRD
b. What is the rate of missing MRD status and are those patients different from those with MRD data available? The answer is not included in this study.
c. Are you going to also study the effect of post-transplant maintenance in AML FLT3, IHD mutations on relapse and overall survival? One of the aims of this study is to have future studies look at post-transplant maintenance from this study.
d. What do you mean by most "recent" pre-conditioning MRD assessment? Would testing need to be completed within a specific time frame before conditioning? All patients who will be receiving a stem cell transplant are required to get a bone marrow biopsy and peripheral blood aspiration before transplantation. Within a month before the transplant, we would look at data point.
e. What is your working definition of MRD? A combination of molecular testing as well as immunotherapy by NFC.
f. Are all mutations equivalent when thinking about MRD? Absolutely not.
g. How sure are you that the MRD patients are really MRD negative? We can never be absolutely sure.
h. How are you going to account for the different sensitivity of methods used to determine MRD? Are ELN risk available at CIBMTR, since when? The way that CIBMTR reports the acute myeloid leukemia data is by reporting their cytogenetics and mutation analysis so we can calculate the data for this population. The point of this study is to look at the commercial availability of these tests and we can rely on it or if we should standardize one testing at all centers.

Additional questions and comments posted via the chat but were unanswered due to limited time can be found in Appendix G.

8. **Racial, ethnicity and socioeconomic disparity in outcome of patients with chronic graft versus host disease.** This proposal was presented by Dr. Nosha Farhadfar. The objectives of this proposal are to determine whether clinical manifestations and severity of chronic GVHD differ based on racial/ethnic and socioeconomical status (SES) differences, to determine whether treatment patterns of chronic GVHD differ based on racial/ethnic and SES differences, and to evaluate whether chronic GVHD treatment outcomes differ based on racial/ethnic and SES differences. The CIBMTR identified 17,665 patients, age 18 years or older, who have received first allogeneic transplant for hematologic malignancy (acute myeloid leukemia, acute lymphoblastic leukemia, myelodysplastic syndrome) between 2008 - 2019. The following questions were answered during the Q&A:
   a. I like the idea for looking at outcomes based on race/ethnicity/SES but not sure if incidence should be a primary outcome because it will be dependent on donor type which is very different amongst the groups. The primary outcome of this study is to look at the outcome of patients who develop chronic graft versus host disease. We need to look at the whole cohort, report the incidence, and then focus on chronic graft versus host disease cohort as the primary endpoint of this study.
   b. How will you correct for the impact of race on HLA mismatch between recipients and donors due to the lower chance of identifying a fully matched donor in non-Hispanic white patients? For the same reason, should cord blood recipients be excluded? We are going to include both the donor type, graft source and degree of HLA matching as covariables in a multi-variable analysis. Cord blood recipients should not be excluded, as there was near 14% of Non-Hispanic black, 14% Hispanic, and 15% Asian who received cord transplant. Approximately 7-8% of cord transplants were received by Non-Hispanic whites. We do have the number to look into cords but if a statistician reviews and determines we don't have the power, then we can eliminate the cords.
   c. Is it possible to access constitutional DNA to look at ancestry information markers in this population? This information is not available for the population. The analysis will focus on self-reported race/ethnicity.
   d. All patients in your cohort from 2008 were not reported with NIH consensus criteria for chronic GVHD. Since you have large numbers, should you limit this to more recent time period? We do have all of the

information on graft versus host disease and whether it was limited or extensive. There is information on whether graft versus host disease is progressive, de-novo or interrupted. We have organ involvement and maximum grade of chronic graft versus host disease. NIH scoring is available for at least the past 4 years and maybe we can look at that group separately. Within the past 4 years, the population limited to NIH grading only in about 1,500 non-Hispanic white, 270 non-Hispanic black, and 200 Hispanic, who have developed chronic graft versus host disease.

Additional questions and comments posted via the chat but were unanswered due to limited time can be found in Appendix H.

9. **Time from diagnosis to transplant as an important contributor for post allogeneic stem cell transplant infections, immune reconstitution and its associated mortality/morbidity**. This proposal was presented by Dr. Lohith Gowda. The objectives of this proposal are to identify density and types of early and late infections (bacterial, viral and fungal) in patients that went to transplant a) <6 months b) between 6- 12 months and c) > 12 months from diagnosis; to identify T cell lymphocyte absolute numbers at days 100 and 180 and CD4/CD8 ratio for the timeline cohorts examining individual donor types; to evaluate the impact of bacterial, viral or fungal infections by day 100 and day 180 on 1-year post-transplant outcomes (relapse, non-relapse mortality, disease free survival, acute and chronic graft versus host disease); and to evaluate quantitative immunoglobulin levels at D+ 100 and + 180 if available. The CIBMTR identified 6,877 ≥ 18 years old patients who underwent first allogeneic transplants for AML in CR1, ALL in CR1 or MDS in the United States from 2012 to 2019. The following questions were answered during the Q&A:
   a. How many patients in the registry have the immune parameters you wish to assess? >2100
   b. How will you account for the type of treatment used prior to transplant? For example, treatments such as hypomethylating agents may require months of treatment before transplant versus induction chemo that works more quickly. We do have some variables that are available, such as types of therapy, and we can analyze levels of intensity of therapy (low to high) and post-transplantation outcomes. The exact number of how many patients who have had different intensities of therapies is not available.

   Additional questions and comments posted via the chat but were unanswered due to limited time can be found in Appendix I.

10. **Efficacy and safety of CD19 directed CAR T-cell therapy for non-Hodgkin B-cell lymphomas with secondary central nervous system involvement**. This proposal was presented by Dr. Hamza Hashmi. The primary objective of this proposal. The CIBMTR identified 55 adult patients (age ≥ 18) who received CD19 CAR T-cell therapy for B-cell NHL with secondary central nervous system (CNS) involvement. The following questions were answered during the Q&A:
   a. How will you differentiate between immune effector cell-associated neurotoxicity syndrome (ICANS) and CNS relapse? ICANS will be documented as a neurotoxicity and CNS relapse will be when the form is filled out.
   b. Is this active CNS disease or previously treated CNS disease? The data received from CIBMTR looks at CNS disease at the time of diagnosis and the CNS disease that is present at the time of cellular therapy.
   c. Do you have any registry information on concomitant CNS therapy (chemo/radiation) pre, peri and post transplantation? Answer was not available at this time.
   d. How many patients are in your study? How will you define whether the patients have cleared their CNS involvement? There are currently 60 patients in the history of this data. Of the 60, 40 had this disease at the time of diagnosis and 20 had this disease at the time of cellular therapy. Whether the patients have cleared their CNS involvement, this information is not available at the time.
   e. Since this is your primary endpoint, how will you account for the differences of frequency of CRS and ICANS across different products (e.g. high in Yescarta, lower in Kymriah, low in Breyanzi)? If you look at the toxicity profile of CD19 therapy, they seem to be relatively similar.

f. Could you please include other agents such as anakinra, siltuximab, and other agents? Dasatinib for this populations for ICANS? Also, was CNS disease under control at CAR-T therapy? As for Anakinra, siltuximab, and other agents, I'm not sure if CIBMTR is capturing this data. As for dasatinib, I'm not sure if this information is available as well. Per Dr. Pasquini of CIBMTR in the live chat, he commented "we capture treatment of ICANS, like siltuximab, dasatinib has been reported as other treatment."
g. Will you have detail on the nature and extender features of secondary CNS involvement to associate with the toxicity and outcome? I only have the essential data with me but am hopeful that this comprehensive research will have further detail.
h. Will all the patients included have active CNS disease at the time of CAR-T or, are treated CNS disease are also included? They are both included, and we are able to tell who has had active disease with a prior history at the time they got the CAR-T therapy.

Additional questions and comments posted via the chat but were unanswered due to limited time can be found in Appendix J.

11. **Haploidentical donor versus matched donor allogeneic hematopoietic cell transplantation in patients with myelofibrosis**. This proposal was presented by Dr. Tania Jain. The primary objective of this proposal is to explore the impact of donor type on overall survival of patients undergoing HCT for myelofibrosis. The CIBMTR identified 1,640 patients ≥18 years old diagnosed with primary, post-ET or post-PV myelofibrosis and undergoing first HCT between 2013 and 2019. The following questions were answered during the Q&A:
    a. Are you also going to compare the effect of pretransplant Ruxo in haplo vs MUD/MRD? Also, are you going to look for graft failures as well in these patient populations? Yes, this will be included. We also do look at graft failures in these populations.
    b. Is there a difference in time from diagnosis to HCT across the groups? The median time from diagnosis to transplant for haploidentical patients was 38 months, while for HLA- identical sibling and URD 8/8 was 21 and 24 months, respectively.
    c. Are you including all conditioning regimens types: MAC, RIC and NMA? Yes, and they will be looked at for comparison in the univariable and may be taken to the multivariable analysis as well.
    d. For the graft failure or rejection analysis are you going to include spleen size? Ideally it should be included but the spleen size measurement has many variables and it may not be a clean assessment. We don't collect precise spleen size in our forms, but it can be analyzed as spleen size as splenomegaly, no splenomegaly or splenectomy.
    e. Can you comment on the bone marrow vs peripheral blood in the three groups? Peripheral blood is more common in the donor source (about 80%).

    Additional questions and comments posted via the chat but were unanswered due to limited time can be found in Appendix K.

12. **Assessing utilization and clinical outcome differences by sex and race in CAR-T for relapsed/refractory NHL**. This proposal was presented by Dr. Arushi Khurana. The objective of this proposal is to enhance our understanding of sex- and race-based differences in utilization of CAR-T vs AutoHCT and outcomes after CAR-T. The CIBMTR identified 1,133 patients to compare sex and race/ethnicity rates for first cellular infusion (AutoHCT vs. CAR-T) for relapsed/refractory non-hodgkins lymphoma patients from 2017 – 2019 (aim 1a). The CIBMTR identified 619 non-hodgkins lymphoma patients who relapse after first AutoHCT to describe subsequent treatment patterns (e.g. CAR-T, second AutoHCT, AlloHCT, other treatment, no treatment) by sex and race/ethnicity (aim 1b). The CIBMTR identified 1,253 patients to identify sex-and race-based differences in response to CD19 CAR-T in aggressive lymphomas (aim 2). The following questions were answered during the Q&A:
    a. Is there gender and race-based difference in SEER data with or without treatment for diffuse large B-cell lymphoma even before CAR T? Yes, that data does exist.

b. Can this be stratified by center/geography (private/public, large urban/rural)? Yes, it will be shown based on zip code (of patient and of recorded center), which will allow us to differentiate from urban/rural as well.
c. We saw almost no neurotoxicity in women so would you be plotting CRS and ICANS based on gender and race? Yes, and we believe CIBMTR is the best resource for this because of the larger numbers
d. How do you differentiate between larger trial centers vs less resourced centers? The information is reported based on the center type. Basing on academic or zip code, or city versus rural center, that will also be a way to differentiate the centers.
e. Would disease response status prior to cellular therapy be taken into account for analysis? Yes, that is one of the co-variants that will be included.
f. How reliable is the data you will get to study "access", as there are many factors, depending on patient specific factors (education, resource, finances, mobility, support, performance, etc.), center specific (criteria), and also access depends on the hematologist/oncologist who sees these patients in the community? Access to a center is not one of the main issues in this study. It is more about why some of these minorities receiving other treatments when they should be receiving cellular therapy at the time of indication.
g. Is there any way to take into account insurance issues? We do look at the insurance statuses as one of the co-variants.
h. Would it be possible to look at differences in access based on commercial CAR T vs. clinical trials? The majority of the patients from the forms received are from commercial CAR T.

Additional questions and comments posted via the chat but were unanswered due to limited time can be found in Appendix L.

13. **Optimal GVHD prevention strategy in older, robust patients with acute leukemias and myeloid malignancies undergoing myeloablative, matched donor hematopoietic cell transplantation**. This proposal was presented by Dr. Richard J. Lin. The primary objective of this proposal is to compare CRFS among patients ≥ 60 years old undergoing myeloablative conditioned, allogeneic hematopoietic cell transplantation with following graft versus host disease prophylaxis in 2 matched-pair analysis and to compare other transplant outcomes in the above 2 matched-pair analysis. The CIBMTR identified 1,301 patients at ≥ 60 years old at the time of first allo-HCT between 2010 and 2019, with any myeloablative conditioning defined by CIBMTR, 8/8 matched related or unrelated donor only, graft versus host disease prophylaxis (ex-vivo TCD/CD34+ selection versus PTCy-based versus Tac/MTX). The following questions were answered during the Q&A:
    a. What do you mean by "robust?" Is it based on KPS, HCT-CI, or just the fact that someone got MA. regimen? We use the definition of a patient getting a myelo-conditioning as a way of saying that they are robust by their transplant centers.
    b. Are patients with In-vivo T cell depletion (Campath or ATG) excluded from this analysis? T cell depletion and CD34 selection does include ATG and does not include Campath.
    c. Why do you pool post-CY and ex vivoCD34+ selection? Can we still consider ex vivoCD34 selection to be a promising transplant modality in 2021? We wanted to compare a 2-match pair analysis and not a direct comparison between CD34 selection and post-CY. We do know which will be better for an older patient.
    d. Why exclude TBI? For older patients, we don't consider TBI to be a conditioning regimen.
    e. How many patients with Tac/methotrexate prophylaxis had ATG? Answer was not available at the time of Q&A.
    f. Do we know GFR (creatinine) coming into allo in these groups? In this study, we didn't include the GFR (creatinine) as a variable but we have some evidence in older patients that does play a major role. I can discuss with our statistician on whether we can include this as a variable.

    Additional questions and comments posted via the chat but were unanswered due to limited time can be found in Appendix M.

