Not for publication or presentation

2021 STATUS REPORT
HEALTH SERVICES AND INTERNATIONAL STUDIES WORKING COMMITTEE

Working Committee Leadership	
Co-Chair:	William Wood; University of North Carolina; william_wood@med.unc.edu
Co-Chair:	Shahrukh Hashmi; Mayo Clinic; sharukh3@gmail.com
Co-Chair:	Leslie Lehmann; Dana Farber Cancer Institute; leslie_lehmann@dfci.harvard.edu
Scientific Director:	Wael Saber; CIBMTR Statistical Center; wsaber@mcw.edu
Statistical Director:	Ruta Brazauskas; CIBMTR Statistical Center; ruta@mcw.edu
Statistician:	Naya He; CIBMTR Statistical Center; nhe@mcw.edu

INTRODUCTION

a. Minutes and overview plan from 2020 TCT meeting (Attachment 1)

PROPOSALS MOVING FORWARD FOR SCORING (click here to cast your score)

a. PROP 2010-32 Racial and ethnic differences in the utilization of CAR-T and autologous HCT for relapsed/ refractory NHL (Megan Herr/ Christine Ho/ Theresa Hahn). (Attachment 2)

b. PROP 2010-272 Gender-based differences in patients undergoing anti-CD19 CAR-T therapy for aggressive lymphomas (Khurana Arushi/ Shahrukh K. Hashmi/ Lin Yi/ N. Nora Bennani). (Attachment 3)

PROPOSALS DROPPED BECAUSE THEY OVERLAP WITH EXISTING STUDIES OR ARE NOT FEASIBLE DUE TO LIMITATIONS OF AVAILABLE PATIENTS OR DATA

a. PROP 2010-114 Racial/ethnic disparities in long-term health outcomes among survivors of allogeneic hematopoietic cell transplant (Neel S. Bhatt/ Akshay Sharma).

b. PROP 2010-268 Health services planning: Impact of allogeneic stem cell transplant center volume on survival within and outside united states: a matched cohort study (Rory M. Shallis/ Lohith Gowda/ Amer M. Zeidan/ Brian Betts).

c. PROP 2010-52 Association between racial and ethnic disparities and outcomes of high-risk acute myeloid leukemia patients receiving an allogeneic hematopoietic cell transplant (Talha Badar/ James Foran/ Mohamed Kharfan Dabaja).

PROPOSALS NOT ACCEPTED FOR CONSIDERATION AT THIS TIME DUE TO RELATIVE SCIENTIFIC IMPACT COMPARED TO ONGOING STUDIES AND/OR OTHER PROPOSALS

a. PROP 2007-02 Racial disparities in access to hematopoietic cell transplantation during COVID-19 pandemic (Zeina Al-Mansour/ Nosha Farhadfar/ John Reid Wingard).

b. PROP 2009-04 Enrollment of adolescents and young adults on blood and marrow transplant clinical trials (Seth Rotz/ Rabi Hanna/ Navneet S Majhail).

c. PROP 2009-12 Changes in international hematopoietic cell transplantation (HCT) practices since publication of choosing wisely BMT (Matthew Seftel/ Sita Bhella).

d. PROP 2010-128 Socioeconomic inequality of a community: a potential determinant for transplant outcomes (Amar Harry Kelkar/ Ellen Fraint/ Navneet S. Majhail).

e. PROP 2010-137 Health care utilization and costs of haploidentical allogeneic stem cell transplants in a contemporary cohort of pediatric patients with acute leukemia and myelodysplastic syndrome (Hemalatha Rangarajan/ Prakash Satwani).

f. PROP 2010-172 Impact of socioeconomic factors on outcomes in allogeneic transplant (Audrey M. Sigmund/ Nidhi Sharma/ Amneet K. Bajwa/ Yvonne A. Efebera/ Samantha Jaglowski).

g. PROP 2010-173 Impact of socioeconomic factors on outcomes in autologous stem cell transplant (Audrey M. Sigmund/ Amneet K. Bajwa/ Nidhi Sharma/ Yvonne A Efebera/ Samantha Jaglowski).

h. PROP 2010-182 Studying the association between neighborhood poverty and geographical distance from the CAR-T treatment center and clinical outcomes in patients with aggressive B-cell lymphoma (Mazyar Shadman/ Jordan Gauthier/ Victor Chow).

i. PROP 2010-203 Evaluation of allogeneic hematopoietic cell transplantation outcomes in underrepresented minorities in the era of haploidentical donor transplant with post-transplant cyclophosphamide (Hany Elmariah/ Taiga Nishihori/ Kedar Kirtane).

j. PROP 2010-210 Assessing top barriers to participate in transplant clinical trials for multiple myeloma patients (Ehsan Malek/ Leland Metheny).

k. PROP 2010-231 Disparity in access to allogeneic hematopoietic cell transplantation patients with AML/MDS in USA: Effect of age (Zeina Al-Mansour/ Yi Guo/ Nosha Farhadfar/ Jiang Bian/ John R. Wingard).

l. PROP 2010-249 Racial differences in outcomes in CD19 targeted chimeric antigen receptor T cell therapy (Brandon J. Blue/ Frederick Locke).

m. PROP 2010-331 Socioeconomic disparities impacting outcomes of CD-19 chimeric antigen receptor T cell therapies (Sayeef Mirza/ Lohith Gowda).

n. PROP 2010-48 Socio-economic determinants of length of stay among pediatric patients undergoing autologous hematopoietic cell transplantation for malignant diseases (Laurie Davis/ Prakash Satwani).

Due to the virtual nature of the 2021 Transplant and Cell Therapy (TCT) Meetings, the CIBMTR leadership changed the Working Committee process for this year. The details were sent previously in a broadcast email to WC members. In summary, each WC could select a maximum of 2 proposals to put forward for voting and only 10 – 15 proposals total from all WC will be presented with only 5 – 10 accepted for this coming year. Within the HSWC, we received 19 proposals. After considering feasibility, novelty, as well as impact, we chose two outstanding proposals but we recognize that several excellent proposals cannot move forward this year due to the maximum number of proposals that were permitted.

