Not for publication or presentation

CIBMTR®
CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH

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;**
	Telephone: 507-284-3417; E-mail: hashmi.shahrukh@mayo.edu
Co-Chair:	**Nandita Khera, MD, Mayo Clinic Arizona, Phoenix, AZ;**
	Telephone: 480-342-0195; Email: khera.nandita@mayo.edu
Co-Chair:	**William A. Wood, MD, MPH, University of North Carolina, Chapel Hill, NC;**
	Telephone: 919-843-6517; E-mail: william_wood@med.unc.edu
Scientific Director:	**Wael Saber, MD, MS, CIBMTR Statistical Center;**
	Telephone: 414-805-0677; Email: wsaber@mcw.edu
Statistical Director:	**Ruta Brazauskas, PhD, CIBMTR Statistical Center;**
	Telephone: 414-955-8687; E-mail: ruta@mcw.edu
Statistician:	**Naya He, MPH, CIBMTR Statistical Center;**
	Telephone: 414-805-0685; E-mail: nhe@mcw.edu

---

1. **Introduction**
   a. Minutes and Overview Plan from February 2019 meeting (Attachment 1)
   b. Instructions for sign-in and voting

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

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 (Attachment 3)

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) (Attachment 4)

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) (Attachment 5)

c. **PROP 1911-160** Predictors of Cost of Initial Hospitalization for Pediatric Allogeneic Hematopoietic Cell Transplantation. (Hemalatha Rangarajan / Prakash Satwani) (Attachment 6)

d. **PROP 1911-215** Access to Allogeneic Hematopoietic Cell Transplant in the United States After Implementation of the Affordable Care Act (Neel S Bhatt/ Akshay Sharma/ Navneet Majhail/ Theresa Hahn) (Attachment 7)

e. **PROP 1911-253** Impact of seasons on outcomes of allogenic hematopoietic cell transplantation (HCT) in North America (Pierre Teira) (Attachment 8)

f. **PROP 1911-265** Assessing Top Barriers to Participate in Transplant Clinical Trials for Multiple Myeloma Patients (Ehsan Malek/ Leland, Metheny) (Attachment 9)

g. **PROP 1912-06** Understanding the costs of cellular immunotherapy for cancer (Doug Rizzo) (Attachment 10)

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

1. HS15-02 Analysis result update (K Bona)

MINUTES AND OVERVIEW PLAN

CIBMTR WORKING COMMITTEE FOR HEALTH SERVICES AND INTERNATIONAL STUDIES
Houston, TX
Thursday, February 21, 2019, 2:45 – 4:45 PM

Co-Chair:	**Shahrukh K. Hashmi, MD, MPH, Mayo Clinic;**
	Telephone: 507-284-3417; E-mail: hashmi.shahrukh@mayo.edu
Co-Chair:	**Nandita Khera, MD, Mayo Clinic Arizona, Phoenix, AZ;**
	Telephone: 480-342-0195; Email: khera.nandita@mayo.edu
Co-Chair:	**William A. Wood, MD, MPH, University of North Carolina, Chapel Hill, NC;**
	Telephone: 919-843-6517; E-mail: william_wood@med.unc.edu
Scientific Director:	**Wael Saber, MD, MS, CIBMTR Statistical Center;**
	Telephone: 414-805-0677; Email: wsaber@mcw.edu
Statistical Director:	**Ruta Brazauskas, PhD, CIBMTR Statistical Center;**
	Telephone: 414-955-8687; E-mail: ruta@mcw.edu
Statistician:	**Naya He, MPH, CIBMTR Statistical Center;**
	Telephone: 414-805-0685; E-mail: nhe@mcw.edu

---

1. Introduction

a. Minutes and Overview Plan from February 2018 meeting (Attachment 1)
b. Instructions for sign-in and voting

The meeting was called to order at 2:45pm by Dr. Nandita Khera. She 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.

Dr. Wael Saber then gave an introduction on center specific analysis research task force and encouraged audiences to submit proposals at TCT 2020.

2. Accrual summary (Attachment 2)

Due to the full agenda, the accrual summary of registration and research cases between 2008 and 2018 were not presented to the committee but were available as part of the Working Committee attachments.

3. Presentations, published or submitted papers

Due to the full agenda, the 2018 presentations and published papers were mentioned, but not presented. One paper was submitted, 2 oral presentations and 2 poster presentations.

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. **Submitted**

b. **HS15-01** D K. Buchbinder, R Brazauskas, K Bo-Subait, K K. Ballen, T E. Hahn, T D John, S K Parsons, S K. Hashmi, N Khera, W A. Wood, W Saber**.** Lost to Follow-up Rates Are Higher in Pediatric Than Adult Survivors, but Not By Transplant Type: A Report from the Center for International Blood and Marrow

Transplant Research. **Poster presentation at ASH in San Diego, CA, December 2018**

c. **HS15-02** K O Bona, R Brazauskas, N He, L E. Lehmann, J Wolfe, J Dalal, S K. Hashmi, T E. Hahn, N Khera, W A. Wood, C Duncan, W Saber. Area-Based Socioeconomic Status and Pediatric Allogeneic Hematopoietic Stem Cell Transplantation Outcomes: A CIBMTR Analysis. **Oral presentation at ASH in San Diego, CA, December 2018**