14. **Outcomes of elderly patients receiving CD-19 directed CAR-T therapy for B-cell lymphomas**. This proposal was presented by Dr. Sayeef Mirza. The primary objectives of this proposal to evaluate cumulative incidence grades, duration and median time to onset of CRS and CRES/ICANS in patients > 65 years of age receiving CD-19 directed CAR-T therapy, describe post CAR-T clinical outcomes and resource utilization in elderly, and identify disease biology, comorbidities and other clinical predictive markers of toxicity, response, and survival in elderly patients. The CIBMTR identified 1,036 patients (<65y,n=612; 65-74y, n=348; >75y, n=76) with the diagnosis of any B-cell lymphoid malignancy (indolent or aggressive lymphoma) receiving CAR-T cell product (CD19 target). The following questions were answered during the Q&A:
    a. Would you please also look at Incidence of pancytopenia, hypogammaglobulinemia and HLH in elderly versus younger in 3 cohorts <60, 60-75 ,>75? I think it's very important to look at this as the data becomes available to us. We are primarily looking at different age groups. We have 81 patients over the age of 75 and five patients over the age of 85. Overall, there are 435 (40 %) of the group are over 65 years old.
    b. How does this defer from the data presented by Dr. Pasquini last year in older patients? This data will be more helpful in including both CAR-T products.
    c. In case of CAR T was used for post-alloHCT relapse, would the donor age of the CART source be analyzed? This is something that we should include in our analysis.
    d. Are data on baseline geriatric scores or HCT-CI available for all? The answer was not available at the time of the Q&A.
    e. Do we have registry information on whether CAR-T production succeeded or not, when attempted? The answer was not available at the time of the Q&A but the moderator did state that on behalf of CIBMTR, this information is not captured.

    Additional questions and comments posted via the chat but were unanswered due to limited time can be found in Appendix N.

15. **Determinants of successful discontinuation of immune suppression following allogeneic hematopoietic cell transplantation**. This proposal was presented by Dr. Joseph Pidala. The primary objective of this proposal is to validate prediction models for immune suppression discontinuation (ISD) and ISD failure developed in prior DISCIS-defined population, explore ISD and ISD failure in a new population inclusive of full range of diversity in current HCT practices, construct and validate dynamic prediction models of ISD and ISD failure in the expanded population. The CIBMTR identified 20,031 patients with a hematologic malignancy who received an allogeneic HCT from matched sibling donor, matched or mismatched unrelated donor, umbilical cord blood or haploidentical donor between 2009-2018. The following questions were answered during the Q&A:
    a. Can you explain how the ISD data information was made feasible? We used CIBMTR follow up data in the previous analysis that led to the development of the prediction model for ISD that we intend to validate in this study.
    b. Can you provide more granularity on how the time of discontinuation of immune suppression will be defined? In the CIBMTR data, there is a hard stop date for a complete discontinuation of immune suppression. That granular data is available, and it was the data we used for the prior project. We used that hard stop of all systemic immune suppression because that's an unambiguous measure of success.
    c. Many with PTCY may be discontinuing by days 100 or 60- likely based on center practice rather than patient response, how will this be addressed? Our prior project was successfully addressed this issue, specifically within that study population. The first step in this project is to validate those findings. We will definitely be studying how immune suppression was performed and what are the subsequent outcomes.
    d. Do you plan to use age as one of the variables regarding likelihood to discontinue IST, or will you have a separate pediatric specific model? Yes, we will consider age as a variable and evaluate the need for a pediatric specific model.

Additional questions and comments posted via the chat but were unanswered due to limited time can be found in Appendix O.

CLOSING:

Dr. Shaw, on behalf of herself and co-chair, Dr. John Wingard, did thank presenters, conference organizers, and the CIBMTR staff for having coordinated this virtual session. She did mention that this session was recorded and encouraged attendees to take survey, as access would be available until Monday, February 15, 2021.

APPENDICES:

A. Risk of subsequent neoplasms in patients with post-transplant cyclophosphamide use for graft-versus-host disease prophylaxis.

1. How will authorship work for these studies? The same as usual, there are fewer studies being accepted but the process otherwise is the same
2. What if a higher risk of cancer is related to the almost uniform use of 2GyTBI in these patients rather than PTCY?
3. What is the breakdown of haploidentical versus matched sib/MUD in the post-transplant cyclophosphamide group?
4. How can we r/o genetic predisposition on samples and variables of TBI based conditioning therapies?
5. What is your sample size and follow-up period?
6. How long post BMT you will follow up? From where will you receive the SN data?
7. Will you be adjusting for chronic GVHD when looking at your outcome of SN?
8. Is this study statistically powered to detect a difference between PTCY and above a certain threshold? What is the threshold?
9. Will analysis be conducted separately for TBI/non-TBI and MAC/RIC conditioning? Are you evaluating all malignancies?
10. Since the total CY exposure is likely not that different in PTCY vs. BU/CY or CY/TBI, is your hypothesis that the timing of exposure to CY may lead to a difference in risk? And if so, why?
11. Information on skin cancers - ssc, bcc available?
12. Matching for HLA matching could be a limitation because the PTCY patients are more likely to receive haploidentical grafts.

B. Outcomes of chimeric antigen receptor-T cell (CAR-T) therapy for patients with antecedent chronic lymphocytic leukemia (Richter's Syndrome).

1. If patients had failed an auto or allo, how do you plan to compare to the results of auto? Isn't it a different group?
2. Can you please provide your thoughts if the small n will be able to generate meaningful results at this time?
3. Would you include both transformed lymphoma from other low-grade lymphoma and Richter's transformation?
4. Are there concerns about underreporting Richter's?
5. Since the numbers are small, can we go back to centers to establish clonality?

C. Impact of graft versus host disease following allogeneic hematopoietic cell transplantation on leukemia free survival in hematologic malignancies. *No additional questions*

D. Effect of HLA evolutionary divergence on survival and relapse following allogeneic hematopoietic cell transplant.

1. Does the HED algorithm take into account variations outside the peptide binding groove?

2. What is the size of the cohort you are looking at?

E. Impact of IDH1 and IDH2 mutations on outcomes of acute myeloid leukemia patients undergoing allogeneic hematopoietic cell transplantation. *No additional questions*

F. Characteristics and outcomes of adolescent and young adults with multiple myeloma treated with autologous hematopoietic cell transplant.

1. How do you plan to control for differences between your AYA group and older control group?

G. Impact of MRD status on outcomes of AML in patients 18-65 years old in CR1 undergoing Allo-HCT.

1. How are you going to account for the different sensitivity of methods used to determine MRD? Are ELN risk available at CIBMTR, since when?
2. Hi Firas, How are defining the MRD?
3. The methods for MRD assessment may be quite heterogeneous, including the threshold of detection. How will you deal with the high likelihood of false MRD negative assessments from using inadequately sensitive quantification?
4. MRD test is different from different centers. How can you control for this?
5. How do you account for different MRD- cut-offs?
6. To clarify, if AML-MRD is to become a "precision medicine tool", does that mean is will be used to guide treatment decisions in addition to being prognostic?
7. How will control for the various methods for detecting MRD as different techniques have different sensitivities/accuracy?
8. if both multiparameter flow and NGS are available and are discordant on the same patient, how will that be analyzed?
9. is the MRD before alloSCT is the one to be analyzed?
10. Will this require more data from centers to answer some of the questions above?

H. Racial, ethnicity and socioeconomic disparity in outcome of patients with chronic graft versus host disease.

1. Is age significantly different in your Hispanic cohort? How do you adjust for it?
2. Was the MMUD recipient cohort limited to single antigen mismatch? Or all mismatches (understanding most MMUD will likely be single antigen MM)?
3. Do you have information on health insurance? Why not to study this question in a more homogeneous patient population to avoid the complexity and interactions in different factors?
4. Are there any other sociodemographic variables available that could be used to adjust for socioeconomic status, or is median income in the patient's ZIP code the only one?
5. Baker et al 2009 demonstrated no impact of household income on GVHD (acute or chronic) and only minimal impact of race on Grade III-IV aGVHD (none of cGVHD). Why do you think this null relationship should be pursued again?
6. Is there a plan to study as per continent distribution?
7. Is there a better index to gauge SES or poverty level?
8. Are Native American/Hawaiian/Pacific islanders being grouped elsewhere?

I. Time from diagnosis to transplant as an important contributor for post allogeneic stem cell transplant infections, immune reconstitution and its associated mortality/morbidity.

1. Do you plan to address the confounding influence of different factors leading to delay in transplant timing?
2. How are you going to account for number of cycles of chemotherapy versus no

chemotherapy as a confounder in the time delay?

J. Efficacy and safety of CD19 directed CAR T-cell therapy for non-Hodgkin B-cell lymphomas with secondary central nervous system involvement.

1. Is site-specific response (CNS vs. other lesions) and pattern of relapse/progression (CNS vs. systemic) available?
2. Why not to consider a comparative group?
3. Will you stratify patients according if they received IT chemo vs radiation therapy?

K. Haploidentical donor versus matched donor allogeneic hematopoietic cell transplantation in patients with myelofibrosis.

1. Availability of somatic mutations?
2. Is pretransplant Splenectomy data available? Are you going to factor this in the outcomes?
3. At least look at splenectomies?
4. What risk stratification is being used? DIPSS or DIPSS+?

L. Assessing utilization and clinical outcome differences by sex and race in CAR-T for relapsed/refractory NHL. *No additional questions*

M. Optimal GVHD prevention strategy in older, robust patients with acute leukemias and myeloid malignancies undergoing myeloablative, matched donor hematopoietic cell transplantation. *No additional questions*

N. Outcomes of elderly patients receiving CD-19 directed CAR-T therapy for B-cell lymphomas. *No additional questions*

O. Determinants of successful discontinuation of immune suppression following allogeneic hematopoietic cell transplantation.

1. How is immune suppression stop defined in the CIBMTR database?
2. How long after HCT do you expect data regarding ongoing IST usage to be reliable since many patients leave the transplant center and are managed elsewhere long-term?
3. How long will you deal with restart IST?

Accrual Summary for the Health Services and International Studies Working Committee

Table 1. Characteristics of recipients who underwent a first allogeneic transplant registered with the CIBMTR

Characteristic	TED N (%)	CRF N (%)
No. of patients	248666	106747
No. of centers	648	575
Age at transplant, years - no. (%)		
Median (min-max)	37 (0-88)	33 (0-88)
0-9	35351 (14)	18179 (17)
10-19	31734 (13)	15634 (15)
20-29	32705 (13)	15120 (14)
30-39	36002 (14)	15908 (15)
40-49	40535 (16)	16043 (15)
50-59	39797 (16)	13878 (13)
60-69	28128 (11)	10071 (9)
70+	4414 (2)	1914 (2)
Recipient gender - no. (%)		
Male	145561 (59)	62691 (59)
Female	103105 (41)	44056 (41)
Recipient race - no. (%)		
Caucasian	167179 (67)	84345 (79)
African-American	11732 (5)	6348 (6)
Asian	18473 (7)	8372 (8)
Pacific islander	520 (0)	257 (0)
Native American	805 (0)	411 (0)
Other	8343 (3)	3927 (4)
Unknown	41614 (17)	3087 (3)
Disease - no. (%)		
Acute myelogenous leukemia	78866 (32)	29738 (28)
Acute lymphoblastic leukemia	42613 (17)	17496 (16)
Other leukemia	6129 (2)	2300 (2)
Chronic myelogenous leukemia	29089 (12)	14750 (14)
Myelodysplastic/myeloproliferative disorders	30382 (12)	14020 (13)
Other acute leukemia	2801 (1)	1012 (1)
Non-Hodgkin lymphoma	16577 (7)	6115 (6)
Hodgkin lymphoma	1593 (1)	614 (1)
Plasma cell disorder/Multiple Myeloma	3264 (1)	1343 (1)
Other Malignancies	1174 (0)	500 (0)
Breast Cancer	179 (0)	90 (0)
Severe aplastic anemia	14203 (6)	7429 (7)
Inherited abnormalities erythrocyte differentiation or function	10296 (4)	5599 (5)

Characteristic	TED N (%)	CRF N (%)
SCID and other immune system disorders	6378 (3)	3197 (3)
Inherited abnormalities of platelets	218 (0)	107 (0)
Inherited disorders of metabolism	2720 (1)	1553 (1)
Histiocytic disorders	1689 (1)	755 (1)
Autoimmune Diseases	131 (0)	47 (0)
Other diseases	364 (0)	82 (0)
Year of transplant - no. (%)		
<1985	4876 (2)	4486 (4)
1985-1989	10451 (4)	9326 (9)
1990-1994	22628 (9)	14566 (14)
1995-1999	35547 (14)	16563 (16)
2000-2004	40227 (16)	16776 (16)
2005-2009	39801 (16)	17647 (17)
2010-2014	46778 (19)	11102 (10)
2015-2019	48358 (19)	16281 (15)
Education - no. (%)	NA	
No primary education		62 (0)
Less than primary or elementary education		84 (0)
Primary of elementary education		717 (1)
Lower secondary education		785 (1)
Upper secondary education		10834 (10)
Post-secondary , non-tertiary education		4023 (4)
Tertiary education, Type A		8202 (8)
Tertiary education, Type B		1806 (2)
Advance research qualification		2104 (2)
Age<18 years old		30675 (29)
Missing		47455 (44)
Health insurance - no. (%)	NA	
No insurance		4245 (4)
Medicaid		9260 (9)
Medicare		5952 (6)
Disability insurance		737 (1)
HMO		2434 (2)
Private health insurance		24393 (23)
National health insurance		15599 (15)
VA/Military		759 (1)
Other		3394 (3)
Missing		39974 (37)
Health insurance - no. (%)	NA	
No insurance		3365 (3)

Characteristic	TED N (%)	CRF N (%)
Disability insurance +/-others		839 (1)
Private health insurance +/- others		29755 (28)
Medicaid +/-others		8169 (8)
Medicare +/-others		3637 (3)
Others		21008 (20)
Missing		39974 (37)
Occupation - no. (%)	NA	
Professional, technical, or related occupation		18992 (18)
Manager, administrator or proprietor		3805 (4)
Clerical or related occupation		2635 (2)
Sales occupation		1977 (2)
Service occupation		3219 (3)
Skilled crafts or related occupation		3161 (3)
Equipment/vehicle operator or related occupation		1466 (1)
Laborer		2051 (2)
Farmer		394 (0)
Member of military		329 (0)
Homemaker		1501 (1)
Student		10819 (10)
Under school age		2490 (2)
Not previously employed		1965 (2)
Other, specify		7823 (7)
Missing		44120 (41)

Table 2. Characteristics of recipients who underwent a first autologous transplant registered with the CIBMTR