STUDIES IN PROGRESS

a. **HS16-01** Trends in utilization and outcomes of autologous and allogeneic hematopoietic cell transplantation in racial and ethnic minorities. Status: Data file preparation. Goal for June 2021: Submitted.

b. **HS16-03** Relationship of race/ethnicity and survival after single and double umbilical cord blood transplantation. Status: Data file preparation. Goal for June 2021: Manuscript preparation.

c. **HS18-01** International collaborative study to compare the prognosis for acute leukemia patients transplanted with intensified myeloablative regimens. Status: Data file preparation. Goal for June 2021: Submitted.

d. **HS18-02** Racial differences in long term survivor outcomes after allogeneic transplants. Status: Data file preparation. Goal for June 2021: Analysis.

e. **HS18-03** Racial/ethnic disparities in receipt of hematopoietic cell transplantation and subsequent resource utilization in children with acute leukemia. Status: Deferred.

f. **HS19-01** Factors associated with clinical trial participation among hematopoietic stem cell transplant patients: A CIBMTR analysis. Status: Protocol development. Goal for June 2021: Protocol development.

g. **HS20-01** Resource intensity of end-of-life care in children after hematopoietic stem cell transplant for acute leukemia: Rates and disparities. Status: Protocol development. Goal for June 2021: No hours were allocated.

PUBLICATIONS, SUBMITTED PAPERS, PRESENTATIONS

a. **HS14-01** Arnold SD, Brazauskas R, He N, Li Y, Hall M, Atsuta Y, Dalal J, Hahn T, Khera N, Bonfim C, Hashmi S, Parsons S, Wood WA, Steinberg A, Freytes CO, Dandoy CE, Marks DI, Lazarus HM, Abdel-Azim H, Bitan M, Diaz MA, Olsson RF, Gergis U, Seber A, Wirk B, LeMaistre CF, Ustun C, Duncan C, Rizzieri D, Szwajcer D, Fagioli F, Frangoul H, Knight JM, Kamble RT, Mehta P, Schears R, Satwani P, Pulsipher MA, Aplenc R, Saber W. The impact of donor type on outcomes and cost of allogeneic hematopoietic cell transplantation for pediatric leukemia: A merged Center for International Blood and Marrow Transplant Research and Pediatric Health Information System analysis. Biology of Blood and Marrow Transplantation: Journal of the American Society for Blood and Marrow Transplantation. 2020 Sep 1; 26(9):1747-1756. doi:10.1016/j.bbmt.2020.05.016. Epub 2020 May 25. PMC7518194.

b. **HS15-02** Bona K, Brazauskas R, He N, Lehmann LE, Abdel-Azim H, Ahmed I, Al-Homsi AS, Aljurf M, Arnold SD, Badawy SM, Battiwalla M, Beattie S, Bhatt NS, Dalal J, Dandoy CE, Diaz MA, Frangoul H, Freytes CO, Ganguly S, George B, Gomez-Almaguer D, Hahn T, Kamble R, Knight JM, LeMaistre CF, Law J, Lazarus HM, Majhail NS, Olsson RF, Preussler JM, Savani BN, Schears R, Seo S, Sharma A, Srivastava A, Steinberg A, Szwajcer D, Wirk B, Yoshimi A, Khera N, Wood WA, Hashmi S, Duncan C, Saber W. Neighborhood-poverty and pediatric allogeneic hematopoietic cell transplantation outcomes: A CIBMTR analysis. Blood. doi:10.1182/blood.2020006252. Epub 2020 Oct 26.

c. **HS17-01** Hong S, Brazauskas R, Hebert KM, Ganguly S, Abdel-Azim H, Diaz MA, Beattie S, Ciurea S, Szwajcer D, Badaway SM, Gratwohl A, LeMaistre C, Aljurf MDSM, Olsson RF, Bhatt NS, Farhadfar N, Yared JA, Yoshimi A, Seo S, Gergis U, Beitinjaneh AM, Sharma A, Lazarus H, Law J, Ulrickson M, Hashem H, Schoemans H, Cerny J, Rizzieri D, Savani BN, Kamble RT, Shaw BE, Khera N, Wood WA, Hashmi S, Hahn T, Lee SJ, Rizzo JD, Majhail NS, Saber W. Community health status and outcomes after allogeneic hematopoietic cell transplantation in the United States. Cancer. doi:10.1002/cncr.33232. Epub 2020 Oct 21.

d. **HS16-02** Tay J, Beattie S, Bredeson C, Brazauskas R, He N, Ahmed IA, Aljurf M, Askar M, Atsuta Y, Badawy S, Barata A, Beitinjaneh A, Bhatt N, Buchbinder D, Cerny J, Ciurea S, D'Souza A, Dalal J, Farhadfar N, Freytes C, Ganguly S, Gergis U, Gerull S, Lazarus H, Hahn T, Hong S, Inamoto Y, Khera N, Kindwall-Keller T, Kamble R, Knight J, Koleva Y, Kumar A, Kwok J, Murthy H, Olsson R, Diaz-Perez MA, Rizzieri D, Seo S, Chhabra S, Schoemans H, Schouten H, Steinberg A, Sullivan K, Szer J, Szwajcer D, Ulrickson M, Verdonck L, Wirk B, Wood W, Yared J, Saber W. Pre-transplant Marital status and Hematopoietic Cell Transplantation Outcomes. Current Oncology. doi:https://doi.org/10.3747/co.27.6327. Epub 2020 Dec.

A G E N D A
CIBMTR WORKING COMMITTEE FOR HEALTH SERVICES AND INTERNATIONAL STUDIES
Orlando, FL
Saturday, February 22, 2020, 12:15 – 2:15 PM

Co-Chair:	**Shahrukh K. Hashmi, MD, MPH, Mayo Clinic;**
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1. Introduction

a. Minutes and Overview Plan from February 2019 meeting
b. Instructions for sign-in and voting

The meeting was called to order at 12:15 pm by Dr. Nandita Khera. Dr. Khera announced that Dr. Leslie Lehmann has been appointed as the co-Chair of the Health Service and International Studies Working Committee starting March 1st. Meanwhile Dr. Khera will be completing her 5-year term as co-Chair at the end of this month. On behalf of the committee, Dr. Saber thanked Dr. Khera for her leadership and service to the committee.

Then Dr. Khera described the goals, expectations, and limitations of the committee, and she gave an introduction of the data that are collected in CRF and TED database. She also explained the voting process, role of working committee members, rules of authorship and statistical hour allocation, and importance of the conference evaluations.

2. Accrual summary

Dr. William A. Wood lead this section. Due to the full agenda, the accrual summary of registration and research cases between 2008 and 2019 were not presented to the committee but were available as part of the Working Committee attachments.