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. The Impact of Marital Status on Hematopoietic Stem Cell Transplant (HCT) Recipient Outcomes: A Surrogate for Consistent Caregiver. a CIBMTR Registry Study. **Poster presentation at ASH in San Diego, CA, December 2018**

e. **HS17-01** S Hong, R Brazauskas, K Herbert, T E. Hahn, N S. Majhail, S J. Lee, D Rizzo, S K. Hashmi, N Khera, W A. Wood, W Saber. Community Health Status and Its Association with Patient Outcome Post Allogeneic Hematopoietic Cell Transplantation. **Oral presentation at TCT in Houston, TX, February 2019**

4. Studies in progress (Attachment 3)

The progress of the ongoing studies during the past year was not presented in order to provide reasonable time to the new proposals for presentation and discussion. A summary of the progress was provided as an attachment to the committee members.

a. **HS14-01** Investigating clinical outcomes and inpatient health care resource utilization of hematopoietic cell transplantation for children with acute leukemia (S Arnold/ R Aplenc/M Pulsipher/P Satwani) **Manuscript preparation**

b. **HS15-01** Who is lost to follow-up in the Center for International Blood and Marrow Transplant Research (CIBMTR) registry? (D Buchbinder/T Hahn/K Ballen/ W Saber/ S Parsons) **Manuscript preparation**

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

d. **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**

e. **HS16-02:** The Impact of Marital Status on Hematopoietic Stem Cell Transplant Recipient Outcomes: A surrogate for consistent caregiver (S M Beattie/ J Tay/ C Bredeson) **Manuscript preparation**

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

g. **HS17-01** Association of community health status and center survival for allogeneic hematopoietic cell transplantation (S Hong/ N Singh Majhail) **Datafile preparation**

5. Future/proposed studies

Dr. Shahrukh K. Hashmi led this section.

a. **PROP 1811-02** Outcomes of autologous stem cell transplantation for patients with multiple myeloma from rural America (Siddhartha Ganguly) (Attachment 7)

Dr. Ganguly presented this study. The specific aims of this study are two-fold: 1. Determine if there are differences in receiving AHCT in Rural patients versus Urban patients with multiple myeloma. 2. Determine if there are differences in outcomes based on residence. Comment received on the definition of “rural America” which should be more specific.

b. **PROP 1811-10** Relative mortality risk in AYA vs younger and older survivors of allogeneic HCT for acute leukemia (Seth Rotz/ Rabi Hanna/ Navneet Majhail) (Attachment 8)
Dr. Rotz presented this study. The specific aims of this study are three-fold: 1. Determine if AYA (age 14-29 at transplant) leukemia patients who are alive and in remission 1yr post-alloHCT will have increased relative risk of mortality compared to the general US population. 2. Determine if the relative risk of mortality compared to the general US population for AYA leukemia patients who are alive and in remission 1yr post-alloHCT is greater than the RR for children age <14, or adults age 30-49. 3. Determine if the risk of late death in AYA survivors is associated with gender and measures of socioeconomic status at the time of HCT. Comment received on if relative risk of mortality AYA population compared to general population is already been studied by other studies. Dr. Rotz replied that there was a CIBMTR study focusing on the whole population survival rate but no age group.

c. **PROP 1811-53** Factors associated with clinical trial participation among HSCT patients: a CIBMTR Analysis (Tamryn Gray, Areej El-Jawahri) (Attachment 9)
Dr. Gray presented this study. The specific aims of this study are three-fold: 1. To describe rates of clinical trial participation based on HCT type. 2. To identify factors that are associated with clinical trial participation in patients with undergoing HCT. 3. To examine the association between clinical trial participation and overall survival (OS) and non-relapse mortality (NRM) in autologous and allogeneic HCT recipients. Comments received on the definition of clinical trial participation. Dr. Gray said the study will include patients participate in clinical trials before transplant based on the forms designed and will not include patients who are go to clinical trials for maintenance. Regarding the center effect Dr. Gray said she can't get the clinical sites' information but she could do sensitivity analysis and patients' zip code will be very informative as well. In response to a question from participant about examine the difference between younger population and adult population, Dr Gray clarified this study will only focus on adult patients because of the different decision-making process between these two groups on participating a clinical trial. In responding to one audience questioning on the disease characteristic of clinical trail participants Dr. Gray said she will look at disease status for each disease. This proposal was accepted by the working committee and leadership, will be HS19-01.

d. **PROP 1811-114** Incidence and Predictors of Post-Transplant Emotional Distress in Patients Undergoing Hematopoietic Cell Transplant (Neel Bhatt/ Heather Tecca/ Aksha Sharma/ Bronwen E. Shaw) (Attachment 10)
Dr. Bhatt presented this study. The specific aims of this study are two-fold: 1. To study the cumulative incidence and predictors of post-transplant emotional distress. 2. To study the association of post-HCT emotional distress at day 100 with total number of inpatient days (in first 100 days), cGVHD (at 1-year), infections (up to 1-year) and overall survival (1-year). Comments received on current CIBMTR forms are lack of anxiety and PSTD information for pre-transplant. Dr. Bhatt said he will not exclude pre-transplant depression patients. One meeting participant expressed concern regarding the data quality of emotional distress questions and how to define these variables. Dr. Saber raised concerns about how to deal with patients who died early before the endpoint. Dr. Bhatt said would treat them as competing risk.

e. **PROP 1811-130** Socioeconomic factors and their impact on non-relapse mortality, GVHD and GVHD survival among patients who received an allogeneic transplant for AML (James Martin/ Henry Fung) (Attachment 11)
Dr. Martin presented this study. The purpose of this study is to determine which socioeconomic variables, if any, impact NRM and acute/chronic GVHD among adult patients with AML who undergo allogeneic hematopoietic stem cell transplant (alloHSCT) while in first or second complete remission (CR1 or CR2). Dr. Khera suggested using data after 2008 since patients' zip code are more complete since then.