Characteristic	TED N (%)	CRF N (%)
No. of patients	240752	46039
No. of centers	612	456
Age at transplant, years - no. (%)		
Median (min-max)	53 (0-86)	50 (0-83)
0-9	10550 (4)	2306 (5)
10-19	7681 (3)	1755 (4)
20-29	16203 (7)	3168 (7)
30-39	24638 (10)	5679 (12)
40-49	43528 (18)	9935 (22)
50-59	65702 (27)	12133 (26)
60-69	59626 (25)	9411 (20)
70+	12824 (5)	1652 (4)
Recipient gender - no. (%)		
Male	130191 (54)	22738 (49)
Female	110561 (46)	23301 (51)
Recipient race - no. (%)		
Caucasian	167537 (70)	36037 (78)
African-American	21151 (9)	5697 (12)
Asian	6075 (3)	1361 (3)
Pacific islander	305 (0)	55 (0)
Native American	699 (0)	217 (0)
Other	5401 (2)	1406 (3)
Unknown	39584 (16)	1266 (3)
Disease - no. (%)		
Acute myelogenous leukemia	8169 (3)	2399 (5)
Acute lymphoblastic leukemia	1619 (1)	474 (1)
Other leukemia	798 (0)	256 (1)
Chronic myelogenous leukemia	701 (0)	290 (1)
Myelodysplastic/myeloproliferative disorders	280 (0)	94 (0)
Other acute leukemia	148 (0)	31 (0)
Non-Hodgkin lymphoma	66376 (28)	11059 (24)
Hodgkin lymphoma	24825 (10)	4021 (9)
Plasma cell disorder/Multiple Myeloma	95190 (40)	15572 (34)
Other Malignancies	19496 (8)	4330 (9)
Breast Cancer	21744 (9)	7294 (16)
Autoimmune Diseases	888 (0)	135 (0)
Other diseases	518 (0)	84 (0)
Year of transplant - no. (%)		

Characteristic	TED N (%)	CRF N (%)
<1985	31 (0)	5 (0)
1985-1989	2066 (1)	672 (1)
1990-1994	19307 (8)	7240 (16)
1995-1999	40356 (17)	12509 (27)
2000-2004	35080 (15)	6061 (13)
2005-2009	37173 (15)	7634 (17)
2010-2014	50132 (21)	4018 (9)
2015-2019	56607 (24)	7900 (17)
Education - no. (%)	NA	
No primary education		16 (0)
Less than primary or elementary education		49 (0)
Primary of elementary education		338 (1)
Lower secondary education		395 (1)
Upper secondary education		6616 (14)
Post-secondary , non-tertiary education		2726 (6)
Tertiary education, Type A		5504 (12)
Tertiary education, Type B		1233 (3)
Advance research qualification		1698 (4)
Age<18 years old		3580 (8)
Missing		23884 (52)
Health insurance - no. (%)	NA	
No insurance		801 (2)
Medicaid		3612 (8)
Medicare		4449 (10)
Missing		37177 (81)
Health insurance - no. (%)	NA	
No insurance		801 (2)
Medicaid +/-others		3612 (8)
Medicare +/-others		4449 (10)
Missing		37177 (81)
Occupation - no. (%)	NA	
Professional, technical, or related occupation		16602 (36)
Manager, administrator or proprietor		1788 (4)
Clerical or related occupation		1286 (3)
Sales occupation		854 (2)
Service occupation		1666 (4)
Skilled crafts or related occupation		1530 (3)
Equipment/vehicle operator or related occupation		847 (2)
Laborer		1023 (2)
Farmer		220 (0)

Characteristic	TED N (%)	CRF N (%)
Member of military		166 (0)
Homemaker		641 (1)
Student		1131 (2)
Under school age		366 (1)
Not previously employed		1012 (2)
Other, specify		3416 (7)
Missing		13491 (29)

Table 3. Characteristics of recipients who received a first transplant from US centers reported to the CIBMTR, 2008 – 2019 (CRF)

Characteristic	Allogeneic N (%)	Autologous N (%)
No. of patients	28573	14129
No. of centers	184	180
Age at transplant, years - no. (%)		
Median (min-max)	51 (0-88)	58 (0-82)
0-9	3719 (13)	552 (4)
10-19	2414 (8)	255 (2)
20-29	2215 (8)	580 (4)
30-39	2190 (8)	801 (6)
40-49	3285 (11)	1818 (13)
50-59	5724 (20)	3993 (28)
60-69	7304 (26)	4980 (35)
70+	1722 (6)	1150 (8)
Recipient gender - no. (%)		
Male	16678 (58)	8159 (58)
Female	11895 (42)	5970 (42)
Recipient race - no. (%)		
Caucasian	22617 (79)	9659 (68)
African-American	3185 (11)	3416 (24)
Asian	1449 (5)	566 (4)
Pacific islander	99 (0)	34 (0)
Native American	195 (1)	118 (1)
Unknown	1028 (4)	336 (2)
Disease - no. (%)		
Acute myelogenous leukemia	9413 (33)	155 (1)
Acute lymphoblastic leukemia	3608 (13)	16 (0)
Other leukemia	756 (3)	14 (0)
Chronic myelogenous leukemia	757 (3)	0 (0)
Myelodysplastic/myeloproliferative disorders	7593 (27)	2 (0)
Other acute leukemia	277 (1)	2 (0)
Non-Hodgkin lymphoma	1690 (6)	3233 (23)
Hodgkin lymphoma	158 (1)	1144 (8)
Plasma cell disorder/Multiple Myeloma	167 (1)	8656 (61)
Other Malignancies	22 (0)	816 (6)
Breast Cancer	0 (0)	2 (0)
Severe aplastic anemia	1270 (4)	1 (0)
Inherited abnormalities erythrocyte differentiation or function	1173 (4)	7 (0)
SCID and other immune system disorders	984 (3)	44 (0)

Characteristic	Allogeneic N (%)	Autologous N (%)
Inherited abnormalities of platelets	35 (0)	0 (0)
Inherited disorders of metabolism	393 (1)	2 (0)
Histiocytic disorders	233 (1)	2 (0)
Autoimmune Diseases	18 (0)	29 (0)
Other diseases	26 (0)	4 (0)
Education - no. (%)		
No primary education	30 (0)	13 (0)
Less than primary or elementary education	53 (0)	27 (0)
Primary of elementary education	110 (0)	83 (1)
Lower secondary education	522 (2)	323 (2)
Upper secondary education	5785 (20)	3493 (25)
Post-secondary , non-tertiary education	1887 (7)	1189 (8)
Tertiary education, Type A	5397 (19)	2950 (21)
Tertiary education, Type B	1256 (4)	864 (6)
Advance research qualification	1016 (4)	556 (4)
Age<18 years old	5708 (20)	748 (5)
Missing	6809 (24)	3883 (27)
Health insurance - no. (%)		
No insurance	459 (2)	145 (1)
Medicaid	5777 (20)	1930 (14)
Medicare	5097 (18)	3085 (22)
Disability insurance	576 (2)	0 (0)
Private health insurance	14902 (52)	0 (0)
National health insurance	160 (1)	0 (0)
VA/Military	362 (1)	0 (0)
Other	520 (2)	0 (0)
Missing	720 (3)	8969 (63)
Health insurance - no. (%)		
No insurance	338 (1)	145 (1)
Disability insurance +/-others	631 (2)	0 (0)
Private health insurance +/- others	17747 (62)	0 (0)
Medicaid +/-others	5033 (18)	1930 (14)
Medicare +/-others	3057 (11)	3085 (22)
Others	1047 (4)	0 (0)
Missing	720 (3)	8969 (63)
Occupation - no. (%)		
Professional, technical, or related occupation	5677 (20)	3245 (23)
Manager, administrator or proprietor	2514 (9)	1384 (10)
Clerical or related occupation	1570 (5)	962 (7)

Characteristic	Allogeneic N (%)	Autologous N (%)
Sales occupation	1239 (4)	631 (4)
Service occupation	2060 (7)	1312 (9)
Skilled crafts or related occupation	1966 (7)	1116 (8)
Equipment/vehicle operator or related occupation	946 (3)	649 (5)
Laborer	1233 (4)	736 (5)
Farmer	205 (1)	139 (1)
Member of military	214 (1)	133 (1)
Homemaker	655 (2)	343 (2)
Student	4786 (17)	559 (4)
Under school age	1396 (5)	292 (2)
Not previously employed	623 (2)	375 (3)
Other, specify	1321 (5)	690 (5)
Missing	2168 (8)	1563 (11)
Recipient zip code - no. (%)		
Not Available	1958 (7)	786 (6)
Available	26615 (93)	13343 (94)

Table 4. Characteristics of recipients who received allogeneic transplants registered with the CIBMTR by WHO region, 2008 – 2019(TED)

Characteristic	Africa	Latin Americas	US / Canada	Eastern Mediterranean	Europe	Southeastern Asia	Western Pacific
No. of patients	36	4469	79473	3680	14111	2033	7804
No. of centers	2	43	208	10	107	14	27
Age, in years - no. (%)							
<10	0 (0)	882 (20)	8415 (11)	1542 (42)	1152 (8)	696 (34)	950 (12)
10-19	6 (17)	877 (20)	6809 (9)	846 (23)	992 (7)	505 (25)	896 (11)
20-29	6 (17)	663 (15)	6769 (9)	607 (16)	1472 (10)	269 (13)	852 (11)
30-39	2 (6)	681 (15)	6858 (9)	358 (10)	1560 (11)	254 (12)	973 (12)
40-49	7 (19)	596 (13)	10236 (13)	219 (6)	2374 (17)	170 (8)	1377 (18)
50-59	9 (25)	505 (11)	17682 (22)	87 (2)	3196 (23)	125 (6)	1701 (22)
60-69	6 (17)	218 (5)	19000 (24)	21 (1)	2967 (21)	14 (1)	1016 (13)
≥70	0 (0)	47 (1)	3704 (5)	0 (0)	398 (3)	0 (0)	39 (0)
Gender - no. (%)							
Male	26 (72)	2640 (59)	45821 (58)	2159 (59)	8311 (59)	1317 (65)	4527 (58)
Female	10 (28)	1829 (41)	33652 (42)	1521 (41)	5800 (41)	716 (35)	3277 (42)
Primary disease - no. (%)							
AML	13 (36)	1204 (27)	30609 (39)	687 (19)	5682 (40)	360 (18)	3103 (40)
ALL	2 (6)	1167 (26)	12559 (16)	600 (16)	2311 (16)	220 (11)	1577 (20)
CML	3 (8)	293 (7)	2635 (3)	116 (3)	505 (4)	72 (4)	206 (3)
Myelodysplastic disorders	7 (19)	517 (12)	14215 (18)	129 (4)	2615 (19)	138 (7)	1242 (16)
NHL	3 (8)	97 (2)	5916 (7)	26 (1)	718 (5)	36 (2)	336 (4)
HL	0 (0)	27 (1)	404 (1)	4 (0)	78 (1)	12 (1)	32 (0)
Multiple myeloma	0 (0)	4 (0)	288 (0)	8 (0)	77 (1)	1 (0)	9 (0)
Other malignancies	1 (3)	115 (3)	3634 (5)	55 (1)	738 (5)	21 (1)	296 (4)
Severe aplastic anemia	4 (11)	559 (13)	2979 (4)	431 (12)	517 (4)	279 (14)	547 (7)
Other non-malignancies	3 (8)	486 (11)	6234 (8)	1624 (44)	870 (6)	894 (44)	456 (6)
Donor type - no. (%)							
HLA-identical sibling	15 (42)	2327 (52)	23911 (30)	2794 (76)	4505 (32)	1308 (64)	2928 (38)
Other Related donor	1 (3)	702 (16)	9536 (12)	538 (15)	849 (6)	460 (23)	961 (12)
Unrelated donor	20 (56)	1440 (32)	46016 (58)	348 (9)	7972 (56)	265 (13)	3915 (50)
Missing	0 (0)	0 (0)	10 (0)	0 (0)	785 (6)	0 (0)	0 (0)

Characteristic	Africa	Latin Americas	US / Canada	Eastern Mediterranean	Europe	Southeastern Asia	Western Pacific
Graft type - no. (%)							
Bone Marrow	1 (3)	2361 (53)	18223 (23)	1906 (52)	2941 (21)	389 (19)	1426 (18)
Peripheral Blood	34 (94)	1904 (43)	53765 (68)	1483 (40)	10605 (75)	1643 (81)	5746 (74)
Cord Blood	1 (3)	203 (5)	7483 (9)	291 (8)	561 (4)	1 (0)	629 (8)
Missing	0 (0)	1 (0)	2 (0)	0 (0)	4 (0)	0 (0)	3 (0)
Year of transplant - no. (%)							
2008	5 (14)	188 (4)	4828 (6)	436 (12)	1613 (11)	55 (3)	496 (6)
2009	11 (31)	313 (7)	5378 (7)	460 (13)	1720 (12)	49 (2)	669 (9)
2010	8 (22)	385 (9)	5605 (7)	451 (12)	1715 (12)	31 (2)	765 (10)
2011	10 (28)	343 (8)	6134 (8)	220 (6)	1568 (11)	123 (6)	861 (11)
2012	1 (3)	409 (9)	6249 (8)	251 (7)	1561 (11)	144 (7)	831 (11)
2013	1 (3)	358 (8)	6745 (8)	209 (6)	1465 (10)	126 (6)	757 (10)
2014	0 (0)	363 (8)	6882 (9)	274 (7)	836 (6)	150 (7)	726 (9)
2015	0 (0)	331 (7)	7076 (9)	253 (7)	689 (5)	189 (9)	567 (7)
2016	0 (0)	318 (7)	7260 (9)	217 (6)	718 (5)	250 (12)	710 (9)
2017	0 (0)	370 (8)	7547 (9)	242 (7)	1344 (10)	289 (14)	485 (6)
2018	0 (0)	537 (12)	7887 (10)	288 (8)	505 (4)	312 (15)	464 (6)
2019	0 (0)	554 (12)	7882 (10)	379 (10)	377 (3)	315 (15)	473 (6)

Table 5. Allogeneic transplant recipients and centers by country registered with the CIBMTR, 2008-2019(TED)

Regions	N	Centers
Africa		
South Africa	36	2
Americas		
USA	74596	192
Argentina	439	7
Brazil	3491	22
Canada	4877	16
Chile	17	2
Venezuela	50	2
Mexico	106	3
Uruguay	57	3
Peru	108	1
Columbia	201	3
Eastern Mediterranean		
Saudi Arabia	2418	4
Egypt	21	2
Iran	671	1
Pakistan	570	3
Europe		
Austria	93	2
Belgium	1062	6
Denmark	1110	1
UK	1934	15
Finland	404	2
France	1086	10
Germany	2464	17
Ireland	157	1