3. Presentations, published or submitted papers

a. **HS12-02** K Paulson, R Brazauskas, N Khera, N He, N Majhail, G Akpek, M Aljurf, D Buchbinder, L Burns, S Beattie, C Freytes, A Garcia, J Gajewski, T Hahn, J Knight, C LeMaistre, H Lazarus, D Szwajcer, M Seftel, B Wirk, W Wood, W Saber. Inferior Access to Allogeneic Transplant in Disadvantaged Populations: A CIBMTR Analysis. **Biology of Blood and Marrow Transplantation. 2019, June. DOI:10.1016/j.bbmt.2019.06.012**

b. **HS14-01** S D. Arnold, R Brazauskas, N He, Y Li, M Hall, Y Atsuta, J Dalal, T Hahn, N Khera, C Bonfim, S Hashmi, S Parsons, W A. Wood, A Steinberg, C O. Freytes, C Dandoy, D I. Marks, H M. Lazarus, H Abdel-Azim, M Bitan, M Angel Diaz, R F. Olsson, U Gergis, A Seber, B Wirk, C. F LeMaistre, C Ustun, C Duncan, D Rizzieri, D Szwajcer, F Fagioli, H A. Frangoul, J M. Knight, P Mehta, R Schears, P Satwani, M Pulsipher, R Aplenc, W Saber The impact of donor type on outcomes and cost of allogeneic hematopoietic cell transplant for pediatric leukemia: a merged CIBMTR and PHIS analysis. **Submitted**

c. **HS15-01** D Buchbinder, R Brazauskas, K Bo-Subait, K Ballen, S Parsons, T John, T Hahn, A Sharma, A Steinberg, A J. Kumar, A Yoshimi, B Wirk, B Shaw, C Freytes, C LeMaistre, C Bredeson, C Dandoy, D Almaguer, D I. Marks, D Szwajcer, G Hale, H Schouten, H Hashem, H Schoemans, H S. Murthy, H M. Lazarus, J Cerny, J Tay, J A. Yared, K Adekola, K R. Schultz, L Lehmann, L Burns, M Aljurf, M A Diaz, N Majhail, N Farhadfar, R Kamble, R Olsson, R Schears, S Seo, S Beattie, S Chhabra, B N. Savani, S Badawy, S Ganguly, S Ciurea, S Marino, U Gergis, Y Kuwatsuka, Y Inamoto, N Khera, S Hashmi, Wi Wood, W Saber. Predictors of Loss to Follow-Up Among Pediatric and Adult Hematopoietic Cell Transplantation Survivors: A Report from the Center for International Blood and Marrow Transplant Research. **Biology of Blood and Marrow Transplantation. 2019, November. doi: 10.1016/j.bbmt.2019.11.003.**

d. **HS16-02** J Tay, R Brazauskas, N He, S Beattie, C Bredeson, J Dalal, S K. Hashmi, T E. Hahn, N Khera, W A. Wood, W Saber, et al. Pre-transplant Marital status and Hematopoietic Cell Transplantation Outcomes. **Submitted**

e. **HS17-01** S Hong, R Brazauskas, K H. Herbert, S Ganguly, H Abdel-Azim, M Angel Diaz, S Beattie, S O. Ciurea, D Szwajcer, S M. Badawy, A A. Gratwohl, C LeMaistre, M D. S. M. Aljurf, R F. Olsson, N S. Bhatt, N Farhadfar, J A. Yared, A Yoshimi-Nöllke, S Seo, U Gergis, N Khera, S Hashmi, A M. Beitinjaneh, B Shaw, W Wood, T Hahn, S J. Lee, J. D Rizzo, N S. Majhail, W Saber. Community Health Status and Outcomes after Allogeneic Hematopoietic Cell Transplantation in the United States. **Submitted**

4. Studies in progress

a. **HS15-02** Impact of socioeconomic status on pediatric stem cell transplant outcomes (K Bona/ J Wolfe/ C Duncan/ L Lehmann) **Manuscript preparation**

b. **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) **Protocol Development**

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

d. **HS18-01** International collaborative study to compare the prognosis for acute leukemia patients transplanted with intensified myeloablative regimens (Y Arai/ Y Atsuta/ S Yano) **Protocol Development**

e. **HS18-02** Racial differences in long term survivor outcomes after allogeneic transplants (B Blue/ N Majhail) **Protocol Development**

f. **HS18-03** Racial/ethnic disparities in receipt of hematopoietic cell transplantation and subsequent resource utilization in children with acute leukemia (L Winestone/ R Aplenc/ K Getz) **Protocol Development**

5. Future/proposed studies

a. **PROP 1903-01** Access to Hematopoietic Stem Cell Transplantation in Pediatric Patients with Acute Lymphoblastic Leukemia and Acute Myeloid Leukemia (Tony H. Truong/ Wael Saber)
Dr. Truong presented this proposal. The specific aims of the study are to determine the prevalence of pediatric ALL and AML using SEER data and determine the transplant rate within the CIBMTR and evaluate factors that are associated with the likelihood of receiving HSCT. Dr. Truong explained he will use SEER data base to find out patients with indications for transplant then match the data with CIBMTR to identify people who received transplant. Regrading one question from meeting participant that if CIBMTR or SEERS has data on chemotherapy before they received transplant, Dr. Truong said this is one limitation for the registry studies. Dr. Khera also added that CIBMTR has lines of treatment for pre transplant but doesn't have very detailed data. One meeting participant pointed out that the SEER data base only covers 20% of the US population, Dr. Truong said this is also anther limitation of the study. Regrading center effect, Dr. Truong explained he will look at the region difference, donor availability based on family size and the access to transplant rate among CAR. T cell centers and non-CAR.T cell centers.

b. **PROP 1911-79** Resource Intensity of End-of-Life Care in Children After Hematopoietic Stem Cell Transplant for Acute Leukemia: Rates and Disparities (Emily E Johnston / Caitlin W. Elgarten / Lena Winestone/ Richard Aplenc)
Dr. Johnston presented this proposal. The specific aims of the study are three-fold: 1. Describe the resource utilization during the 30 days before death. 2. Determine the prevalence of patients with a resource intense phenotype in the last 30 days of life. 3. Determine the clinical and sociodemographic characteristics associated with a resource intense phenotype. Regarding discharge disposition code in PHIS data base, Dr. Johnston said in PHIS it's not very actually used but she will check it. In responding a participant questioning if PHIS data base has the date of cost to use for predicting mortality, Dr. Johnston explained that this study is not interested in prediction of mortality but tease out disparities in health care utilization. Dr. Saber added that the cost data in PHIS is reported by date. Regarding the differential utilization on relapse, Dr. Johnston said patient will be coded as relapse or no relapse for model building.
This proposal was accepted by the working committee and leadership, will be HS20-01.

c. **PROP 1911-160** Predictors of Cost of Initial Hospitalization for Pediatric Allogeneic Hematopoietic Cell Transplantation. (Hemalatha Rangarajan / Prakash Satwani)
Dr. Rangarajan presented this proposal. The specific aims of the study are two-fold: 1. To determine the cost associated with first admission for children undergoing allogeneic HCT for malignant and non-malignant diseases from 2010-2019. 2. To validate and test a predictive model of cost for the transplant admission for patients ≤ 21 years of age undergoing allogeneic HCT for malignant and non-malignant disease. Dr. Wood suggested to test center effect in the model. Dr. Rizzo questioned why only looking at index of admission rather than certain period time to build a more robust model, Dr. Satwani said it's a good idea but the challenge in real world is the they don't know the transplant rate for each center. But this study could provide data to educate people whether to get transplant. Dr. Saber questioned the risk factors in the model for predicting cost, Dr. Rangarajan explained she will use post-transplant variables such as GVHD. Dr. Khera suggested to look at the cost distribution after building the model, examine the 10% of outliers then define that as cut off for the cost.