Dropped proposed studies

a. **PROP 1811-15** Comparison of specific ethnic population (Pakistan) with western population for GVHD outcomes. *Dropped due to feasibility.*
b. **PROP 1811-44** 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.*
c. **PROP 1811-84** Evaluation of Factors that Contribute to Cancellation or Delay of planned Hematopoietic Stem Cell Transplantation (HSCT). *Dropped due to feasibility and small sample size*.
d. **PROP 1811-87** Variations in the use of myeloablative versus reduced intensity conditioning in different countries among patients more than 50 years of age using the CIBMTR database. *Dropped due to low scientific impact.*
e. **PROP 1811-149** Cost Effective Analysis of Allogeneic bone marrow transplantation with cyclophosphamide–total body irradiation versus Bulsulphan–cyclophosphamide conditioning regimens. *Dropped due to feasibility.*
f. **PROP 1811-177** Predictors of Cost of Initial Hospitalization for Pediatric Allogeneic Hematopoietic Cell Transplantation. *Dropped due to overlapped with previous studies.*

6. CIBMTR strategic initiative: Fostering international collaboration

Dr. Wood led this section. Dr. Pasquini gave a brief introduction of CIBMTR international program and three international studies which were presented later.

a. **PROP 1811-31** Haploidentical stem cell transplantation for malignant and non-malignant hematological diseases in patients without sibling donor: a multicenter prospective longitudinal study of the Brazilian bone marrow transplantation study group (Nelson Hamerschlak/ Mariana Kerbauy/ Anrezea Riberio) (Attachment 4)
   Dr. Kerbauy presented this study. The specific aims of this study are two-fold: 1. 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. 2. Compare the 1year incidences of Acute GVHD (grades II-IV, and III-IV), Chronic GVHD (NIH moderate to severe), Non-relapse-related Mortality, Disease Relapse (only Arm 1), time to Neutrophil engraftment, time to Platelet Engraftment and Event-free survival between recipients of Haplo plus Post-CY and of matched related and unrelated donors. Comments received about the process of Brazilian centers report to CIBMTR and data quality control. Dr. Pasquini also explained the challenges that Brazil transplant centers faced: 1) Data manager is not a part of transplant program recognized by the government. Hospitals can't directly hire data manager. 2) People in Brazil don't speak English but FormsNet is only in English. Dr. Saber suggested comparing Brazil Haplo patients to other countries in the future when data is complete. Other discussions are about explaining Brazilian health care system and how this study can improve Brazilian transplant program.
b. **PROP 1811-116** 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), Program Nacional de Apoio à Atenção Oncológica (Pronon), and CIBMTR (Adriana Seber/ Nelson Hamerschlak/ Mary Flowers/ Marcelo Pasquini) (Attachment 5)
   Dr. Seber presented this study. The specific aims of this study are two-fold: 1. Compare 1-year overall survival after allogeneic HCT performed in Brazil from URD, Haplo and MSD. 2. 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. Comment received on how the study itself funded. One participant suggested to include as many transplant centers as possible.

c. **PROP 1811-32** Comparing outcomes of myeloablative T-replete haploidentical transplantation with PT-CY protocol and ATG+G-CSF Protocol in patients with cytogenetic intermediate/high risk acute myeloid leukemia in first complete remission (Xiao-Jun Huang) (Attachment 6)
Dr. Huang presented this study. The purpose of this study is to compare post-transplant outcomes in adult patients with int/high risk AML in CR1 undergoing T-replete haplo-HCT with PT-CY versus ATG+G-CSF. Regarding the graft type in the population of Peking University, Dr. Huang said in recent 2 years for Haplo was PB only but mixed grafts before that. Regarding adjust age group difference, Dr. Huang said he will do a subgroup analysis.

7. Other Business

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

Working Committee Overview Plan for 2019-20

Study number and title	Current status	Goal with date	Total hours to complete	Total hours to goal	Hours allocated to 6/30/2019	Hours allocated 7/1/2019-6/30/2020	Total Hours allocated
HS14-01 Investigating clinical outcomes and inpatient health care resource utilization of hematopoietic cell transplantation for children with acute leukemia	Manuscript Preparation	Submitted – July 2019	10	10	10	10	20
HS15-01 Who is lost to follow-up in the Center for International Blood and Marrow Transplant Research (CIBMTR) registry?	Manuscript Preparation	Submitted – July 2019	50	50	50	10	60
HS15-02 Impact of Socioeconomic Status on Pediatric Stem Cell Transplant Outcomes	Manuscript Preparation	Submitted – July 2019	70	70	70	10	80
HS16-01 Trends in Utilization and Outcomes of Autologous and Allogeneic Hematopoietic Cell Transplantation in Racial and Ethnic Minorities	Protocol Development	Data File Preparation – July 2019	280	30	30	180	210
HS16-02 The Impact of Marital Status on Hematopoietic Stem Cell Transplant Recipient Outcomes: A surrogate for consistent caregiver	Manuscript Preparation	Submitted – July 2019	70	70	70	10	80
HS16-03 Relationship of Race/Ethnicity and Survival after Single and Double Umbilical Cord Blood Transplantation	Protocol Development	Analysis– July 2019	280	130	130	150	280
HS17-01 Association of community health status and center survival for allogeneic hematopoietic cell transplantation	Analysis	Submitted – July 2019	100	100	100	10	110
HS18-01 International collaborative study to compare the prognosis for acute leukemia patients transplanted with intensified myeloablative regimens	Draft Protocol Received	Manuscript Preparation – July 2020	310	240	0	240	240