Regions	N	Centers
Israel	945	7
Italy	546	7
Netherlands	554	8
Norway	78	1
Poland	374	4
Portugal	130	2
Spain	618	8
Sweden	817	4
Switzerland	649	3
Russia	91	1
Turkey	421	3
Greece	3	1
Czech Republic	460	3
Slovak Republic	115	1
Southeastern Asia		
India	2012	13
Thailand	21	1
Western Pacific		
Australia	3452	15
Korea	2660	3
New Zealand	879	4
Taiwan	62	1
Hong Kong	39	1
Singapore	712	3

Table 6. Number of patients who received a first allogeneic transplant registered with the CIBMTR between 2000 and 2019 by country

	CRF		TED	
Country	Malignant disease	Non-malignant disease	Malignant disease	Non-malignant disease
Argentina	100-500	<100	501-999	100-500
Australia	501-999	100-500	≥1000	501-999
Austria	<100	<100	100-500	<100
Belgium	100-500	<100	≥1000	100-500
Brazil	501-999	501-999	≥1000	≥1000
Canada	501-999	100-500	≥1000	≥1000
Colombia	<100	<100	100-500	<100
Czech Republic	100-500	<100	501-999	<100
Denmark	100-500	<100	≥1000	100-500
Egypt	<100	NA	501-999	100-500
Finland	<100	<100	501-999	<100
France	100-500	<100	≥1000	100-500
Germany	≥1000	<100	≥1000	501-999
Hong Kong	<100	<100	100-500	<100
India	100-500	501-999	≥1000	≥1000
Iran	100-500	100-500	≥1000	501-999
Ireland	100-500	<100	100-500	<100
Israel	100-500	<100	≥1000	100-500
Italy	<100	<100	≥1000	100-500
Japan	501-999	<100	501-999	<100
Korea	501-999	100-500	≥1000	501-999
Mexico	<100	<100	100-500	<100
Netherlands	<100	<100	501-999	<100
New Zealand	100-500	100-500	≥1000	100-500
Pakistan	<100	100-500	100-500	501-999
Peru	<100	<100	100-500	<100

Country	CRF		TED	
	Malignant disease	Non-malignant disease	Malignant disease	Non-malignant disease
Poland	100-500	<100	501-999	100-500
Portugal	<100	<100	100-500	<100
Russia	<100	<100	100-500	<100
Saudi Arabia	501-999	501-999	≥1000	≥1000
Singapore	100-500	<100	501-999	<100
Slovak Republic	<100	<100	100-500	<100
South Africa	100-500	<100	100-500	<100
Spain	100-500	<100	≥1000	100-500
Sweden	100-500	100-500	≥1000	100-500
Switzerland	<100	<100	≥1000	100-500
Taiwan	<100	NA	100-500	<100
Turkey	<100	<100	501-999	<100
UK	100-500	100-500	≥1000	501-999
USA	≥1000	≥1000	≥1000	≥1000
Uruguay	<100	<100	100-500	<100
Venezuela	<100	<100	100-500	<100

Countries with <100 patients in both CRF and TED dataset are not included in this report.

Table 7. Number of patients who received a first autologous transplant registered to the CIBMTR between 2000 and 2019 by country

	CRF		TED	
Country	Malignant disease	Non-malignant disease	Malignant disease	Non-malignant disease
Argentina	100-500	NA	≥1000	<100
Australia	100-500	<100	≥1000	<100
Austria	<100	NA	100-500	<100
Belgium	<100	NA	501-999	<100
Brazil	100-500	<100	≥1000	<100
Canada	501-999	<100	≥1000	100-500
Colombia	<100	NA	100-500	<100
Czech Republic	<100	NA	501-999	<100
Denmark	<100	NA	<100	NA
Finland	<100	NA	100-500	NA
France	<100	NA	501-999	<100
Germany	<100	<100	≥1000	<100
India	<100	NA	100-500	<100
Iran	<100	NA	100-500	<100
Israel	<100	<100	501-999	<100
Italy	<100	NA	≥1000	<100
Japan	<100	NA	<100	NA
Korea	<100	NA	501-999	<100
Mexico	<100	NA	100-500	100-500
Netherlands	NA	NA	100-500	<100
New Zealand	<100	NA	100-500	<100
Pakistan	<100	NA	<100	NA
Poland	<100	NA	100-500	<100
Portugal	NA	NA	100-500	NA
Russia	<100	<100	100-500	<100
Saudi Arabia	<100	NA	501-999	<100

	CRF		TED	
Country	**Malignant disease**	**Non-malignant disease**	**Malignant disease**	**Non-malignant disease**
Singapore	100-500	<100	501-999	<100
South Africa	<100	NA	100-500	<100
Spain	<100	<100	≥1000	<100
Sweden	<100	NA	100-500	<100
Switzerland	NA	NA	100-500	<100
Turkey	<100	NA	501-999	<100
UK	<100	NA	≥1000	<100
USA	≥1000	100-500	≥1000	501-999
Uruguay	100-500	NA	>=1000	<100
Venezuela	<100	NA	100-500	NA

Countries with <100 patients in both CRF and TED dataset are not included in this report.

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TO: Health Services and International Studies Working Committee Members

FROM: Wael Saber, MD, MS; Scientific Director for Health Services and International Studies Working Committee

RE: Studies in Progress Summary

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) This study will evaluate the trends in utilization and clinical outcomes of autologous and allogeneic HCT in patients of different race/ ethnicity utilizing data collected by the Center for International Blood and Marrow Transplant Research (CIBMTR). This study is in the analysis phase. The goal of this study is to have the manuscript submitted by June 2022.

HS16-03 Relationship of Race/Ethnicity and Survival after Single and Double Umbilical Cord Blood Transplantation (K Ballen) This study will compare overall and disease free survivals for White, Hispanic, Asian, and Black patients after single and double umbilical cord blood transplantation; and determine if survival for White, Hispanic, Asian, and Black patients is comparable if transplanted with units of similar cell dose and HLA match. This study is in the analysis phase. The goal of this study is to have the manuscript submitted by June 2022.

HS18-01 International collaborative study to compare the prognosis for acute leukemia patients transplanted with intensified myeloablative regimens (Y Arai/ Y Atsuta/ S Yano). The aims of this study are: 1) To determine whether intensified myeloablative regimens of AraC or VP16 added to CY/TBI can improve the clinical outcomes (overall survival; OS) in allo-HSCT for acute leukemia. 2) To confirm the prognostic differences (OS, non-relapse mortality, and relapse) between the conventional and intensified myeloablative regimens in each patient's characteristic such as age, comorbidity, disease risk/status, donor source, GVHD prophylaxis and so on. 3)To compare the OS, non-relapse mortality, and relapse of intensified regimen between the US and Japan. This study is in the analysis phase. The goal of this study is to have the manuscript submitted by June 2022.

HS18-02 Racial differences in long term survivor outcomes after allogeneic transplants (B Blue/ N Majhail) The aims of this study are: 1) To determine association of ethnicity/race and socioeconomic status (SES) on OS among adult allogeneic HCT recipients with hematologic malignancies who have survived for at least 1 year in remission. 2)To investigate the cumulative incidence of NRM and relapse post-transplant by ethnicity/race and SES in allogeneic HCT recipients who have survived in remission

for at least 1 year. 3)To compare standardized mortality ratio between our cohort of 1-year transplant survivors with that of their age- and gender-matched peers in general population (analyses will be stratified by ethnicity/race). This study is in the manuscript preparation phase. The goal of this study is to have the manuscript submitted by June 2022.

HS19-01 Factors Associated with Clinical Trial Participation among HCT Patients: A CIBMTR Analysis (T F. Gray/ A El-Jawahri) The primary aims of this study are: 1) To describe rates of clinical trial participation based on HCT type; 2) To explore factors that are associated with clinical trial participation in patients with undergoing HCT; 3) To assess the impact of clinical trial participation on overall survival (OS) and non-relapse mortality (NRM) in autologous and allogeneic HCT recipients. This study is in the data file preparation phase. The goal of this study is to have the manuscript submitted by June 2022.

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). The primary objective of this study is determine if the 1year Overall Survival after Hematopoietic Stem Cell Transplantation (HCT) plus post-Cy from Haploidentical related donor (Haplo – HCT) for acute myeloid leukemia, Hodgkin Disease (Study Arm 1) and Severe Aplastic Anemia (Arm 2) is not inferior compared to matched related or unrelated allogeneic HCT donor with 10/10 and 9/10 compatibility. This study is in the data collecting phase.

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). The primary objective of this study is to compare 1-year overall survival after allogeneic HCT performed in Brazil from URD, Haplo and MSD. The secondary objective of this study is to compare the 100-day transplant-related mortality (TRM) and the 1-year event-free survival (EFS) after allogeneic HCT performed in Brazil from URD, Haplo and MSD. This study is in the data file preparation phase.

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) The primary aims of this study are: 1) Describe the resource utilization during the 30 days before death among children who received a HSCT for a hematologic malignancy and then died within 5

years at the same PHIS hospital. 2) Determine the prevalence of patients with a resource intense phenotype in the last 30 days of life among children who received a HSCT for a hematologic malignancy and then died within 5 years at the same PHIS hospital. 3) Determine the clinical and sociodemographic characteristics associated with a resource intense phenotype among children who received a HSCT for a hematologic malignancy and then died within 5 years at the same PHIS hospital. This study is in the protocol development phase. The goal of this study is to have the manuscript submitted by June 2022.

Response Summary:

This form is intended to be completed by a physician/researcher for the purpose of proposing a study. Content should not include Personal Identifiable Information (PII) or Protected Health Information (PHI). If you are a patient, do not complete this form. Patients: Contact your healthcare provider immediately for reports of problems with your treatment or problems with products received for your treatment. The CIBMTR uses de-identified data and is unable to associate reported treatment problems, adverse events, or corrections of information with a center, clinical trial, or healthcare provider.

Q1. Study Title

Health Care Utilization and costs of haploidentical allogeneic stem cell transplants in a contemporary cohort of pediatric patients with acute leukemia and myelodysplastic syndrome.

Q2. Key Words

Health Care Utilization, Costs, Haploidentical Transplant, Pediatrics

Q3. PRINCIPAL INVESTIGATOR

Provide the following information for each investigator:

Principal Investigator #1:

First and last name, degree(s):	Hemalatha Rangarajan
Email address:	hemalatha.rangarajan@nationwidechildrens.org
Institution name:	Nationwide Children's Hospital
Academic rank:	Clinical Assistant Professor of Pediatrics

Q4. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- No

Q5. Do you identify as an underrepresented/minority?

- Yes

Q6. Principal Investigator #2 (If applicable):

First and last name, degree(s):	Prakash Satwani, MD
Email address:	ps2087@columbia.edu
Institution name:	Division of Pediatric Hematology, Oncology, and Stem Cell Transplantation
Academic rank:	Associate Professor of Pediatrics

Q7. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- No

Q8. Do you identify as an underrepresented/minority?

- Yes

Q9. We encourage a maximum of two Principal Investigators per study. If more than one author is listed, please indicate who will be identified as the corresponding PI below:

Hemalatha Rangarajan

Q10. If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:

N/A

LETTER OF COMMITMENT:

Please note: *A letter of commitment will be signed by Lead and Last authors as it describes the expectations for filling that role. By signing the letter of commitment, the authors accept their responsibilities and will be held accountable for timely completion of all steps in the project. More details regarding author responsibilities can be found here:* *https://www.cibmtr.org/Studies/Observational/StudyManagement/p*

Q12. CURRENT ONGOING WORK WITH CIBMTR: Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.

I have completed the following study with CIBMTR
IB17-02: Outcomes of Pediatric patients with JMML following unrelated donor transplant: The impact of Donor KIR Gene Content and KIR Ligand Matching
Manuscript Published. Transplantation and Cellular Therapy. PMID: 34407489. Role : Principal investigator
The following proposals that I have submitted have been accepted and are at varying stages of development. I am one of the co-principal investigators on all these protocols.
1. IN20-01: Incidence, Risk Factors, and Outcomes of Infections post CD19 CAR T therapies. February 2020. Data analysis is ongoing.
2. CT20-02: Resource utilization in patients receiving CAR-T Therapy. February 2020. Protocol development is in progress.
3. PC19-03: Outcomes of allogeneic hematopoietic cell transplantation in pediatric patients with AML and CNS involvement. February 2019. Data analysis is ongoing.

Q13. PROPOSED WORKING COMMITTEE:

- Health Services and International Studies

Q14. Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.

- No

Q15. RESEARCH QUESTION:

How does costs and health care utilization (HCU) of haploidentical allogeneic stem cell transplants in pediatric patients with acute leukemia and myelodysplastic syndrome (MDS) compare with costs of matched sibling and other alternative donor transplants? are they comparable?

Q16. RESEARCH HYPOTHESIS:

Costs and health Care utilization (HCU) of haploidentical allogeneic hematopoietic stem transplants (HaploHCT) in pediatric patients with acute leukemia and myelodysplastic syndrome (MDS) are higher than matched sibling donors (MSD) transplants but comparable to costs of other alternative donor transplants namely: matched unrelated donors (MURD), mismatched unrelated donor (MMUD) and umbilical cord blood (UCB) transplants.

Q17. SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.)

Suggested word limit of 200 words:

Aim 1. To determine the cost and HCU associated with HaploHCT for pediatric patients (≤ 21 years) patients with acute leukemia (ALL, AML) and MDS from 2010-2020.
Aim 2. To compare the costs and health care utilization of HaploHCT with that of MSD, MUD, MMURD and UCB transplants.

Q18. SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.

Allogeneic HCT irrespective of donor source is a highly specialized, resource intensive and costly medical procedure. The financial burden and subsequent bankruptcy (financial toxicity) a complication experienced by HCT recipients leads to noncompliance and hesitancy in accepting medical care [1, 2]. Data on costs of HCT have traditionally focused on MSD and alternative donors HCTs namely: MURD, MMURD including umbilical cord blood (UCB). There is no data available currently on costs and HCU associated with HaploHCT. Given the increasing use of HaploHCTs it would be important to ascertain the associated costs and HCU associated with this donor source and how it compares to other donor HCTs. Through our proposed CIBMTR-Pediatric health information system (PHIS) merged study, we plan to study this question in a systematic fashion. Results from this study may not only provide data on costs associated with HaploHCT but also enable hospitals and health insurance companies to allocate appropriate resources and reimbursement. It may also lay the groundwork for future robust cost effectiveness analysis studies based on donor source.