d. **PROP 1911-215** Access to Allogeneic Hematopoietic Cell Transplant in the United States After Implementation of the Affordable Care Act (Neel S Bhatt/ Aks' cdhay Sharma/ Navneet Majhail/ Theresa Hahn)
Dr. Bhatt presented this proposal. The specific aims of the study are two-fold: 1. To assess the association between ACA Medicaid expansion and the rate of allogeneic HCT in females, racial

and ethnic minority populations and those living in high poverty areas. 2. To assess the association between ACA Medicaid expansion and the rates of uninsured patients undergoing allogeneic HCT. Dr. Khera questioned how to address other factors could influence the rate of transplant, Dr. Bhatt explained this is the limitation of the study and he can't address it yet. In response to the question that if the rate of renal transplant increased after implementation of the ACA, Dr. Bhatt replied he has looked at the oncology literature which shows transplant rate was increased but need to check solid organ transplant literature. Regrading how to catch patients diagnosed with cancer but didn't go to transplant, Dr. Bhatt replied he did think about using SEER data base before. Since SEER data base only cover 20% of US population until 2016 in some certain states so he did not use it at last. Dr. Brazauskas commented regardless policy changing, the rate of transplant keep going up. One meeting participant suggested that he can look at the population of the state as substitute data.

e. **PROP 1911-253** Impact of seasons on outcomes of allogenic hematopoietic cell transplantation (HCT) in North America (Pierre Teira)
Dr. Teira presented this proposal. The specific aim of the study is to assess the impact of the season where the HSCT is done on cumulative incidence of Relapse, aGVHD, cGVHD, NRM, EFS and OS in HSCT in North America. Dr. Truong questioned how to identify the infection was due to seasonal virus or other virus, Dr. Teira said he doesn't have the data for this. Dr. Phelan suggested to look at non-malignant patients since hospitals do the transplant in summer on purpose to avoid viral infection. Dr. Rizzo questioned how to use the result, DR. Teira replied it depends on what he finds in the outcome and it may be used for guidelines.

f. **PROP 1911-265** Assessing Top Barriers to Participate in Transplant Clinical Trials for Multiple Myeloma Patients (Ehsan Malek/ Leland Metheny)
Dr. Metheny presented this proposal. The specific aims of the study are three-fold: 1. To assess the difference in age, renal function, performance status, socioeconomic characteristics between enrolled patients on STAMINA trial and patients in CIBMTR registry. 2. To determine the percentage of patients in the CIBMTR registry who do not meet eligibility criteria for BMT CTN 0702. 3. To assess the significance of each eligibility criteria in leading to potential exclusion to BMT CTN 0702. Dr. Saber commented the CIBMTR population are not general oncology patients but patients who passed the transplant screening tests and underwent transplants and there are other factors that center could not directly control for patients to enroll into a clinical trial. Dr. Khera suggested to include all clinical trials done for multiple myeloma and compare to the whole autologous transplant patients.

g. **PROP 1912-06** Understanding the costs of cellular immunotherapy for cancer (Doug Rizzo)
Dr. Rizzo presented this proposal. The specific aims of the study are four-fold: 1. Describe costs of care within 100d of cellular immunotherapy. 2. Evaluate patient, disease and transplant characteristics that affect costs of care. 3. Determine how post transplant complications, including CRS and ICANS impact costs of care. 4. Describe site of infusion (IP or OP) and impact on costs of care. Comments received on how to get centers' engagement. Dr. Rizzo also expressed the concerns of reliability of the billing from centers. Meeting participants also suggested to collaborate with Cellular Immunotherapy for Cancer committee since they received a similar proposal, Dr. Rizzo replied happy to collaborate.

6. Dropped proposed studies

a. **PROP 1911-97** Evaluating the effect of delay in allogeneic stem cell transplantation due to donor unavailability on recipient stem cell transplantation outcomes. *Dropped due to feasibility and small sample size.*

7. Study Presentation

a. **HS15-02** Analysis result update (K Bona)

Dr. Duncan briefly updated the committee on analysis result of the study. Meeting participants suggested that Dr. Duncan could look at the cause of death for the study population and Dr. Duncan agreed. Dr. Duncan explained that 20% cut off for poverty level is based on the poverty level that people who can get support for national poverty level and there are also different ways to look at it.

Not for publication or presentation ***Attachment 1***

Working Committee Overview Plan for 2020-2021

Study number and title	Current status	Goal with date	Total hours to complete	Total hours to goal	Hours allocated to 6/30/2020	Hours allocated 7/1/2020-6/30/2021	Total Hours allocated
HS14-01: Investigating clinical outcomes and inpatient health care resource utilization of hematopoietic cell transplantation for children with acute leukemia	Submitted	Published – July 2021	10	10	10	0	10
HS15-02: Impact of Socioeconomic Status on Pediatric Stem Cell Transplant Outcomes	Submitted	Published – July 2021	20	20	10	10	20
HS16-01: Trends in Utilization and Outcomes of Autologous and Allogeneic Hematopoietic Cell Transplantation in Racial and Ethnic Minorities	Protocol Development	Submitted – July 2021	280	280	210	70	280
HS16-02: The Impact of Marital Status on Hematopoietic Stem Cell Transplant Recipient Outcomes: A surrogate for consistent caregiver	Submitted	Published – July 2020	10	10	10	0	10
HS16-03: Relationship of Race/Ethnicity and Survival after Single and Double Umbilical Cord Blood Transplantation	Protocol Development	Submitted – July 2021	250	250	180	70	250
HS17-01: Association of community health status and center survival for allogeneic hematopoietic cell transplantation	Submitted	Published – July 2020	10	10	10	0	10
HS18-01: International collaborative study to compare the prognosis for acute leukemia patients transplanted with intensified myeloablative regimens	Protocol Development	Submitted – July 2021	310	310	240	70	310
HS18-02: Racial differences in long term survivor outcomes after Allogeneic hematopoietic cell transplantation	Protocol Development	Manuscript Preparation – July 2021	310	240	100	140	240