HS18-02 Racial differences in long term survivor outcomes after Allogeneic hematopoietic cell transplantation	Draft Protocol Received	Analysis– July 2020	310	160	0	160	160
HS18-03 Racial/ethnic disparities in receipt of hematopoietic cell transplantation and subsequent resource utilization in children with acute leukemia	Draft Protocol Received	Data File Preparation – July 2020	310	100	0	100	100

Oversight Assignments for Working Committee Leadership (March 2019)	
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
Nandita Khera	**HS15-01** Who is lost to follow-up in the Center for International Blood and Marrow Transplant Research (CIBMTR) registry?
	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
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

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	244367	104180
No. of centers	640	566
Age at transplant, years - no. (%)		
Median (min-max)	36.9 (0-87.8)	32.7 (0-87.8)
0-9	34812 (14.2)	17800 (17.1)
10-19	31263 (12.8)	15344 (14.7)
20-29	32312 (13.2)	14870 (14.3)
30-39	35654 (14.6)	15725 (15.1)
40-49	40087 (16.4)	15814 (15.2)
50-59	39028 (16)	13487 (12.9)
60-69	27094 (11.1)	9444 (9.1)
70+	4117 (1.7)	1696 (1.6)
Recipient gender - no. (%)		
Male	143093 (58.6)	61195 (58.7)
Female	101274 (41.4)	42985 (41.3)
Recipient race - no. (%)		
Caucasian	164592 (67.4)	82730 (79.4)
African-American	11461 (4.7)	6023 (5.8)
Asian	18105 (7.4)	8081 (7.8)
Pacific islander	501 (0.2)	233 (0.2)
Native American	785 (0.3)	389 (0.4)
Other	8347 (3.4)	3927 (3.8)
Unknown	40576 (16.6)	2797 (2.7)
Disease - no. (%)		
Acute myelogenous leukemia	77315 (31.6)	29166 (28)
Acute lymphoblastic leukemia	41925 (17.2)	17206 (16.5)
Other leukemia	6100 (2.5)	2275 (2.2)
Chronic myelogenous leukemia	28966 (11.9)	14715 (14.1)
Myelodysplastic/myeloproliferative disorders	29471 (12.1)	13282 (12.7)
Other acute leukemia	2732 (1.1)	987 (0.9)
Non-Hodgkin lymphoma	16366 (6.7)	5945 (5.7)
Hodgkin lymphoma	1572 (0.6)	585 (0.6)
Plasma cell disorder/Multiple Myeloma	3263 (1.3)	1335 (1.3)
Other Malignancies	1173 (0.5)	500 (0.5)
Breast Cancer	179 (0.1)	90 (0.1)
Severe aplastic anemia	14002 (5.7)	7220 (6.9)
Inherited abnormalities erythrocyte differentiation or function	9982 (4.1)	5255 (5)

Characteristic	TED N (%)	CRF N (%)
SCID and other immune system disorders	6236 (2.6)	3103 (3)
Inherited abnormalities of platelets	212 (0.1)	106 (0.1)
Inherited disorders of metabolism	2686 (1.1)	1533 (1.5)
Histiocytic disorders	1654 (0.7)	741 (0.7)
Autoimmune Diseases	120 (0)	45 (0)
Other diseases	413 (0.2)	91 (0.1)
Year of transplant - no. (%)		
<1985	4876 (2)	4486 (4.3)
1985-1989	10451 (4.3)	9325 (9)
1990-1994	22628 (9.3)	14566 (14)
1995-1999	35549 (14.5)	16562 (15.9)
2000-2004	40230 (16.5)	16771 (16.1)
2005-2009	39805 (16.3)	17646 (16.9)
2010-2014	46728 (19.1)	11084 (10.6)
2015-2019	44100 (18)	13740 (13.2)
Education - no. (%)	NA	
No primary education		55 (0.1)
Less than primary or elementary education		77 (0.1)
Primary of elementary education		708 (0.7)
Lower secondary education		733 (0.7)
Upper secondary education		10400 (10)
Post-secondary, non-tertiary education		3890 (3.7)
Tertiary education, Type A		7779 (7.5)
Tertiary education, Type B		1719 (1.7)
Advance research qualification		2031 (1.9)
Age<18 years old		30005 (28.8)
Missing		46783 (44.9)
Health insurance - no. (%)	NA	
No insurance		3081 (3)
Disability insurance +/-others		800 (0.8)
Private health insurance +/- others		28566 (27.4)
Medicaid +/-others		7841 (7.5)
Medicare +/-others		3371 (3.2)
Others		20705 (19.9)
Missing		39816 (38.2)
Occupation - no. (%)	NA	
Professional, technical, or related occupation		18379 (17.6)
Manager, administrator or proprietor		3597 (3.5)
Clerical or related occupation		2509 (2.4)
Sales occupation		1882 (1.8)