Q19. SCIENTIFIC JUSTIFICATION: Provide a background summary of previous related research and their strengths and weaknesses, justification of your research and why your research is still necessary.

Background:
Use of haploidentical donors has expanded the donor pool for patients in need of life saving allogeneic HCT for both malignant as well as nonmalignant disorders. [3] Common strategies for HaploHCTs include ex-vivo T cell depletion (CD34 depletion, alpha beta T cell depletion, CD45 RA depletion etc.) and use of post-transplant cyclophosphamide (PT-CY). A recent CIBMTR study revealed that 80% of these HCTs used PTCY for GVHD prophylaxis. [3] In a survey[4] of 315 HCT physicians, 21% of respondents predicted that haploidentical donors would be the preferred donors in the coming years. Additionally, studies are now showing that transplant outcomes post haploHCT are similar if not better than other alternative donors including MUD, MMUD and UCB HCTs [5-8]and even MSD[9].
Healthcare utilization and cost is at the forefront of the national debate in the US. In this setting having accurate information regarding the cost associated with newer and popular treatment strategies is crucial for making informed decisions in our healthcare system. In United States according to an Agency for Health Care Research and Quality [10] report, overall hospital costs grew by 6.3% to $344 billion from 2004-2007. HCT accounted for the most rapid increase in total hospital costs with a growth rate of 84.9% and 1.3 billion dollars were spent in 2007, due to the increased number of transplants and increased lengths of hospital stay (LOS).[10]
A recent CIBMTR- PHIS based study [11]analyzed the impact of donor on costs and outcomes of allogeneic HCT performed between 2004-2011 in 632 pediatric patients (<21 years) with acute leukemia. The author observed that by 2 years the total adjusted costs (TAC) remained significantly lower for MSD alloHCT compared to MUD alloHCT but higher for UCB HCT compared to MUD alloHCT. Although UCB and MUD alloHCT provided similar survival outcomes, MUD alloHCT had a significant survival advantage in cost by day 100 and 2 years. We the PIs have also published similar studies on costs associated with HCTs at pediatric centers. [12-14]. We also found that UCB and increasing age major drives of HCT related costs. However, none of the pediatric studies described to date have analyzed costs associated with haploHCTs.
A more detailed understanding of costs for HaploHCT would be more relevant in this current era. It will also important to ascertain how this alternative donor transplant compares UCB HCT, currently identified to be the most expensive graft source[14]. Therefore, we propose merging data from PHIS with that of the CIBMTR for the purpose of this study whereby we will able to identify patients who underwent haploHCTs, their HCU and costs. We will compare this data on costs and HCU of HaploHCTS with that of a contemporary cohort of MSD, MUD, MMUD and UCB HCTs, also extracted from the CIBMTR-PHIS databases.
Study Design. We will conduct a retrospective study of a multi-center, national cohort of pediatric patients undergoing alloHCT for acute leukemia/MDS during the period of time from 1/1/2010 to 12/31/2020 We will identify patients who underwent HaploHCT and compare their outcomes (costs and HCU utilization) with those patients who underwent MSD, MUD, MMUD and UCB transplants. We will also further sub-categorize patients who underwent HaploHCT as T cell replete (PTCY based) vs T cell deplete (ex vivo T cell depleted) recipients. If the number of patients with ex vivo T cell depleted haplo allografts are few, we will exclude them in the final analysis.

Q19a. SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF)

N/A

Q20. PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.

Inclusion:
- Age who ≤ 21 years of age at the time of alloHCT with 2 years of follow-up
- Recipients with diagnosis of ALL, AML, MDS
- Transplant during Years 2010-2020
- Patients must be represented in both CIBMTR and PHIS databases

Exclusion
- Patients with < 2 years of follow up data.
- Recipients of 2nd allogeneic HCT or prior autologous stem cell transplant
- Exclude patients that received grafts from multiple donors
- Exclude non-consented patients

Q21. Does this study include pediatric patients?

- Yes

Q22. DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Data collection forms available at: http://www.cibmtr.org/DataManagement/DataCollectior Outline any supplementary data required. Additional data collection is extremely difficult and will make your proposal less feasible.

Variables to be included from CIBMTR database:
• Age ≤ 21 years
• Sex, Race
• Performance score < 90 vs ≥ 90
• Transplant comorbidity index 0-2 vs ≥ 3
• CMV status Negative/Positive/Not reported
• Disease AML/ALL/MDS
• Disease status: CR1, CR2, Relapse, refractory anemia with blasts, Partial response/Chemo resistant.
• Disease risk index Low/intermediate/high/very high/unknown
• HLA matching: MSD, MUD, MMUD, Haploidentical (> 2 antigen MM and related)
• Conditioning regimen and intensity MA/RIC/NMA
• Serotherapy Y/N : if Y Campath/ATG/both
• Cell source: PB/BM/GCSF primed BM/ UCB
• T cell depletion strategy: PTCY/ CD45 RA /Alpha beta T / CD34 selection /others
• Other GVHD prophylaxis agents: Calcineurin inhibitors (CNI) + MMF, CNI+ MTX, Sirolimus ± others, CNI only, PTCY ± others
Outcomes
• Day of Neutrophil and platelet engraftment
• Graft failure Y/N
• Relapse Y/N if Y months from HCT
• Acute GVHD Grade I-II vs II-IV
• Chronic GVHD Y/N
• Alive or dead at last follow up Y/N
• Cause of death if applicable
Variables to be collected PHIS database: PHIS Financial and HCU variables starting from admission through two-year post-HCT will be pulled from the PHIS database.
• Age
• Sex
• Ethnicity
• Diagnosis ALL, AML or MDS
• Treatment center
• LOS for initial and subsequent admissions
• Need for ICU care, ICU LOS
• Number of hospital admissions up to 1 years post HCT
• Costs incurred in the 1st year post HCT categorized under the following: total adjusted charges, pharmacy charges, imaging charges, laboratory charges, room charges, physician fees.
• Need for mechanical ventilation and dialysis in the first-year post HCT
Statistical Analysis: Descriptive statistics will be used to summarize all data. Median costs incurred during the first-year post HCT along with interquartile ranges will be calculated. Median and Range will be calculated for the following health care utilization variables: LOS, ICU LOS and ICU utilization rate. Percentages representing frequency of usage will be calculated for the following variables, rates of ICU utilization, need for mechanical ventilation, dialysis. The impact of the following variables on costs and HCU will be analyzed by a multivariate analysis: age, disease status pre HCT, comorbidity index, performance score, occurrence of post-transplant complications namely GVHD and graft failure. Total adjusted costs and total adjusted costs per day will be summarized using descriptive statistics and reported as median and interquartile range by donor type for AML/MDS and ALL separately. Differences in total adjusted costs and adjusted costs per day by donor type will be tested using the Kruskal- Wallis test.

Q23. **PATIENT REPORTED OUTCOME (PRO) REQUIREMENTS: If the study requires PRO data collected by CIBMTR, the proposal should include: 1) A detailed description of the PRO domains, timepoints, and proposed analysis of PROs; 2) A description of the hypothesis specific to PROS.**

For additional information on what PRO measures have been collected and timepoints of collection, please reach out to the Late Effects and Quality of Life or Health Services Working Committee leadership: https://www.cibmtr.org/About/WhoWeAre/Com

Not applicable

Q24. **SAMPLE REQUIREMENTS: If the study requires biologic samples from the CIBMTR Repository, the proposal should also include: 1) A detailed description of the proposed testing methodology and sample requirements; 2) A summary of the investigator's previous experience with the proposed assay systems. PIs should be encouraged to review the inventory details, sample types collected and reach out to research_repos@nmdp.org with any questions.**

More information can be found at: https://www.cibmtr.org/Samples/Inventory/Pages/index

Not applicable

Q25. NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required, i.e., neither database contains all the data required to answer the study question.

PHIS database.

Inpatient charges will be obtained from the Pediatric Health Information System Database (PHIS).[15] PHIS is a confidential database of patient data from 50 member hospitals in the United States. Participating hospitals submit de-identified data. An encrypted medical record number (MRN) permits identification of readmissions at the same hospital; it can also be used to identify patient with their institution specific MRN. Charges reported from the hospital perspective are divided into specific categories of clinical, pharmacy, laboratory, and imaging services. Charges reported to PHIS are adjusted by geographical region based on the wage and price index (published annually in the Federal Register). All charges will be adjusted for inflation using the medical component of the consumer price index to 2019 dollars. Data on costs are not available in the CIBMTR database.

Merging and validating. Patients in PHIS database who received alloHCT will be identified using relevant ICD9 and ICD10 codes. These patients are identified within CIBMTR using a probabilistic algorithm. A target of 85% merge accuracy will be set, in accordance with previously published reports.[16, 17] Once linked, merge accuracy will be assessed with institution level validation at Columbia university medical center (CUMC) and Nationwide Children's Hospital. This process will be similar to our recently published studies. [11, 17, 18]

The following variables will be used to link patient data from PHIS with that of the CIBMTR database

- Age (Date of birth) and Sex
- Diagnosis ALL
- Date of HCT
- Center where treatment given

Feasibility:

We the PIs have extensive experience in working with the PHIS database and have independently extracted data from PHIS database for several published studies. [11, 13, 19-21] Therefore, our prior experience conducting healthcare utilization studies in children and adolescents with hematologic disorders and cancers is testament to our ability to successfully complete the proposed project. At our center (CUMC), we recently conducted a study of cost-effectiveness and HCU in patients undergoing alloHCT for the treatment of sickle cell disease[18] . In projects as mentioned above we merged the robust data from our center with that from the PHIS database[21]. This enabled us to analyze the cost of unrelated donor alloHCT at our center. Additionally, it allowed us to examine the fiscal trends and treatment patterns around alloHCT at our center over an 11-year period (2005-2016). As a testament to the success of our early studies, we were granted permission to merge thousands of records from the Center of International Blood and Marrow Transplant Research (CIBMTR) with data from PHIS. With this unique linked dataset, we examined HCU in a larger cohort of patients undergoing alloHCT for treatment of sickle cell disease as well as in a separate cohort of patients undergoing alloHCT for treatment of leukemia (CIBMTR study HS13-02[18] and HS 14-01[11]).

Q26. REFERENCES:

References
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3. D'Souza, A., et al., Current Use and Trends in Hematopoietic Cell Transplantation in the United States. Biol Blood Marrow Transplant, 2017. 23(9): p. 1417-1421.
4. Farhadfar, N., et al., Hematopoietic Cell Transplantation (HCT) Predictions for the Year 2023. Biology of Blood and Marrow Transplantation, 2020. 26(3, Supplement): p. S201.
5. Fuchs, E.J., et al., Double unrelated umbilical cord blood versus HLA-haploidentical bone marrow transplantation (BMT CTN 1101). Blood, 2020.
6. Symons, H.J., et al., Myeloablative haploidentical BMT with posttransplant cyclophosphamide for hematologic malignancies in children and adults. Blood Adv, 2020. 4(16): p. 3913-3925.
7. Ciurea, S.O., et al., Haploidentical transplant with posttransplant cyclophosphamide vs matched unrelated donor transplant for acute myeloid leukemia. Blood, 2015. 126(8): p. 1033-40.
8. Bertaina, A., et al., Unrelated donor vs HLA-haploidentical α/β T-cell- and B-cell-depleted HSCT in children with acute leukemia. Blood, 2018. 132(24): p. 2594-2607.
9. Rashidi, A., et al., Outcomes of haploidentical vs matched sibling transplantation for acute myeloid leukemia in first complete remission. Blood Adv, 2019. 3(12): p. 1826-1836.
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13. Rangarajan, H.G., et al., Increased Health Care Utilization and Costs during Allogeneic Hematopoietic Cell Transplantation for Acute Leukemia and Myelodysplastic Syndromes in Adolescents and Young Adults Compared with Children: A Multicenter Study. Biol Blood Marrow Transplant, 2019. 25(5): p. 1031-1038.
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15. PHIS. 2017. (Accessed May 31, 2017, 2017, at https://www.childrenshospitals.org/programs-and-services/data-analytics-and-research/pediatric-analytic-solutions/pediatric-health-information-system.).
16. Arnold, S.D., et al., Clinical risks and healthcare utilization of haematopoietic cell transplantation for sickle cell disease in the U.S. using merged databases. Haematologica, 2017.
17. Berry, J.G., et al., Hospital utilization and characteristics of patients experiencing recurrent readmissions within children's hospitals. Jama, 2011. 305(7): p. 682-90.
18. Arnold, S.D., et al., Clinical risks and healthcare utilization of hematopoietic cell transplantation for sickle cell disease in the USA using merged databases. Haematologica, 2017. 102(11): p. 1823-1832.
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20. Rangarajan, H.G., et al., Venous Thromboembolism in Pediatric Hematopoietic Cell Transplant: A Multicenter Cohort Study. Biol Blood Marrow Transplant, 2018. 24(2): p. 337-342.
21. Bourgeois, W., et al., Health care utilization and cost among pediatric patients receiving unrelated donor allogeneic hematopoietic cell transplantation. Bone Marrow Transplant, 2018.

Q27. **CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning:**

1. Employment (such as an independent contractor, consultant or providing expert testimony)?
2. Relationships (such as executive and advisory committee positions, medical consultant, speaker's bureau)?
3. Ownership (such as equity, ownership or financial interests)?
4. Transactions (such as honoraria, patents, royalties and licenses)?
5. Legal (such as pending or current arbitration or legal proceedings)?

- No, I do not have any conflicts of interest pertinent to this proposal

Q27a. **If yes, provide detail on the nature of employment, name of organization, role, entity, ownership, type of financial transaction or legal proceeding and whether renumeration is >$5000 annually.**

N/A

BEFORE FINAL SUBMISSION, please review the PI checklist to ensure that you have completed all necessary steps. This will increase the likelihood of submitting a feasible and successful proposal.