HS18-03: Racial/ethnic disparities in receipt of hematopoietic cell transplantation and subsequent resource utilization in children with acute leukemia	Protocol Development	Analysis – July 2021	310	180	100	80	180
HS19-01: Factors associated with clinical trial participation among HSCT patients: a CIBMTR Analysis	Protocol Development	Manuscript Preparation – July 2021	330	260	0	260	260
HS20-01: Resource Intensity of End-of-Life Care in children after hematopoietic stem cell transplant for Acute Leukemia: rates and disparities	Protocol Development	Data File Preparation – July 2021	330	100	0	100	100

Oversight assignments for Working committee leadership (March 2020)

William Wood	**HS14-01:** Investigating clinical outcomes and inpatient health care resource utilization of hematopoietic cell transplantation for children with acute leukemia
	HS15-02: Impact of Socioeconomic Status on Pediatric Stem Cell Transplant Outcomes
	HS16-03: Relationship of race/ethnicity and survival after single and double umbilical cord blood transplantation
	HS17-01: Association of community health status and center survival for allogeneic hematopoietic cell transplantation
	HS19-01: Factors associated with clinical trial participation among HSCT patients: a CIBMTR Analysis
Leslie Lehmann	**HS16-01:** Trends in utilization and outcomes of autologous and allogeneic hematopoietic cell transplantation in racial and ethnic minorities
	HS16-02: The impact of marital status on hematopoietic stem cell transplant recipient outcomes: a surrogate for consistent caregiver
	HS20-01: Resource Intensity of End-of-Life Care in children after hematopoietic stem cell transplant for Acute Leukemia: rates and disparities
Shahrukh Hashmi	**HS18-01:** International collaborative study to compare the prognosis for acute leukemia patients transplanted with intensified myeloablative regimens
	HS18-02: Racial differences in long term survivor outcomes after Allogeneic hematopoietic cell transplantation
	HS18-03: Racial/ethnic disparities in receipt of hematopoietic cell transplantation and subsequent resource utilization in children with acute leukemia

Proposal: 2010-32

Title:
Racial and ethnic differences in the utilization of CAR-T and autologous HCT for relapsed/refractory NHL.

Megan Herr, PhD, Megan.Herr@RoswellPark.org, Roswell Park Comprehensive Cancer Center (Junior investigator)
Christine Ho, MD, Christine.Ho@RoswellPark.org, Roswell Park Comprehensive Cancer Center (Junior investigator)
Theresa Hahn, PhD, Theresa.Hahn@RoswellPark.org, Roswell Park Comprehensive Cancer Center

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) will describe treatment patterns of non-Hodgkin lymphoma (NHL) patients after they relapse or are refractory to an autoHCT.

Specific aims:
- Aim 1: Compare race and ethnicity rates for first autoHCT vs CAR T for relapsed/refractory NHL patients.
- Aim 2: Describe treatment patterns of NHL autoHCT patients who relapse after autoHCT (e.g. CAR T, second autoHCT, allogeneic HCT (alloHCT), other treatment, no treatment) by race and ethnicity.

Scientific impact:
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.

Scientific justification:
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.

Proposal 1911-267: Comparison of outcomes of DLBCL patients with partial response after salvage therapy who underwent CAR-T vs. ASCT.

Baseline characteristics for patients undergoing 1st commercial CAR-T prior to HCT or 1st auto-HCT for DLBCL in PR

Characteristic	CAR-T	AutoHCT
No. of patients	165	251
No. of centers	49	85
Race - no. (%)		
White	143 (87)	160 (64)
African-American	8 (5)	53 (21)
Asian	6 (4)	21 (8)
Pacific Islander	0	2 (1)
Native American	0	5 (2)
More than one race	5 (3)	5 (2)
Not reported	3 (2)	5 (2)
Ethnicity - no. (%)		
Hispanic or Latino	15 (9)	21 (8)
Non Hispanic or non-Latino	142 (86)	211 (84)
Non-resident of the U.S.	3 (2)	12 (5)
Not reported	5 (3)	7 (3)

Proposal 1911-51: CAR-T cell Therapy versus Autologous Transplant in Early Rituximab Failure Patients with Diffuse Large B-cell Lymphoma.

Baseline characteristics for patients undergoing 1st commercial CAR-T or 1st AutoHCT for DLBCL who had early frontline rituximab failure

Characteristic	CAR-T	AutoHCT
No. of patients	448	141
No. of centers	59	66
Recipient race - no. (%)		
White	383 (86)	91 (65)
African-American	21 (5)	23 (16)
Asian	17 (4)	16 (11)
Other	1 (<1)	6 (4)
More than one race	13 (3)	3 (2)
Not reported	13(3)	2 (1)
Recipient ethnicity - no. (%)		
Hispanic or Latino	48 (11)	13 (9)
Non Hispanic or non-Latino	378 (84)	116 (82)
Non-resident of the U.S.	6 (1)	11 (8)
Unknown	16 (4)	1 (1)

Patient eligibility population:

Aim 1

- Patients diagnosed with diffuse large B-cell lymphoma (DLBCL) not otherwise specified, high grade B-cell lymphoma or DLBCL arising from follicular lymphoma
- Disease status at CAR T-cell infusion or HCT: relapsed/refractory (CR2+, Rel1+, PIF)
- All ages at time of CAR T-cell infusion or HCT
- Patients who received therapy between 1/1/2017-12/31/2020

Aim 2:

- Patients who received an autoHCT for DLBCL, not otherwise specified, high grade B-cell lymphoma or DLBCL arising from follicular lymphoma
- All ages at time of autoHCT
- Patients who received their first autoHCT between 1/1/2010-12/31/2018 and relapsed or progressed after HCT between 1/1/2016 and 12/31/2019.

Data requirements:

- Information requested includes data on demographics, previous HCT, and treatments after autoHCT.
- Data on the following CIBMTR data collection forms will be needed:
  - 4000
  - 4003
  - 2000
  - 2018
  - 2118
  - 2100
  - 2402
  - 2900

Sample requirements:

None

Study design (scientific plan):

Aim 1:

Compare race and ethnicity rates for first autoHCT vs CAR T for relapsed/refractory NHL patients.

- The first aim will compare the rate of first autoHCT to CAR T by race and ethnicity. Data will be analyzed for relapsed/refractory NHL patients who received treatment (autoHCT or CAR T) from 2017-2020.
- Main results may be presented as:

		1st AutoHCT	CAR T-cell
		N=323	N=1176
Total number of patients		N (%)	N (%)
Race			
	White	202 (63)	987 (84)
	African American	70 (22)	55 (5)
	Asian	32 (10)	53 (5)
	Other	8 (3)	0
	More than one race	0	3 (0)
	Missing/Unknown	11 (4)	78 (6)
Ethnicity			
	Hispanic	29 (9)	108 (9)
	Non-Hispanic	281 (87)	1006 (86)
	N/A - Not a resident of the U.S.	3 (1)	18 (2)
	Unknown	10 (3)	44 (4)

Aim 2:

Describe treatment patterns of NHL patients who relapsed after an autologous HCT (e.g. CAR T, second autoHCT, alloHCT, other treatment, no treatment) by race and ethnicity.