Characteristic	TED N (%)	CRF N (%)
Service occupation		3005 (2.9)
Skilled crafts or related occupation		3033 (2.9)
Equipment/vehicle operator or related occupation		1388 (1.3)
Laborer		1921 (1.8)
Farmer		372 (0.4)
Member of military		299 (0.3)
Homemaker		1417 (1.4)
Student		10332 (9.9)
Under school age		2494 (2.4)
Not previously employed		1851 (1.8)
Other, specify		7741 (7.4)
Missing		43960 (42.2)

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

Characteristic	TED N (%)	CRF N (%)
No. of patients	236674	44934
No. of centers	601	449
Age at transplant, years - no. (%)		
Median (min-max)	52.9 (0-86.4)	50 (0-83.2)
0-9	10357 (4.4)	2284 (5.1)
10-19	7609 (3.2)	1733 (3.9)
20-29	16036 (6.8)	3097 (6.9)
30-39	24425 (10.3)	5594 (12.4)
40-49	43112 (18.2)	9774 (21.8)
50-59	64716 (27.3)	11860 (26.4)
60-69	58122 (24.6)	9049 (20.1)
70+	12297 (5.2)	1543 (3.4)
Recipient gender - no. (%)		
Male	127761 (54)	22091 (49.2)
Female	108913 (46)	22843 (50.8)
Recipient race - no. (%)		
Caucasian	164910 (69.7)	35444 (78.9)
African-American	20684 (8.7)	5355 (11.9)
Asian	5923 (2.5)	1269 (2.8)
Pacific islander	298 (0.1)	49 (0.1)
Native American	680 (0.3)	206 (0.5)
Other	5404 (2.3)	1406 (3.1)
Unknown	38775 (16.4)	1205 (2.7)
Disease - no. (%)		
Acute myelogenous leukemia	8157 (3.4)	2393 (5.3)
Acute lymphoblastic leukemia	1614 (0.7)	473 (1.1)
Other leukemia	796 (0.3)	255 (0.6)
Chronic myelogenous leukemia	701 (0.3)	290 (0.6)
Myelodysplastic/myeloproliferative disorders	281 (0.1)	95 (0.2)
Other acute leukemia	149 (0.1)	31 (0.1)
Non-Hodgkin lymphoma	65404 (27.6)	10809 (24.1)
Hodgkin lymphoma	24525 (10.4)	3846 (8.6)
Plasma cell disorder/Multiple Myeloma	92762 (39.2)	14938 (33.2)
Other Malignancies	19210 (8.1)	4300 (9.6)
Breast Cancer	21744 (9.2)	7293 (16.2)
Autoimmune Diseases	830 (0.4)	134 (0.3)
Other diseases	501 (0.2)	77 (0.2)
Year of transplant - no. (%)		

Characteristic	TED N (%)	CRF N (%)
<1985	31 (0)	5 (0)
1985-1989	2066 (0.9)	672 (1.5)
1990-1994	19307 (8.2)	7237 (16.1)
1995-1999	40356 (17.1)	12507 (27.8)
2000-2004	35082 (14.8)	6056 (13.5)
2005-2009	37184 (15.7)	7625 (17)
2010-2014	50212 (21.2)	3976 (8.8)
2015-2019	52436 (22.2)	6856 (15.3)
Education - no. (%)	NA	
No primary education		15 (0)
Less than primary or elementary education		45 (0.1)
Primary of elementary education		327 (0.7)
Lower secondary education		363 (0.8)
Upper secondary education		6388 (14.2)
Post-secondary, non-tertiary education		2651 (5.9)
Tertiary education, Type A		5316 (11.8)
Tertiary education, Type B		1168 (2.6)
Advance research qualification		1662 (3.7)
Age<18 years old		3527 (7.8)
Missing		23472 (52.2)
Health insurance - no. (%)	NA	
No insurance		755 (1.7)
Medicaid +/-others		3481 (7.7)
Medicare +/-others		4227 (9.4)
Missing		36471 (81.2)
Occupation - no. (%)	NA	
Professional, technical, or related occupation		16329 (36.3)
Manager, administrator or proprietor		1720 (3.8)
Clerical or related occupation		1238 (2.8)
Sales occupation		814 (1.8)
Service occupation		1559 (3.5)
Skilled crafts or related occupation		1456 (3.2)
Equipment/vehicle operator or related occupation		779 (1.7)
Laborer		1016 (2.3)
Farmer		203 (0.5)
Member of military		157 (0.3)
Homemaker		617 (1.4)
Student		1104 (2.5)
Under school age		373 (0.8)
Not previously employed		966 (2.1)

Characteristic	TED N (%)	CRF N (%)
Other, specify		3332 (7.4)
Missing		13271 (29.5)