Embedded Data:

N/A

Baseline characteristics for patients who undergoing Allo HCT for acute leukemia and myelodysplastic syndrome in PHIS centers

Characteristic	**CRF**	**TED**
No. of patients	633	1906
No. of centers	35	36
Age of recipient - no. (%)		
Median (min-max)	9 (1-21)	10 (0-21)
0 - 9	337 (53)	917 (48)
10 - 19	281 (44)	931 (49)
20 - 29	15 (2)	58 (3)
Sex - no. (%)		
Male	378 (60)	1126 (59)
Female	255 (40)	780 (41)
Disease - no. (%)		
Acute myelogenous leukemia	294 (46)	710 (37)
Acute lymphoblastic leukemia	272 (43)	959 (50)
Myelodysplastic/myeloproliferative disorders	67 (10)	237 (13)
Donor type – no. (%)		
HLA-identical sibling	103 (16)	481 (25)
Mismatched related		
1 Ag/allele	4 (1)	16 (1)
>=2 Ag/allele	57 (9)	133 (7)
Other related(matching TBD)	5 (1)	40 (2)
Well-matched unrelated (8/8)	125 (20)	585 (31)
Partially-matched unrelated (7/8)	59 (9)	212 (11)
Mis-matched unrelated (<=6/8)	6 (1)	14 (1)
Unrelated (matching TBD)	2 (0)	20 (1)
Cord blood	272 (43)	401 (21)
Missing	0(0)	4 (0)
GVHD prophylaxis - no. (%)		
Ex-vivo T-cell depletion	21 (3)	95(5)
CD34 selection	11 (2)	35(2)
Post-CY + other(s)	38 (6)	95(5)
Post-CY alone	1 (0)	2 (0)
CNI (TAC/CSA) + MMF +/- Other(except post-CY)	282 (45)	508(28)
CNI (TAC/CSA) + MTX +/- Other(except MMF, post-CY)	234 (37)	1022(54)
CNI (TAC/CSA) +/- Other (except MMF, MTX, post-CY)	29 (5)	52(3)
TAC alone	2 (0)	19 (1)
CSA alone	9 (1)	32 (2)
Others	4 (1)	20 (1)
Missing	2 (0)	26(1)

Characteristic	CRF	TED
Stem cell source - no. (%)		
Bone Marrow	279 (44)	1162 (61)
Peripheral Blood	82 (13)	343 (18)
Cord Blood	272 (43)	401 (21)
Year of transplant - no. (%)		
2010	94 (15)	203 (11)
2011	29 (5)	202 (11)
2012	49 (8)	195 (10)
2013	82 (13)	216 (11)
2014	93 (15)	219 (11)
2015	118 (19)	236 (12)
2016	79 (12)	219 (11)
2017	46 (7)	214 (11)
2018	34 (5)	153 (8)
2019	9 (1)	49 (3)
Follow-up - median (range)	62 (24-128)	60 (24-128)

Response Summary:

This form is intended to be completed by a physician/researcher for the purpose of proposing a study. Content should not include Personal Identifiable Information (PII) or Protected Health Information (PHI). If you are a patient, do not complete this form. Patients: Contact your healthcare provider immediately for reports of problems with your treatment or problems with products received for your treatment. The CIBMTR uses de-identified data and is unable to associate reported treatment problems, adverse events, or corrections of information with a center, clinical trial, or healthcare provider.

Q1. Study Title

Utilization of chimeric antigen receptor (CAR) T-cells differs by race and ethnicity compared to autologous hematopoietic cell transplant (autoHCT)

Q2. Key Words

Race and ethnicity
Chimeric antigen receptor (CAR) T-cells
Autologous hematopoietic cell transplant (autoHCT)

Q3. PRINCIPAL INVESTIGATOR

Provide the following information for each investigator:

Principal Investigator #1:

First and last name, degree(s):	Megan Herr, PhD
Email address:	Megan.Herr@RoswellPark.org
Institution name:	Roswell Park Comprehensive Cancer Center
Academic rank:	Assistant Professor of Oncology

Q4. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- Yes

Q5. Do you identify as an underrepresented/minority?

- No

Q6. Principal Investigator #2 (If applicable):

First and last name, degree(s):	Christine Ho
Email address:	Christine.Ho@RoswellPark.org
Institution name:	Roswell Park Comprehensive Cancer Center
Academic rank:	Assistant Professor of Oncology

Q7. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- Yes

Q8. Do you identify as an underrepresented/minority?

- No

Q9. We encourage a maximum of two Principal Investigators per study. If more than one author is listed, please indicate who will be identified as the corresponding PI below:

Megan Herr

Q10. If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:

N/A

LETTER OF COMMITMENT:

Please note: *A letter of commitment will be signed by Lead and Last authors as it describes the expectations for filling that role. By signing the letter of commitment, the authors accept their responsibilities and will be held accountable for timely completion of all steps in the project. More details regarding author responsibilities can be found here:* *https://www.cibmtr.org/Studies/Observational/StudyManagement/p*

Q12. CURRENT ONGOING WORK WITH CIBMTR: Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.

Current ongoing work: PI: IN20-01
CO-I: CT20-01, CT19-01, SC17-07, IN19-01, LE17-01, LE18-01, LE20-02, IB19-02, CV20-04b

Q13. PROPOSED WORKING COMMITTEE:

- Health Services and International Studies

Q14. Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.

- Yes

Q14a. If you have already spoken with a scientific director or working committee chair regarding this study, then please specify who:

Dr. Wael Saber (last year)

Q15. RESEARCH QUESTION:

Does the utilization of chimeric antigen receptor (CAR) T-cells differ by race and ethnicity compared to autologous hematopoietic cell transplant (autoHCT)?

Q16. RESEARCH HYPOTHESIS:

We hypothesize that 1) racial disparities exist in the utilization of chimeric antigen receptor (CAR) T-cells compared to autologous hematopoietic cell transplant (autoHCT) and 2) treatment patterns of non-Hodgkin lymphoma (NHL) patients differ after they relapse or are refractory to an autoHCT.

Q17. SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.)

Suggested word limit of 200 words:

Aim 1: primary objective: compare the rate of first autoHCT to the rate of first CAR T by race and ethnicity. Data will be analyzed for relapsed/refractory NHL patients who received treatment (autoHCT or CAR T) from 2017-2021. Additionally, COVID-19 impact on utilization will be described in a sensitivity analysis of 2020-2021 patients.
Aim 2: primary objective: describe therapy choices after a failed autologous HCT for NHL by race and ethnicity. Data will be analyzed for patients who received their first autoHCT from 2010-2019 and relapsed or progressed between 2016-2020. Therapies following autoHCT for relapsed/refractory patients will be compared by race and ethnicity and include second autoHCT, first alloHCT, CAR T-cell, other, and no therapy. This post-autoHCT therapy will be assessed for an association with the covariates listed (including age, sex, etc.) to determine if results should be stratified.

Q18. SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.

Treatment with CD19-targeted CAR T-cell immunotherapy is novel for relapsed/refractory B-cell lymphoma and the number of patients treated will increase as more CAR T-cell therapies get approved. Unfortunately, this therapy is underutilized in minority populations. Many of these patients have received a previous autoHCT, suggesting this difference is not an access to care issue. Describing the patterns of care after autoHCT for relapsed/refractory NHL patients will help identify the alternative therapies, if any, minority patients are receiving instead of CAR T and if this differs from patients of white race.

Q19. SCIENTIFIC JUSTIFICATION: Provide a background summary of previous related research and their strengths and weaknesses, justification of your research and why your research is still necessary.

Treatment with CAR T-cell therapy is novel for relapsed/refractory B-cell lymphoma, but racial/ethnic differences exist. Patients treated with CAR T-cell therapy were less likely to be African American race than autoHCT (5% vs 21% per CIBMTR Lymphoma Working Committee Minutes 2020 Proposal: 1911-267; see table below) and more likely to be white (87% CAR T compared to 64% AutoHCT). Proposal: 1911-51 supports these racial disparities and also depicts a difference for therapies in those of Asian race (4% in CAR T vs 11% in autoHCT). Furthermore, racial differences have been described in autoHCT (Joshua et al. Access to hematopoietic stem cell transplantation- Effect of race and sex. Cancer. 2010) suggesting these percentages should be even higher for minorities. We seek to expand upon this research into the CAR T-cell setting to compare utilization of these treatments (either CAR T-cell therapy or second autoHCT or first alloHCT) by race/ethnicity. Additionally, we will investigate potential reasons for these racial and ethnic differences. Although no differences existed by sex and minimal differences existed by age, these will be investigated as well.

Q19a. SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF)

[Click here]

Q20. PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.

Aim 1
Patients eligible for Aim 1a must meet the eligibility criteria for commercial CAR-T:
• Patients diagnosed with diffuse large B-cell lymphoma (DLBCL) not otherwise specified, high grade B-cell lymphoma, mediastinal large B-cell lymphoma, or DLBCL arising from follicular lymphoma
• Disease status at CAR-T cell infusion or autoHCT: relapsed/refractory (CR2+, Rel1+, PIF)
• Age 18 years or older at time of CAR-T cell infusion or HCT
• Patients who received commercial CAR-T cell (axi-cel or tisa-cel) therapy or autoHCT between 1/1/2017-12/31/2019
Aim 2 (distinct population from Aim 1)
Patients eligible for Aim 1b include those who failed first autoHCT with the following:
• Patients who received an autoHCT for DLBCL, not otherwise specified, high grade B-cell lymphoma, mediastinal large B-cell lymphoma, or DLBCL arising from follicular lymphoma
• Age 18 years or older at time of autoHCT
• Patients who received their first autoHCT between 1/1/2010-12/31/2018
• Patients who relapsed or progressed between 1/1/2016 and 12/31/2019 after their first autoHCT.

Q21. Does this study include pediatric patients?

- No

Q21a. If this study does not include pediatric patients, please provide justification:

Axi-cel and Tisa-cel use is limited to adult patients.

Q22. DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Data collection forms available at: http://www.cibmtr.org/DataManagement/DataCollectior Outline any supplementary data required. Additional data collection is extremely difficult and will make your proposal less feasible.

• Information requested includes data on demographics, previous HCT, and treatments after autoHCT.
• Data on the following CIBMTR data collection forms will be needed:
o 4000
o 4003
o 2000
o 2018
o 2118
o 2100
o 2402
o 2900
• No additional data is requested.

Q23. **PATIENT REPORTED OUTCOME (PRO) REQUIREMENTS: If the study requires PRO data collected by CIBMTR, the proposal should include: 1) A detailed description of the PRO domains, timepoints, and proposed analysis of PROs; 2) A description of the hypothesis specific to PROS.**

For additional information on what PRO measures have been collected and timepoints of collection, please reach out to the Late Effects and Quality of Life or Health Services Working Committee leadership: https://www.cibmtr.org/About/WhoWeAre/Com

None

Q24. **SAMPLE REQUIREMENTS: If the study requires biologic samples from the CIBMTR Repository, the proposal should also include: 1) A detailed description of the proposed testing methodology and sample requirements; 2) A summary of the investigator's previous experience with the proposed assay systems. PIs should be encouraged to review the inventory details, sample types collected and reach out to research_repos@nmdp.org with any questions.**

More information can be found at: https://www.cibmtr.org/Samples/Inventory/Pages/index

None

Q25. NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required, i.e., neither database contains all the data required to answer the study question.

None

Q26. REFERENCES:

Joshua TV, Rizzo JD, Zhang M-J, et al. Access to hematopoietic stem cell transplantation- Effect of race and sex. Cancer. 2010:116(14):3469-3476.

Q27. CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning:

1. Employment (such as an independent contractor, consultant or providing expert testimony)?
2. Relationships (such as executive and advisory committee positions, medical consultant, speaker's bureau)?
3. Ownership (such as equity, ownership or financial interests)?
4. Transactions (such as honoraria, patents, royalties and licenses)?
5. Legal (such as pending or current arbitration or legal proceedings)?

- No, I do not have any conflicts of interest pertinent to this proposal

Q27a. If yes, provide detail on the nature of employment, name of organization, role, entity, ownership, type of financial transaction or legal proceeding and whether renumeration is >$5000 annually.

N/A

BEFORE FINAL SUBMISSION, please review the PI checklist to ensure that you have completed all necessary steps. This will increase the likelihood of submitting a feasible and successful proposal.

Embedded Data:

N/A

Table for Aim 1

Baseline characteristics for patients who undergoing 1st commercial CAR-T or 1st AutoHCT for DLBCL in relapsed or refractory

Characteristic	CAR-T	Auto
No. of patients	1025	227
No. of centers	81	71
Age at infusion/ HCT, by category - no. (%)		
Median (min-max)	63 (18-91)	61 (18-79)
10-19	3 (0)	1 (0)
20-29	32 (3)	9 (4)
30-39	57 (6)	13 (6)
40-49	100 (10)	22 (10)
50-59	223 (22)	66 (29)
60-69	370 (36)	80 (35)
>= 70	240 (23)	36 (16)
Gender - no. (%)		
Male	636 (62)	159 (70)
Female	389 (38)	68 (30)
Product - no. (%)		
Kymriah	213 (21)	NA
Yescarta	739 (72)	NA
Other	73 (7)	NA
Recipient race - no. (%)		
White	848 (83)	144 (63)
African American	54 (5)	45 (20)
Asian	48 (5)	22 (10)
Pacific Islander	3 (0)	2 (1)
Native American	5 (0)	5 (2)
More than one race	5 (0)	0
Unknown	38 (4)	4 (2)
Missing	24 (2)	5 (2)
Recipient ethnicity - no. (%)		
Hispanic or Latino	106 (10)	21 (9)
Non-Hispanic or non-Latino	868 (85)	200 (88)
N/A - Not a resident of the U.S.	11 (1)	1 (0)
Unknown	40 (4)	5 (2)
Sub-disease indication of DLBCL - no. (%)		
NHL diffuse, large B-cell	237 (23)	118 (52)
T-cell / histiocytic rich large B-cell lymphoma	14 (1)	15 (7)
Primary mediastinal large B-cell	31 (3)	4 (2)
Diffuse, large B-cell lymphoma- Germinal center B-cell type	374 (36)	33 (15)

Characteristic	CAR-T	Auto
Diffuse, large B-cell lymphoma- Activated B-cell type	233 (23)	35 (15)
EBV+ DLBCL	7 (1)	2 (1)
High-grade B-cell lymphoma	17 (2)	2 (1)
High-grade B-cell lymphoma, with MYC and BCL2 and/or BCL6 rearrangements	112 (11)	18 (8)
Disease status prior to CT - no. (%)		
CR2 +	19 (2)	121 (53)
< CR, chemosensit	200 (20)	95 (42)
< CR, chemoresist	806 (79)	11 (5)
Year of CT - no. (%)		
2017	8 (1)	76 (33)
2018	343 (33)	85 (37)
2019	674 (66)	66 (29)
Follow-up of survivors, months - median (range)	23 (1-49)	24 (2-49)