- The second aim will describe therapy after an autologous HCT for NHL patients who relapsed or progressed after the autoHCT by race and ethnicity. Data will be analyzed for patients who received their first autoHCT from 2010-2018 and relapsed or progressed between 2016-2019. 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.
- Main results may be presented as:

Total number of patients		2nd AutoHCT	CAR T-cell	1st AlloHCT	Other therapy	No therapy
		N (%)	N (%)	N (%)	N (%)	N (%)
Race						
	White	N (%)	N (%)	N (%)	N (%)	N (%)
	African American	N (%)	N (%)	N (%)	N (%)	N (%)
	Asian	N (%)	N (%)	N (%)	N (%)	N (%)
	Other	N (%)	N (%)	N (%)	N (%)	N (%)
	More than one race	N (%)	N (%)	N (%)	N (%)	N (%)
	Missing					
Ethnicity						
	Hispanic	N (%)	N (%)	N (%)	N (%)	N (%)
	Non-Hispanic	N (%)	N (%)	N (%)	N (%)	N (%)
	N/A - Not a resident of the U.S.	N (%)	N (%)	N (%)	N (%)	N (%)
	Unknown	N (%)	N (%)	N (%)	N (%)	N (%)

Study details and outcome definitions are as follows:

- Retrospective cohort
- Exposure of interest: race/ethnicity
- Impact of covariates:
  - Age
  - Sex
  - HCT comorbidity index
  - Insurance
  - Disease
  - Disease status at CAR T-cell infusion or HCT
  - Number of lines of prior therapy
  - Type of product (Yescarta vs Kymriah, if possible)
  - Conditioning regimen
  - Delayed engraftment or non-engraftment

Please note: as this study is descriptive, and most of the work has been completed by generating the data tables for this proposal the statistical effort is minimal. Due to COVID and the amount of work the CIBMTR statistical team is currently under, we would be willing to conduct the analyses ourselves with oversight from the CIBMTR stats team (including sharing of SAS code and final data etc.). The analyses are simple assessments of interactions between the covariates and race/ethnicity – no outcomes will be analyzed with this proposal. Both Drs. Herr and Hahn have conducted analyses on CIBMTR data with past proposals and therefore are familiar with the intricacies of these data.

Data source:
The CIBMTR Research Database will be used in this study. No external data or data linkage will be required.

Conflicts of interest:
None

References:
1. 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.

Data 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	1176	323
No. of centers	81	79
Age at infusion, by category - no. (%)		
Median (min-max)	63 (18-91)	59 (18-79)
10-19	3 (0)	1 (0)
20-29	29 (2)	13 (4)
30-39	65 (6)	18 (6)
40-49	115 (10)	38 (12)
50-59	266 (23)	94 (29)
60-69	447 (38)	114 (35)
>= 70	251 (21)	45 (14)
Gender - no. (%)		
Male	759 (65)	216 (67)
Female	417 (35)	107 (33)
Product - no. (%)		
Kymriah	219 (19)	NA
Yescarta	957 (81)	NA
Recipient race - no. (%)		
White	987 (84)	202 (63)
African American	55 (5)	70 (22)
Asian	53 (5)	32 (10)
Pacific Islander	0	3 (1)
Native American	0	5 (2)
More than one race	3 (0)	0
Unknown	41 (3)	5 (2)
Missing	37 (3)	6 (2)
Recipient ethnicity - no. (%)		
Hispanic or Latino	108 (9)	29 (9)
Non-Hispanic or non-Latino	1006 (86)	281 (87)
N/A - Not a resident of the U.S.	18 (2)	3 (1)
Unknown	44 (4)	10 (3)
Karnofsky/Lansky performance score prior to CT - no. (%)		
90-100	445 (38)	161 (50)
<90	576 (49)	156 (48)
Missing	155 (13)	6 (2)
Sub-disease indication of DLBCL - no. (%)		
NHL diffuse, large B-cell	326 (28)	211 (65)

Characteristic	CAR-T	Auto
T-cell / histiocytic rich large B-cell lymphoma	14 (1)	20 (6)
Primary mediastinal large B-cell	35 (3)	5 (2)
Diffuse, large B-cell lymphoma- Germinal center B-cell type	404 (34)	32 (10)
Diffuse, large B-cell lymphoma- Activated B-cell type	263 (22)	35 (11)
EBV+ DLBCL	8 (1)	2 (1)
High-grade B-cell lymphoma, NOS	15 (1)	1 (0)
High-grade B-cell lymphoma, with MYC and BCL2 and/or BCL6 rearrangements	111 (9)	17 (5)
Disease status prior to CT - no. (%)		
CR2 +	32 (3)	169 (52)
< CR, chemosensit	232 (20)	135 (42)
< CR, chemoresist	912 (78)	18 (6)
Missing		1 (0)
Types of prior HCTs - no. (%)		NA
No prior HCT	810 (69)	
Prior allo-HCT(s)	18 (2)	
Prior auto-HCT(s)	324 (28)	
Prior auto and allo-HCT(s)	7 (1)	
Missing	17 (1)	
Year of CT or Transplant - no. (%)		
2016	0	102 (32)
2017	5 (0)	75 (23)
2018	453 (39)	85 (26)
2019	718 (61)	61 (19)

Data 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	243	4	376
No. of centers	91	4	73
Age at HCT - no. (%)			
Median (min-max)	55 (3-75)	62 (61-72)	62 (22-82)
< 10	1 (0)	0 (0)	0 (0)
10-19	6 (2)	0 (0)	0 (0)
20-29	14 (6)	0 (0)	3 (1)
30-39	15 (6)	0 (0)	23 (6)
40-49	56 (23)	0 (0)	35 (9)
50-59	88 (36)	0 (0)	92 (24)
60-69	57 (23)	3 (75)	157 (42)
>= 70	6 (2)	1 (25)	66 (18)