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	26622	13167
No. of centers	181	178
Age at transplant, years - no. (%)		
Median (min-max)	50.8 (0-87.8)	58 (0.2-82.4)
0-9	3517 (13.2)	535 (4.1)
10-19	2247 (8.4)	240 (1.8)
20-29	2048 (7.7)	528 (4)
30-39	2060 (7.7)	734 (5.6)
40-49	3111 (11.7)	1685 (12.8)
50-59	5400 (20.3)	3758 (28.5)
60-69	6729 (25.3)	4645 (35.3)
70+	1510 (5.7)	1042 (7.9)
Recipient gender - no. (%)		
Male	15560 (58.4)	7599 (57.7)
Female	11062 (41.6)	5568 (42.3)
Recipient race - no. (%)		
Caucasian	21226 (79.7)	9117 (69.2)
African-American	2883 (10.8)	3094 (23.5)
Asian	1312 (4.9)	513 (3.9)
Pacific islander	87 (0.3)	28 (0.2)
Native American	178 (0.7)	109 (0.8)
Unknown	936 (3.5)	306 (2.3)
Disease - no. (%)		
Acute myelogenous leukemia	8942 (33.6)	152 (1.2)
Acute lymphoblastic leukemia	3373 (12.7)	15 (0.1)
Other leukemia	738 (2.8)	13 (0.1)
Chronic myelogenous leukemia	731 (2.7)	0
Myelodysplastic/myeloproliferative disorders	6921 (26)	3 (0)
Other acute leukemia	253 (1)	2 (0)
Non-Hodgkin lymphoma	1544 (5.8)	3022 (23)
Hodgkin lymphoma	141 (0.5)	1008 (7.7)
Plasma cell disorder/Multiple Myeloma	159 (0.6)	8077 (61.3)
Other Malignancies	22 (0.1)	792 (6)
Breast Cancer	0	2 (0)
Severe aplastic anemia	1149 (4.3)	1 (0)
Inherited abnormalities erythrocyte differentiation or function	1047 (3.9)	3 (0)

Characteristic	Allogeneic N (%)	Autologous N (%)
SCID and other immune system disorders	921 (3.5)	40 (0.3)
Inherited abnormalities of platelets	34 (0.1)	0
Inherited disorders of metabolism	378 (1.4)	2 (0)
Histiocytic disorders	223 (0.8)	2 (0)
Autoimmune Diseases	16 (0.1)	28 (0.2)
Other diseases	30 (0.1)	5 (0)
Education - no. (%)		
No primary education	25 (0.1)	12 (0.1)
Less than primary or elementary education	49 (0.2)	24 (0.2)
Primary of elementary education	104 (0.4)	80 (0.6)
Lower secondary education	489 (1.8)	307 (2.3)
Upper secondary education	5401 (20.3)	3294 (25)
Post-secondary, non-tertiary education	1793 (6.7)	1117 (8.5)
Tertiary education, Type A	5026 (18.9)	2780 (21.1)
Tertiary education, Type B	1175 (4.4)	803 (6.1)
Advance research qualification	945 (3.5)	520 (3.9)
Age<18 years old	5329 (20)	704 (5.3)
Missing	6286 (23.6)	3526 (26.8)
Health insurance - no. (%)		
No insurance	312 (1.2)	137 (1)
Disability insurance +/-others	594 (2.2)	0
Private health insurance +/- others	16641 (62.5)	0
Medicaid +/-others	4705 (17.7)	1799 (13.7)
Medicare +/-others	2791 (10.5)	2864 (21.8)
Others	997 (3.7)	0
Missing	582 (2.2)	8367 (63.5)
Occupation - no. (%)		
Professional, technical, or related occupation	5163 (19.4)	2977 (22.6)
Manager, administrator or proprietor	2322 (8.7)	1315 (10)
Clerical or related occupation	1472 (5.5)	913 (6.9)
Sales occupation	1157 (4.3)	594 (4.5)
Service occupation	1900 (7.1)	1220 (9.3)
Skilled crafts or related occupation	1847 (6.9)	1060 (8.1)
Equipment/vehicle operator or related occupation	887 (3.3)	585 (4.4)
Laborer	1155 (4.3)	733 (5.6)
Farmer	190 (0.7)	127 (1)
Member of military	194 (0.7)	126 (1)
Homemaker	602 (2.3)	324 (2.5)
Student	4404 (16.5)	533 (4)

Characteristic	Allogeneic N (%)	Autologous N (%)
Under school age	1473 (5.5)	300 (2.3)
Not previously employed	551 (2.1)	337 (2.6)
Other, specify	1250 (4.7)	614 (4.7)
Missing	2055 (7.7)	1409 (10.7)
Recipient zip code - no. (%)		
Not Available	1669 (6.3)	659 (5)
Available	24953 (93.7)	12508 (95)