Table for Aim 2

Baseline characteristics for **NHL** patients who relapsed after an autologous HCT

Characteristic	1st AlloHCT	2nd AutoHCT	CAR T-cell
No. of patients	257	4	520
No. of centers	95	4	79
Age at HCT - no. (%)			
Median (min-max)	55 (18-75)	62 (61-72)	62 (22-82)
10-19	3 (1)	0 (0)	6 (1)
20-29	15 (6)	0 (0)	28 (5)
30-39	18 (7)	0 (0)	55 (11)
40-49	59 (23)	0 (0)	128 (25)
50-59	96 (37)	0 (0)	216 (42)
60-69	60 (23)	3 (75)	87 (17)
>= 70	6 (2)	1 (25)	
Recipient sex - no. (%)			347 (67)
Male	172 (67)	3 (75)	173 (33)
Female	85 (33)	1 (25)	520
Karnofsky/Lansky performance score prior to HCT - no. (%)			
90-100	174 (68)	2 (50)	231 (44)
80	57 (22)	1 (25)	142 (27)
<80	18 (7)	1 (25)	67 (13)
Missing	8 (3)	0 (0)	80 (15)
Race - no. (%)			

Characteristic	1st AlloHCT	2nd AutoHCT	CAR T-cell
White	189 (74)	2 (50)	448 (86)
African-American	25 (10)	1 (25)	24 (5)
Asian	12 (5)	0 (0)	23 (4)
Pacific Islander	1 (0)	0 (0)	1 (0)
Native American	0	0	1 (0)
More than one race	1 (0)	0 (0)	2 (0)
Missing	29 (11)	1 (25)	21 (4)
Ethnicity - no. (%)			
Hispanic or Latino	23 (9)	0 (0)	40 (8)
Not Hispanic or Latino	200 (78)	3 (75)	447 (86)
Non-resident of the U.S.	31 (12)	1 (25)	11 (2)
Missing	3 (1)	0 (0)	22 (4)
Year of HCT - no. (%)			
2016	121 (47)	1 (25)	20 (4)
2017	83 (32)	2 (50)	28 (5)
2018	48 (19)	1 (25)	197 (38)
2019	5 (2)	0 (0)	275 (53)

Response Summary:

This form is intended to be completed by a physician/researcher for the purpose of proposing a study. Content should not include Personal Identifiable Information (PII) or Protected Health Information (PHI). If you are a patient, do not complete this form. Patients: Contact your healthcare provider immediately for reports of problems with your treatment or problems with products received for your treatment. The CIBMTR uses de-identified data and is unable to associate reported treatment problems, adverse events, or corrections of information with a center, clinical trial, or healthcare provider.

Q1. Study Title

Changes in international Hematopoietic Cell Transplantation (HCT) Practices since publication of "Choosing Wisely BMT"

Q2. Key Words

Health Services; Guidelines; Hematopoietic Cell Transplantation

Q3. PRINCIPAL INVESTIGATOR

Provide the following information for each investigator:

Principal Investigator #1:

First and last name, degree(s):	Matthew Seftel
Email address:	matthew.seftel@blood.ca
Institution name:	University of British Columbia
Academic rank:	Professor

Q4. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- No

Q5. Do you identify as an underrepresented/minority?

- No

Q6. Principal Investigator #2 (If applicable):

First and last name, degree(s):	N/A
Email address:	N/A
Institution name:	N/A
Academic rank:	N/A

Q7. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

N/A

Q8. Do you identify as an underrepresented/minority?

N/A

Q9. We encourage a maximum of two Principal Investigators per study. If more than one author is listed, please indicate who will be identified as the corresponding PI below:

N/A

Q10. If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:

N/A

LETTER OF COMMITMENT:

Please note: *A letter of commitment will be signed by Lead and Last authors as it describes the expectations for filling that role. By signing the letter of commitment, the authors accept their responsibilities and will be held accountable for timely completion of all steps in the project. More details regarding author responsibilities can be found here:* *https://www.cibmtr.org/Studies/Observational/StudyManagement/p*

Q12. CURRENT ONGOING WORK WITH CIBMTR: Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.

N/A

Q13. PROPOSED WORKING COMMITTEE:

- Health Services and International Studies

Q14. Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.

- Yes

Q14a. If you have already spoken with a scientific director or working committee chair regarding this study, then please specify who:

Dr William Wood

Q15. RESEARCH QUESTION:

What is the effect of "Choosing Wisely BMT" recommendations on clinical practice in HCT?

Q16. RESEARCH HYPOTHESIS:

Since the publication and dissemination of the "Choosing Wisely BMT" recommendations in 2018, we hypothesize that the clinical HCT community has modified its HCT practices in temporal association with these recommendations.

Q17. SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.)

Suggested word limit of 200 words:

To measure trends in HCT practice in the three following categories:
1. Bone Marrow (BM) vs. peripheral blood stem cells (PBSCs) for matched unrelated donor (MUD) HCT after myeloablative conditioning (MAC) in patients with hematological malignancies.
2. Use of BM vs. PBSCs as the cell source for HCT in patients with aplastic anemia.
3. Use of single vs. double cord blood units for cord blood transplantation (CBT).

Q18. SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.

An evaluation of the effects of a major Quality Improvement project such as Choosing Wisely BMT is important as a tool to measure the effectiveness of such campaigns, and to determine whether further knowledge dissemination or recommendations are necessary.

Q19. SCIENTIFIC JUSTIFICATION: Provide a background summary of previous related research and their strengths and weaknesses, justification of your research and why your research is still necessary.

The mission of "Choosing Wisely" is to promote dialogue between clinicians and patients by helping them identify care that is (i) supported by evidence (ii) not duplicative of other tests or procedures already received (iii) as free from harm as possible (iv) necessary. National organizations representing medical specialists, including the ASTCT and its Canadian counterpart CTTC (previously CBMTG) have asked their members to identify tests or procedures commonly used in their field whose necessity should be questioned and discussed.
The Choosing Wisely BMT campaign was formulated in 2017 as a combined effort between ASTCT and CTTC with approval and oversight by Choosing Wisely in the USA (ABIM) and Choosing Wisely Canada. This campaign culminated in a peer-reviewed set of recommendations that were published and disseminated on relevant websites, and at the 2018 ASTCT and CTTC annual conferences. Despite these initial steps, it is unknown whether the Choosing Wisely BMT recommendations have been implemented, and whether relevant practice changes have subsequently occurred within the internatioanal HCT community.
The purpose of the current CIBMTR research proposal is to evaluate whether there have been temporal changes in HCT practice in three domains of HCT practice that were highlighted by Choosing Wisely BMT: Choice of cell source in MUD MA HCT; choice of cell source in aplastic anemia; choice of number of umbilical cord blood units in CBT. The effect of the two other domains encompassed by Choosing Wisely BMT (pertaining to the use of IVIG after HCT and the dose of corticosteroids in the treatment of graft-versus-host disease) cannot readily be captured using CIBMTR data, and thus these recommendations will not be analyzed.
This study will review HCT characteristics for the 4 years before and after the publication of Choosing Wisely BMT in order to determine any change of practice that occurred in temporal association with these recommendations.An evaluation of the effects of a major Quality Improvement project such as Choosing Wisely BMT is important as a tool to measure the effectiveness of such campaigns, and to determine whether further knowledge dissemination or recommendations are necessary.

Q19a. SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF)

N/A

Q20. PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.

1. Recipients of matched (8/8) unrelated donor HCT hematological malignancies from January 1 2014 to December 31 2021.
a. Recipients of (i) ex-vivo T-cell depletion; (ii) in-vivo T-cell depletion using alemtuzumab are excluded.
b. Recipients of non-myeloablative conditioning regimens are excluded.
2. Recipients of first related donor and MUD HCT for aplastic anemia from January 1 2014 to December 31 2021
a. Recipients of (i) ex-vivo T-cell depletion; (ii) in-vivo T-cell depletion using alemtuzumab are excluded.
b. Recipients of haploidentical HCT are excluded
3. Recipients of CBT (for any indication) from January 1 2014 to December 31 2021

Q21. Does this study include pediatric patients?

- Yes

Q22. DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Data collection forms available at: http://www.cibmtr.org/DataManagement/DataCollectior Outline any supplementary data required. Additional data collection is extremely difficult and will make your proposal less feasible.

HCT characteristics as reported to CIBMTR for the 8 year period January 1 2014 to December 31 2021 in the following categories:

1. Recipients of first Matched (8/8) unrelated donor HCT using MAC for hematological malignancies (AML, MDS, ALL, CML, MPN/MF, NHL, CLL) from January 1 2014 to December 31 2021.

Specific data required:

- Age at HCT
- Month/Year of HCT
- Indication for HCT
- CIBMTR disease risk index (DRI) at HCT
- KPS at HCT (<80% vs > 80%)
- Conditioning regimen
- Cell source (BM vs. PBSCs)
- ATG used as part of conditioning regimen (Y vs N)
- GVHD prophylaxis

2. Recipients of first related and unrelated donor HCT for aplastic anemia, excluding haploidentical HCT, from January 1 2014 to December 31 2021

- Age at HCT
- Month/Year of HCT
- Previous IST (Yes, No)
- KPS at HCT (<80% vs > 80%)
- Conditioning regimen
- Cell source (BM vs PBSCs)
- ATG used as part of conditioning regimen (Y vs N)
- GVHD prophylaxis

3. Recipients of first CBT of any age and for any indication from January 1 2014 to December 31 2021.

- Age at HCT
- Month/Year of HCT
- Indication for HCT
- CIBMTR disease risk index (DRI) at HCT
- KPS at HCT (<80% vs > 80%)
- Conditioning regimen
- Single vs Double CBT units
- ATG used as part of conditioning regimen (Y vs N)
- GVHD prophylaxis

Q23. **PATIENT REPORTED OUTCOME (PRO) REQUIREMENTS: If the study requires PRO data collected by CIBMTR, the proposal should include: 1) A detailed description of the PRO domains, timepoints, and proposed analysis of PROs; 2) A description of the hypothesis specific to PROS.**

For additional information on what PRO measures have been collected and timepoints of collection, please reach out to the Late Effects and Quality of Life or Health Services Working Committee leadership: https://www.cibmtr.org/About/WhoWeAre/Com

N/A

Q24. **SAMPLE REQUIREMENTS: If the study requires biologic samples from the CIBMTR Repository, the proposal should also include: 1) A detailed description of the proposed testing methodology and sample requirements; 2) A summary of the investigator's previous experience with the proposed assay systems. PIs should be encouraged to review the inventory details, sample types collected and reach out to research_repos@nmdp.org with any questions.**

More information can be found at: https://www.cibmtr.org/Samples/Inventory/Pages/index

N/A

Q25. NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required, i.e., neither database contains all the data required to answer the study question.

N/A

Q26. REFERENCES:

1. Bhella S.Majhail NS, Betcher J, et al. Choosing Wisely BMT: American Society for Blood and Marrow Transplantation and Canadian Blood and Marrow Transplant Group's List of 5 Tests and Treatments to Question in Blood and Marrow Transplantation. Biol Blood Marrow Transplant 2018 May;24(5):909-913. doi: 10.1016/j.bbmt.2018.01.017. Epub 2018 Jan 31.
2. Choosing Wisely: American Society for Transplantation and Cellular Therapy & Cell Therapy Transplant Canada. Released January 30 2018. https://www.choosingwisely.org/societies/american-society-for-transplantation-and-cellular-therapy-and-cell-therapy-transplant-canada/
3. Choosing Wisely Canada. Blood and Marrow Transplant: Five things Physicians and Patients Should Question. Released January 30 2018. https://choosingwiselycanada.org/blood-marrow-transplant/

Q27. CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning:

1. Employment (such as an independent contractor, consultant or providing expert testimony)?
2. Relationships (such as executive and advisory committee positions, medical consultant, speaker's bureau)?
3. Ownership (such as equity, ownership or financial interests)?
4. Transactions (such as honoraria, patents, royalties and licenses)?
5. Legal (such as pending or current arbitration or legal proceedings)?

- No, I do not have any conflicts of interest pertinent to this proposal

Q27a. If yes, provide detail on the nature of employment, name of organization, role, entity, ownership, type of financial transaction or legal proceeding and whether renumeration is >$5000 annually.

N/A

BEFORE FINAL SUBMISSION, please review the PI checklist to ensure that you have completed all necessary steps. This will increase the likelihood of submitting a feasible and successful proposal.

Embedded Data:

N/A

Response Summary:

This form is intended to be completed by a physician/researcher for the purpose of proposing a study. Content should not include Personal Identifiable Information (PII) or Protected Health Information (PHI). If you are a patient, do not complete this form. Patients: Contact your healthcare provider immediately for reports of problems with your treatment or problems with products received for your treatment. The CIBMTR uses de-identified data and is unable to associate reported treatment problems, adverse events, or corrections of information with a center, clinical trial, or healthcare provider.

Q1. Study Title

The impact of ethnicity, race, and socio-economic status (SES) in mismatched unrelated donor (MMUD) allogeneic hematopoietic cell transplantation (HCT)

Q2. Key Words

mismatched donor transplant socio-economic status racial ethnic disparity

Q3. PRINCIPAL INVESTIGATOR

Provide the following information for each investigator:

Principal Investigator #1:

First and last name, degree(s):	Trent Wang, DO
Email address:	trentwang@med.miami.edu
Institution name:	University of Miami
Academic rank:	Assistant Professor of Medicine

Q4. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- Yes

Q5. Do you identify as an underrepresented/minority?

- No

Q6. Principal Investigator #2 (If applicable):

First and last name, degree(s):	Antonio Jimenez
Email address:	amjimenez@med.miami.edu
Institution name:	University of Miami
Academic rank:	Assistant Professor of Medicine

Q7. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- No

Q8. Do you identify as an underrepresented/minority?