Characteristic	1st AlloHCT	2nd AutoHCT	CAR T-cell
Recipient sex - no. (%)			
Male	164 (67)	3 (75)	247 (66)
Female	79 (33)	1 (25)	129 (34)
Karnofsky/Lansky performance score prior to HCT/CT - no. (%)			
90-100	163 (67)	2 (50)	158 (42)
80	54 (22)	1 (25)	105 (28)
<80	18 (7)	1 (25)	53 (14)
Missing	8 (3)	0 (0)	60 (16)
Race - no. (%)			
White	180 (74)	2 (50)	325 (86)
Black or African-American	22 (9)	1 (25)	17 (5)
Asian	11 (5)	0 (0)	16 (4)
Native Hawaiian or other Pacific Islander	1 (0)	0 (0)	0 (0)
American Indian or Alaska Native	1 (0)	0 (0)	0 (0)
Other	1 (0)	0 (0)	0 (0)
Missing	27 (11)	1 (25)	18(4)
Ethnicity - no. (%)			
Hispanic or Latino	24 (10)	0 (0)	25 (7)
Not Hispanic or Latino	189 (78)	3 (75)	325 (86)
Non-resident of the U.S.	27 (11)	1 (25)	9 (2)
Missing	3 (1)	0 (0)	17(4)
Year of HCT - no. (%)			
2016	120 (49)	1 (25)	0(0)
2017	79 (33)	2 (50)	4 (1)
2018	40 (16)	1 (25)	157 (42)
2019	4 (2)	0 (0)	215 (57)

Proposal: 2010-272

Title:
Assessing sex and race-based disparities in response and toxicities of Anti CD19 CAR-T therapy in aggressive lymphomas.

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Research hypothesis:
No studies have explored possible differences in the outcomes and incidence of toxicities related to CAR-T therapy based on sex and racial groups. Many lines of evidence describes differences in immune responses between women and men, higher incidence of autoimmune disorders in women and the effect of sex hormones on the immune system.[1-7] Women mount a more vigorous antibody- and cell-mediated immune responses than men following either infection or vaccination. Estradiol is associated with upregulation of CD4 T cells and dendritic cells, increased survival of autoreactive B cells, and decreased tumor necrosis factor production. Another possible mechanism may lie in the immunosuppressive properties of androgens: a recent study showed that androgen-deprivation therapy allows male mice to mount a more robust immune response, and in humans, genes associated with poor virus-response are up-regulated by androgens.[8] Also men presenting with high serum androgen levels display the weakest influenza immune responses.[9] In addition, association of CAR-T specific toxicities with response to therapy remains unclear. Race based differences also exist, with African Americans presenting with diffuse large B-cell lymphoma at a much younger age, with more advanced stage disease, B-symptoms and poorer overall survival compared to Caucasians.
Therefore, we aim to study the gender-based differences in patients undergoing Anti-CD19 CAR-T therapy for aggressive lymphomas and their potential link with response in patients.

Specific aims:
- Identify sex and race based differences in response to CD19 CAR-T in aggressive lymphomas
- Identify sex and race based differences in CAR-T therapy toxicities

Scientific impact:
Pivotal clinical trials that led to the approval of two Anti-CD19 CAR-T products for the treatment of aggressive B-cell Non-Hodgkin lymphoma did not specify the outcomes or toxicities based on gender. There is ample evidence to suggest immunological and pharmacokinetic differences based on gender. Dosing both men and women with the same exact dose of an immunological therapy without consideration of these differences can impact outcomes and needs to be addressed. This clinical data will help design future studies which will take into account these differences and collect information to decipher the reasons underneath.

Scientific justification:
Epidemiologic studies suggest that the sex difference in DLBCL is more pronounced when premenopausal women are compared with men of the same age.[10] While examining global transcriptome DLBCL data from The Cancer Genome Atlas, female sex was associated with decreased interferon signaling, transcription, cell cycle, and PD-1 signaling, and JUN and CYCX signaling were the

most critical factors associated with tumor progression in older and male patients.[11] The sex-specific differences in elderly patients with DLBCL appear to have increased with the introduction of the monoclonal CD20 antibody rituximab into the therapeutic armamentarium as seen in the RICOVER-60 study.[12] Several clinical trials since then have tried to optimize the rituximab dosing and timing to improve on the outcomes of patients.[14-16] Solid tumor studies with immune checkpoint inhibitors also suggest differences in the response and toxicities based on gender. Data remains scarce in lymphoma especially with cellular therapy.

Patient eligibility population:

- Age 18 or older
- Received regulatory approved CAR-T: axicabtagene ciloleucel or tisagenlecleucel

Data requirements: Forms 4000 V4, 4003 V1, 4006 V2 and 4100 V3

Patient related	**Disease related**	**Outcomes**	**Toxicity**
Date of birth Date of diagnosis Date of CAR-T infusion Gender Ethnicity Race Prior co-morbidities Name of the product (Treated with regulatory approved CAR-T) - functional status – karnofsky prior to CAR-T -specify coexisiting disease or organ impairment prior to cellular therapy	-Lymphoma histology (at diagnosis) -Cytogenetics FISH – bcl2, bcl6, myc re-arrangements, amplification -date of transformation (if transformed lymphoma) -Stage -Extranodal involvement -B-symptoms -LDH -IPI -Bone marrow involvement -Prior HCT -Specify HSC source -Date of prior HCT -Prior lines of therapy -Intrathecal therapy -Intraocular therapy -Radiation -did recipient achieve a CR after 1st line of therapy -was the disease status assessed by	-Date of contact to determine last status -Recipients' survival status at last contact -What was the **best response** to cellular therapy, date of best response established -**Peripheral blood count recovery:** was there evidence of initial recovery, date of ANC > 500/mm^3, date of platelets >20x10^9 -was a disease relapse or progression detected? Date documented. -Did a **new malignancy,** myelodysplasia/myeloproliferative or lymphoproliferative disorder occur that is different from the disease for which cellular therapy was performed	-did the recipient develop: date of CRS diagnosis, was therapy given, specify therapy given for CRS -**CRS symptoms**, **fever:** date of onset; **hypotension:** date of onset, intravenous fluids, vasopressors, other therapy, date of resolution of CRS; **hypoxia** requiring supplemental oxygen > fiO2 40%, date of onset, ventilator support -**Neurotoxicity:** date of onset, cognitive assessment, which assessment, lowest score, depressed level of consciousness, most severe level, seizure, cerebral edema, hemiparesis, cerebral vascular event, did neurotoxicity resolve, date of resolution, was therapy given, specify the therapy -**Other toxicities Hypogammaglobulinemia**: date of onset previously reported, did it resolve, replacement therapy; **Tumor lysis syndrome:** date of onset, grade, did it resolve

	radiological assessment prior to CAR-T – date, was disease detected - was the disease status assessed by clinical/hematologic assessment prior to CAR-T – date, was disease detected -recipient's Disease status immediately prior to CAR-T -Systemic therapy prior to CAR-T – was lymphodepleting therapy given?, drugs? Date started		**-Other grade 3,4 organ toxicity:** date of onset, resolution specify organ **-specify maximum Lab results:** total serum ferritin, C-reactive protein **-Infection:** Did the recipient develop a clinically significant infection, organism, site, date of diagnosis,

Sample requirements:
No samples are required from the NMDP repository

Study design:
Aim 1: Identify sex and race-based differences in response to CD19 CAR-T in aggressive lymphomas

- Primary endpoint: best response complete remission (CR) rate
- Secondary endpoint: best response overall response rate (ORR), progression-Free survival (PFS), and overall survival (OS)

Definitions:

- *Best response CR Rate:* percentage of patients who had a complete response at any point after infusion of CAR-T
- *Best response ORR:* calculated as the percentage of patients who had a complete or partial response
- *OS:* Date of cellular therapy infusion to death from any cause
- *PFS:* Date of cellular therapy infusion to progression/relapse or death from any cause.
- Analysis: Kaplan Meier curves and Cox models will be used to compare PFS and OS outcomes between sex and race. Between patient cohorts, categorical variables will be compared by the χ^2 or Fisher's exact test.