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	4114	76403	3526	13788	1806	7521
No. of centers	2	39	205	9	107	12	27
Age, in years - no. (%)							
<10	0	806 (19.6)	8185 (10.7)	1485 (42.1)	1120 (8.1)	603 (33.4)	892 (11.9)
10-19	6 (16.7)	806 (19.6)	6561 (8.6)	802 (22.7)	978 (7.1)	445 (24.6)	858 (11.4)
20-29	6 (16.7)	624 (15.2)	6500 (8.5)	581 (16.5)	1445 (10.5)	246 (13.6)	830 (11)
30-39	2 (5.6)	629 (15.3)	6625 (8.7)	344 (9.8)	1541 (11.2)	234 (13)	955 (12.7)
40-49	7 (19.4)	556 (13.5)	9925 (13)	214 (6.1)	2334 (16.9)	154 (8.5)	1334 (17.7)
50-59	9 (25)	467 (11.4)	17050 (22.3)	82 (2.3)	3133 (22.7)	114 (6.3)	1656 (22)
60-69	6 (16.7)	189 (4.6)	18130 (23.7)	18 (0.5)	2865 (20.8)	10 (0.6)	961 (12.8)
≥70	0	37 (0.9)	3427 (4.5)	0	372 (2.7)	0	35 (0.5)
Gender - no. (%)							
Male	26 (72.2)	2429 (59)	44096 (57.7)	2063 (58.5)	8098 (58.7)	1176 (65.1)	4370 (58.1)
Female	10 (27.8)	1685 (41)	32307 (42.3)	1463 (41.5)	5690 (41.3)	630 (34.9)	3151 (41.9)
Primary disease - no. (%)							
AML	13 (36.1)	1091 (26.5)	29419 (38.5)	669 (19)	5532 (40.1)	330 (18.3)	3013 (40.1)
ALL	2 (5.6)	1075 (26.1)	12063 (15.8)	582 (16.5)	2282 (16.6)	199 (11)	1533 (20.4)
CML	3 (8.3)	273 (6.6)	2560 (3.4)	114 (3.2)	495 (3.6)	66 (3.7)	193 (2.6)
Myelodysplastic disorders	7 (19.4)	471 (11.4)	13457 (17.6)	125 (3.5)	2546 (18.5)	123 (6.8)	1182 (15.7)
NHL	3 (8.3)	86 (2.1)	5740 (7.5)	25 (0.7)	706 (5.1)	35 (1.9)	321 (4.3)
HL	0	25 (0.6)	394 (0.5)	3 (0.1)	73 (0.5)	10 (0.6)	30 (0.4)
Multiple myeloma	0	4 (0.1)	287 (0.4)	8 (0.2)	77 (0.6)	1 (0.1)	9 (0.1)
Other malignancies	1 (2.8)	108 (2.6)	3564 (4.7)	55 (1.6)	729 (5.3)	20 (1.1)	284 (3.8)
Severe aplastic anemia	4 (11.1)	534 (13)	2858 (3.7)	416 (11.8)	510 (3.7)	253 (14)	536 (7.1)
Other non-malignancies	3 (8.3)	447 (10.9)	6061 (7.9)	1529 (43.4)	838 (6.1)	769 (42.6)	420 (5.6)
Donor type - no. (%)							
HLA-identical sibling	15 (41.7)	2205 (53.6)	23210 (30.4)	2678 (76)	4420 (32.1)	1183 (65.5)	2835 (37.7)
Other Related donor	1 (2.8)	604 (14.7)	8935 (11.7)	507 (14.4)	796 (5.8)	385 (21.3)	908 (12.1)
Unrelated donor	20 (55.6)	1305 (31.7)	44250 (57.9)	341 (9.7)	7787 (56.5)	238 (13.2)	3778 (50.2)
Missing	0	0	8 (0)	0	785 (5.7)	0	0

Characteristic	Africa	Latin Americas	US / Canada	Eastern Mediterranean	Europe	Southeastern Asia	Western Pacific
Graft type - no. (%)							
Bone Marrow	1 (2.8)	2176 (52.9)	17541 (23)	1815 (51.5)	2910 (21.1)	324 (17.9)	1376 (18.3)
Peripheral Blood	34 (94.4)	1738 (42.2)	51524 (67.4)	1420 (40.3)	10317 (74.8)	1481 (82)	5534 (73.6)
Cord Blood	1 (2.8)	199 (4.8)	7336 (9.6)	291 (8.3)	557 (4)	1 (0.1)	606 (8.1)
Missing	0	1 (0)	2 (0)	0	4 (0)	0	5 (0.1)
Year of transplant - no. (%)							
2008	5 (13.9)	188 (4.6)	4831 (6.3)	436 (12.4)	1612 (11.7)	56 (3.1)	496 (6.6)
2009	11 (30.6)	313 (7.6)	5377 (7)	460 (13)	1720 (12.5)	49 (2.7)	667 (8.9)
2010	8 (22.2)	385 (9.4)	5609 (7.3)	451 (12.8)	1715 (12.4)	31 (1.7)	764 (10.2)
2011	10 (27.8)	343 (8.3)	6135 (8)	220 (6.2)	1567 (11.4)	122 (6.8)	860 (11.4)
2012	1 (2.8)	409 (9.9)	6251 (8.2)	251 (7.1)	1561 (11.3)	136 (7.5)	828 (11)
2013	1 (2.8)	357 (8.7)	6747 (8.8)	209 (5.9)	1465 (10.6)	116 (6.4)	756 (10.1)
2014	0	346 (8.4)	6881 (9)	274 (7.8)	836 (6.1)	140 (7.8)	724 (9.6)
2015	0	323 (7.9)	7073 (9.3)	253 (7.2)	687 (5)	186 (10.3)	565 (7.5)
2016	0	317 (7.7)	7261 (9.5)	215 (6.1)	705 (5.1)	242 (13.4)	704 (9.4)
2017	0	355 (8.6)	7531 (9.9)	242 (6.9)	1331 (9.7)	287 (15.9)	470 (6.2)
2018	0	453 (11)	7632 (10)	274 (7.8)	410 (3)	294 (16.3)	426 (5.7)