- Yes

Q9. We encourage a maximum of two Principal Investigators per study. If more than one author is listed, please indicate who will be identified as the corresponding PI below:

Trent Wang

Q10. If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:

- Yes, I am a junior investigator and would like assistance identifying a senior mentor for my project

LETTER OF COMMITMENT:

Please note: *A letter of commitment will be signed by Lead and Last authors as it describes the expectations for filling that role. By signing the letter of commitment, the authors accept their responsibilities and will be held accountable for timely completion of all steps in the project. More details regarding author responsibilities can be found here:* *https://www.cibmtr.org/Studies/Observational/StudyManagement/p*

Q12. CURRENT ONGOING WORK WITH CIBMTR: Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.

No PI projects

Q13. PROPOSED WORKING COMMITTEE:

- Health Services and International Studies

Q14. Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.

- No

Q15. RESEARCH QUESTION:

Do disparities in ethnicity, race, and SES impact outcomes in mismatched unrelated donor HCT

Q16. RESEARCH HYPOTHESIS:

Disparities in ethnicity/race and SES may result in differences in MMUD HCT outcomes.

Q17. SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.)

Suggested word limit of 200 words:

1-To compare MMUD HCT outcomes among recipients of varying backgrounds in ethnicity/race and SES
3-To describe the racial/ethnic and SES composition of MMUD recipients
2-To evaluate the impact of ATG vs PTCy GVHD prophylaxis regimens relative to ethnicity/race and SES

Q18. SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.

We wish to study the impact of SES, ethnicity, and race disparities on MMUD HCT outcomes to highlight potential areas in need for additional directed focus and resource.

Q19. SCIENTIFIC JUSTIFICATION: Provide a background summary of previous related research and their strengths and weaknesses, justification of your research and why your research is still necessary.

Disparities in cancer outcomes have been increasingly described based on racial/ethnic and socioeconomic status. Cancer biology may play a role in disparate outcomes among different ethnicities, however likely in conjunction with a multitude of other factors including socioeconomic status. Studies have demonstrated minority racial/ethnic groups were associated with lower likelihood of receiving cancer care such as chemotherapy, radiation and surgery in multiple cancers including pancreatic (Nipp 2018), ovarian cancer (Sherry 2017), and other solid tumors (also include auto MM data).

Within allogeneic transplant, racial disparities have been noted in outcomes such that minorities have been described as having increased GVHD, increased NRM, and decreased overall survival. Most studies demonstrated that Caucasians had improved survival as compared to African American and Hispanic populations (Easaw 1996, Serna 2003, Baker 2009). GVHD differences were also noted with lower rates of acute GVHD among Japanese and Scandanavian cohorts compared to white Americans, African Americans and Irish cohorts (Oh 2005). Single umbilical cord blood transplant studies in children found worse survival among black patients (Ballen 2012), possibly attributed to HLA mismatch and cell dose. Kuwatsuka in 2014 found that in children undergoing umbilical cord transplant, there was no different in acute GVHD but more chronic among white children receiving ATG. No difference in overall survival was noted.

Among persons that describe themselves as of Euro-caucasian background the probability of identifying an HLA matched unrelated donor is 75%, compared to 15-45% in patients that identify as from racial or ethnic minority backgrounds (Gragert 2014, Barker 2019). Therefore, MMUD HCT is required in a significant fraction of adult patients, particularly within non-Caucasian minority populations (Pidala 2015).

Historically, clinical outcomes following MMUD transplantation were inferior, given higher rates of NRM and GVHD when traditional GVHD prophylaxis is used. (Saber 2012). Post-transplant cyclophosphamide (PTCy) has allowed for use of increasingly mismatched HLA donors, first described in the haploidentical setting. The recent NMDP's MMUD-15 study (Shaw 2021) evaluating the use of PTCy in recipients of a BM-mismatched grafts found that PTCy provided encouraging survival and acceptable rates of GVHD and NRM, despite high degree of HLA mismatch. Importantly, 48% of enrolled patients belonged to an ethnic/racial minority)

Within an already heterogeneous patient population receiving MMUD HCT, clinical outcomes are variable and treatment related mortality and GVHD risk remain significant concerns. There is limited study of the racial/ethnic and SES characteristics of MMUD recipients given the relative infrequency of this type of transplant. It is unknown whether certain SES characteristics or race/ethnicity confer increased risk. In addition, with the promising data reported from PTCy based conditioning in this MMUD HCT, it is conceivable that PTCy may mitigate SES/racial/ethnic risk factors when compared to ATG-based GVHD prophylaxis

We hypothesize that disparities in race/ethnicity and SES impact clinical outcomes among patients undergoing MMUD HCT. Through improved understanding of health outcome disparities, we can inform health policy to shape targeted interventions.

Q19a. SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF)

N/A

Q20. PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.

-Patients aged 18 years or older
-Available data 2000-2020 (may consider 2010 – 2020 based on numbers available of MMUD)
-Recipients of MMUD HCT (>1 mismatch at -A, -B, -C, -DRB1 alleles)

Q21. Does this study include pediatric patients?

- No

Q21a. If this study does not include pediatric patients, please provide justification:

SES impact in pediatric population not accounted for here, but can be added

Q22. DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Data collection forms available at: http://www.cibmtr.org/DataManagement/DataCollectior Outline any supplementary data required. Additional data collection is extremely difficult and will make your proposal less feasible.

2000 (baseline), 2006 (hsct infusion), 2005 (HLA), 2100 (post HLA infusion follow up2200 (follow up), 2300 (late follow up), 2455 (Selective follow up), 2900 (death data).
Variables
Main Effect:
-Race/ethnicity: Non-Hispanic white vs. Non-Hispanic black vs. Hispanic vs. Asian
-SES (median annual household income based on ZIP code of residence): < 20,000, 20,000-39,999, 40,000-59,999, 60,000 – 79,999, > 80,000 , Marital status, Insurance, Education
Patient-related:
-Age, 18-40, 40-60, 60+
-Gender: Male vs Female
-Race: white non-hispanic, white Hispanic, black non-hispanic, black Hispanic, Asian
-Karnofsky performance score: ≥90% <90
-Disease: malignant disease vs non-malignant
-CMV serostatus donor and recipient
Transplant Related
-ASBMT RFI disease risk category: Low vs Intermediate vs High
-Year of transplant: 2000 – 2010 vs 2010 – 2020
-Graft type: Bone marrow vs peripheral blood
-Conditioning intensity: Myeloablative (MA) vs RIC/NMA
-TBI-based conditioning: Yes vs No
- GVHD prophylaxis: CNI, CNI+MMF, CNI+MTx, CNI+MTX+ATG, CNI+PTCY
- Donor Ethnicity
-Acute GVHD: grade 0-1 vs. 2-4
-Chronic GVHD: limited vs extensive vs none

Q23. **PATIENT REPORTED OUTCOME (PRO) REQUIREMENTS: If the study requires PRO data collected by CIBMTR, the proposal should include: 1) A detailed description of the PRO domains, timepoints, and proposed analysis of PROs; 2) A description of the hypothesis specific to PROS.**

For additional information on what PRO measures have been collected and timepoints of collection, please reach out to the Late Effects and Quality of Life or Health Services Working Committee leadership: https://www.cibmtr.org/About/WhoWeAre/Com

None

Q24. **SAMPLE REQUIREMENTS: If the study requires biologic samples from the CIBMTR Repository, the proposal should also include: 1) A detailed description of the proposed testing methodology and sample requirements; 2) A summary of the investigator's previous experience with the proposed assay systems. PIs should be encouraged to review the inventory details, sample types collected and reach out to research_repos@nmdp.org with any questions.**

More information can be found at: https://www.cibmtr.org/Samples/Inventory/Pages/index

None

Q25. NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required, i.e., neither database contains all the data required to answer the study question.

None

Q26. REFERENCES:

Nipp, et al. Disparities in cancer outcomes across age, sex, and race/ethnicity among patients with pancreatic cancer. Cancer Med 2018. 7(2):525-535.
Sherri L, et al. Disparities in ovarian cancer survival in the United States (2001-2009): Findings from the CONCORD-2 study. Cancer, 2017.
Easaw SJ, Lake DE, Beer M, Seiter K, Feldman EJ, Ahmed T. Graft-versus-host disease. Possible higher risk for African American patients. Cancer. 1996;78:1492–1497
Serna DS, Lee SJ, Zhang MJ, et al. Trends in survival rates after allogeneic hematopoietic stem-cell transplantation for acute and chronic leukemia by ethnicity in the United States and Canada. JCO. 2003;21:3754–3760
Baker KS, Davies SM, Majhail NS, et al. Race and socioeconomic status influence outcomes of unrelated donor hematopoietic cell transplantation. BBMT. 2009;15:1543–1554
Oh H, Loberiza FR Jr, Zhang MJ, et al. Comparison of graft-versus-host-disease and survival after HLA-identical sibling bone marrow transplantation in ethnic populations. Blood. 2005 Feb 15;105(4):1408-16.
Ballen K, et al. Relationship of race/ethnicity and survival after single umbilical cord blood transplantation for adults and children with leukemia and myelodysplastic syndromes. Biol Blood Marrow Transplant. 2012; 18: 903–912
Kuwatsuka Y, et al. Graft-versus-host disease and survival after cord blood transplantation for acute leukemia: a comparison of Japanese versus White populations. Biol Blood Marrow Transplant. 2014 May;20(5):662-7.
Gragert L et al. HLA Match Likelihoods for Hematopoietic Stem-Cell Grafts in the U.S. Registry. New England Journal of Medicine. 2014;371(4):339-348.
Barker JN, et al. Racial disparities in access to HLA-matched unrelated donor transplants: a prospective 1312-patient analysis. Blood Advances. 2019;3(7):939-944.
Pidala J, et al. Race/ethnicity affects the probability of finding an HLA-A, -B, -C and -DRB1 allele-matched unrelated donor and likelihood of subsequent transplant utilization. BMT. 2015;48(3):346-350.
Saber W, et al. Outcomes after matched unrelated donor versus identical sibling hematopoietic cell transplantation in adults with acute myelogenous leukemia. Blood. 2012;119(17):3908-3916.
Shaw BE, et al. National Marrow Donor Program–Sponsored Multicenter, Phase II Trial of HLA-Mismatched Unrelated Donor Bone Marrow Transplantation Using Post-Transplant Cyclophosphamide. JCO. 2021;39(18):1971-1982.

Q27. CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning:

1. Employment (such as an independent contractor, consultant or providing expert testimony)?
2. Relationships (such as executive and advisory committee positions, medical consultant, speaker's bureau)?
3. Ownership (such as equity, ownership or financial interests)?
4. Transactions (such as honoraria, patents, royalties and licenses)?
5. Legal (such as pending or current arbitration or legal proceedings)?

- No, I do not have any conflicts of interest pertinent to this proposal

Q27a. If yes, provide detail on the nature of employment, name of organization, role, entity, ownership, type of financial transaction or legal proceeding and whether renumeration is >$5000 annually.

N/A

BEFORE FINAL SUBMISSION, please review the PI checklist to ensure that you have completed all necessary steps. This will increase the likelihood of submitting a feasible and successful proposal.

Embedded Data:

N/A

Baseline characteristics for patients who undergoing first Allo HCT reported to CIBMTR (CRF)

Characteristic	
No. of patients	4345
No. of centers	160
Age of recipient - no. (%)	
Median (min-max)	48 (18-81)
10 - 19	169 (4)
20 - 29	635 (15)
30 - 39	658 (15)
40 - 49	950 (22)
50 - 59	1078 (25)
60 - 69	740 (17)
70+	115 (3)
Sex - no. (%)	
Male	2466 (57)
Female	1879 (43)
Disease - no. (%)	
Acute myelogenous leukemia	1701 (39)
Acute lymphoblastic leukemia	653 (15)
Other leukemia	178 (4)
Chronic myelogenous leukemia	400 (9)
Myelodysplastic/myeloproliferative disorders	717 (17)
Other acute leukemia	25 (1)
Non-Hodgkin lymphoma	320 (7)
Hodgkin lymphoma	26 (1)
Plasma cell disorder/Multiple Myeloma	19 (0)
Severe aplastic anemia	109 (3)
Inherited abnormalities erythrocyte differentiation or function	29 (1)
SCID and other immune system disorders	4 (0)
Myeloproliferative Neoplasms	164 (4)
Donor type - no. (%)	
Partially-matched unrelated (7/8)	3630 (84)
Mis-matched unrelated (<=6/8)	715 (16)
Ethnicity - no. (%)	
Hispanic or Latino	444 (10)
Non Hispanic or non-Latino	3066 (71)
Non-resident of the U.S.	9 (0)
Missing	826 (19)
Race - no. (%)	
White	3533 (81)
Black or African American	424 (10)

Characteristic	
Asian	130 (3)
Native Hawaiian or other Pacific Islander	4 (0)
American Indian or Alaska Native	30 (1)
Other	7 (0)
More than one race	34 (1)
Missing	183 (4)
GVHD prophylaxis - no. (%)	
Ex-vivo T-cell depletion	228 (5)
CD34 selection	99 (2)
Post-CY + other(s)	192 (4)
Post-CY alone	3 (0)
CNI (TAC/CSA) + MMF +/- Other(except post-CY)	927 (21)
CNI (TAC/CSA) + MTX +/- Other(except MMF, post-CY)	2447 (56)
CNI (TAC/CSA) +/- Other (except MMF, MTX, post-CY)	219 (5)
TAC alone	131 (3)
CSA alone	30 (1)
Others	40 (1)
Missing	29 (1)
Stem cell source - no. (%)	
Bone Marrow	1464 (34)
Peripheral Blood	2881 (66)
Insurance type - no. (%)	
No insurance	16 (0)
Disability insurance +/-others	69 (2)
Private health insurance +/- others	2128 (49)
Medicaid +/-others	649 (15)
Medicare +/-others	451 (10)
Others	190 (4)
Missing	842 (19)
Zip code availability - no. (%)	
No	207 (5)
Yes	4138 (95)
Year of transplant - no. (%)	
2000	337 (8)
2001	306 (7)
2002	263 (6)
2003	334 (8)
2004	329 (8)
2005	363 (8)
2006	318 (7)

Characteristic	
2007	309 (7)
2008	301 (7)
2009	252 (6)
2010	121 (3)
2011	71 (2)
2012	73 (2)
2013	170 (4)
2014	188 (4)
2015	172 (4)
2016	137 (3)
2017	126 (3)
2018	126 (3)
2019	49 (1)
Follow-up - median (range)	120 (0-245)