Aim 2: Identify sex and race-based differences in toxicities associated with CD19 CAR-T in aggressive lymphomas

- Primary endpoint: rate of severe CRS, rate of severe ICANS
- Secondary endpoint: Rate of tocilizumab use, rate of steroid use, other AE including cytopenias, time to hematological recovery, hypogammaglobulinemia, infections, any other grade 3-4 organ toxicities.

Definitions:

- Severe CRS: defined as those that required vasopressor, CPAP/BiPAP/intubation, and high O2 supplementation.
- Severe ICANS: defined as those that received intervention (including steroid, tocilizumab, intubation), or seizure, cerebral edema

Analysis:

CRS and neurotoxicity rates – will be calculated as percentage of patients who developed these toxicities removing any patients who are deceased prior to 7 days post infusion. In addition specific interventions such as use of vasopressor, tocilizumab, steroids, intubation or high O2 supplementation will be captured as categorical variables. Based on the interventions listed CRS will be graded based on ASTCT grading when possible. Inflammatory markers as correlates of toxicities, such as ferritin and CRP when available will be obtained.

Comparison between sex and race-based groups will be done (categorical variables will be compared by the χ^2 or Fisher's exact test, and the Student t-test will be used to compare continuous variables). The nonparametric independent samples median test will be used to compare median values between 2 groups when appropriate. We will assess co-variates to make sure the groups are balanced. Age/decade matched analysis will be considered to evaluate potential differences between pre/post-menopausal women, and old vs. young (<60 years) males. Comparisons in the responses and toxicities will also be made based on both race and sex eg. Caucasian male vs. Caucasian female etc.

To avoid confounding factors from different CAR-T products, we will also perform these analyses for patients who received axi-cel or tisa-cel separately for gender based differences. As CART product selection consideration for each patient is variable among providers and institutions, we will not compare outcomes between axi-cel and tisa-cel.

Non-CIBMTR data source:

No external data source needed

Conflicts of interest:

- Yi Lin: research funding from Janssen, Kite/Gilead, Celgene, BlueBird Bio; consultancy with Kite/Gilead, Novartis, Janssen, Legend Biotech, BlueBird Bio, Celgene, JUNO, AlloGene, Gamida Cells. DSMB: Sorrento. Steering Committee: Legend Biotech, Janssen, Celgene. All funds paid to Mayo, no personal compensation.
- Nora Bennani: Advisory board activity with Verastem, Daiishi Sankyo Inc .All funds paid to Mayo, no personal compensation

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Characteristic of adult patients(age≥18) who received first commercial CAR-T therapy for DLBCL reported to CIBMTR

Characteristic	Male	Female
No. of patients	811	442
No. of centers	82	71
Age at infusion, by category - no. (%)		
Median (min-max)	62.65 (18.45-90.82)	62.44 (19.56-86.01)
10-19	2 (0)	1 (0)
20-29	20 (2)	9 (2)
30-39	46 (6)	26 (6)
40-49	78 (10)	45 (10)
50-59	188 (23)	98 (22)
60-69	303 (37)	166 (38)
≥ 70	174 (21)	97 (22)
Product - no. (%)		
Kymriah	146 (18)	92 (21)
Yescarta	665 (82)	350 (79)
Recipient race - no. (%)		
White	692 (85)	360 (81)
African American	35 (4)	24 (5)
Asian	30 (4)	26 (6)
More than one race	2 (0)	1 (0)
Unknown	27 (3)	15 (3)
Missing	25 (3)	16 (4)
Recipient ethnicity - no. (%)		
Hispanic or Latino	76 (9)	41 (9)
Non-Hispanic or non-Latino	696 (86)	371 (84)
N/A - Not a resident of the U.S.	13 (2)	10 (2)
Unknown	24 (3)	20 (5)
Missing	2 (0)	0
Country - no. (%)		
US	808 (100)	441 (100)
Other	3 (0)	1 (0)
Karnofsky/Lansky performance score prior to CT - no. (%)		
90-100	320 (39)	164 (37)
80	240 (30)	133 (30)
< 80	138 (17)	97 (22)
Missing	113 (14)	48 (11)
Sub-disease indication of DLBCL - no. (%)		

Characteristic	Male	Female
NHL diffuse, large B-cell	222 (27)	130 (29)
T-cell / histiocytic rich large B-cell lymphoma	15 (2)	2 (0)
Primary mediastinal large B-cell	16 (2)	22 (5)
Diffuse, large B-cell lymphoma- Germinal center B-cell type	282 (35)	145 (33)
Diffuse, large B-cell lymphoma- Activated B-cell type	184 (23)	95 (21)
EBV+ DLBCL, NOS	6 (1)	2 (0)
High-grade B-cell lymphoma, NOS	9 (1)	7 (2)
High-grade B-cell lymphoma, with MYC and BCL2 and/or BCL6 rearrangements	77 (9)	39 (9)
Disease transformation at diagnosis - no. (%)		
No transformation	576 (71)	316 (71)
Transformation from CLL	17 (2)	10 (2)
Transformation from a different lymphoma histology	218 (27)	115 (26)
Missing	0	1 (0)
Disease status prior to CT - no. (%)		
CR1	8 (1)	0
CR2 +	20 (2)	12 (3)
< CR, chemosensit	152 (19)	81 (18)
< CR, chemoresist	590 (73)	325 (74)
Unknown	25 (3)	15 (3)
Missing	16 (2)	9 (2)
Types of prior HCTs - no. (%)		
No prior HCT	541 (67)	310 (70)
Prior allo-HCT(s)	14 (2)	6 (1)
Prior auto-HCT(s)	236 (29)	121 (27)
Prior auto and allo-HCT(s)	4 (0)	3 (1)
Missing	16 (2)	2 (0)
Year of CT - no. (%)		
2017	1 (0)	4 (1)
2018	316 (39)	165 (37)
2019	494 (61)	273 (62)
Follow-up - median (min-max)	11.35 (0.89-26.97)	11.45 (0.95-27.93)