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	71973	189
Argentina	413	6
Brazil	3187	19
Canada	4430	16
Chile	11	2
Venezuela	50	2
Mexico	95	3
Uruguay	50	3
Peru	108	1
Columbia	200	3
Eastern Mediterranean		
Saudi Arabia	2300	4
Egypt	20	2
Iran	671	1
Pakistan	535	2
Europe		
Austria	93	2
Belgium	896	6
Denmark	1088	1
UK	1879	15
Finland	404	2
France	1086	10
Germany	2463	17
Ireland	157	1

Regions	N	Centers
Israel	903	7
Italy	546	7
Netherlands	554	8
Norway	78	1
Poland	374	4
Portugal	130	2
Spain	618	8
Sweden	818	4
Switzerland	633	3
Russia	91	1
Turkey	400	3
Greece	3	1
Czech Republic	460	3
Slovak Republic	114	1
Southeastern Asia		
India	1785	11
Thailand	21	1
Western Pacific		
Australia	3263	15
Korea	2659	3
New Zealand	832	4
Taiwan	62	1
Hong Kong	29	1
Singapore	676	3

Table 6. Number of patients who received a first allogeneic transplant registered with the CIBMTR between 2000 and 2018 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	501-999
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	100-500
Hong Kong	<100	<100	100-500	<100
India	100-500	100-500	501-999	≥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	501-999	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
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	≥1000	100-500
Switzerland	<100	<100	≥1000	<100
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 2018 by country

	CRF		TED	
Country	**Malignant disease**	**Non-malignant disease**	**Malignant disease**	**Non-malignant disease**
Argentina	100-500	NA	≥1000	<100
Australia	<100	<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
Colombia	NA	NA	100-500	<100
Czech Republic	<100	NA	501-999	<100
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
Korea	<100	NA	501-999	<100
Mexico	<100	NA	100-500	<100
Netherlands	NA	NA	100-500	<100
New Zealand	<100	NA	100-500	<100
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
Singapore	100-500	<100	501-999	<100
South Africa	<100	NA	100-500	<100
Spain	<100	<100	≥1000	<100

	CRF		TED	
Country	**Malignant disease**	**Non-malignant disease**	**Malignant disease**	**Non-malignant disease**
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	501-999	<100
Venezuela	<100	NA	100-500	NA

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

CIBMTR®
CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH

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

HS15-02 Impact of socioeconomic status on pediatric stem cell transplant outcomes (K Bona/J Wolfe/ C Duncan/ L Lehmann) The objective of this study is to determine the relationship between poverty (neighborhood and household) and pediatric stem cell transplant outcomes. The study protocol is under manuscript preparation phase. We expect to submit the manuscript by the end of March 2020.

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 protocol development phase. The goal is to have the analysis completed by the end of June 2020.

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 between White and Black patients after single and double umbilical cord blood transplantation; and determine if survival is comparable if transplanted with units of similar cell dose and HLA match. This study is in the protocol development phase. The goal is to have the analysis completed by the end of June 2020.

HS18-01 International collaborative study to compare the prognosis for acute leukemia patients transplanted with intensified myeloablative regimens (Y Arai/ Y Atsuta/ S Yano) First objective of this study is to determine the type and frequency of intensified myeloablative regimens used in the conditioning regimens for acute leukemia in the US and Japan. Second objective of this study is to compare the outcomes after intensified regimen between the US and Japan. This study is in the protocol development phase. The goal is to have the analysis completed by the end of June 2020.

HS18-02 Racial differences in long term survivor outcomes after allogeneic transplants (B Blue/ N Majhail) This study will evaluate OS by ethnicity/race after allogeneic HCT in adult recipients with hematologic malignancies who have survived for at least 2 years in remission. Furthermore this study will investigate the cumulative incidence of NRM and relapse at 7 years post-transplant by ethnicity/race in allogeneic HCT recipients who have survived in remission for at least 2 years. This study is in the protocol development phase. The goal is to have the protocol completed by then end of June 2020.

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) Black and Hispanic patients undergo hematopoietic cell transplantation (HCT) less frequently than White non-Hispanic patients. Additionally, Black patients more frequently utilize alternative donor sources. Minority children have greater ICU utilization, increased total length of stay, and more frequent readmissions. This study will compare the rate of hematopoietic cell transplant by donor source between racial/ethnic minorities compared to the white non-Hispanic populations among a cohort of pediatric acute leukemia patients. This study is in the protocol development phase. The goal is to have the protocol completed by then end of June 2020.

Proposal: 1903-01

Title:
Access to Hematopoietic Stem Cell Transplantation in Pediatric Patients with Acute Lymphoblastic Leukemia and Acute Myeloid Leukemia

Tony H. Truong, MD, MPH, tony.truong@ahs.ca, Alberta Children's Hospital/University of Calgary
Wael Saber, MD, MS, wsaber@mcw.edu, Medical College of Wisconsin, Milwaukee, USA

Hypothesis:
Access to hematopoietic stem cell transplantation (HSCT) in children with acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML) is *not* affected by factors extrinsic to the disease, including race, payer status, socio-economic status, and distance to treating center.
Unlike their adult counterparts, pediatric patients with ALL and AML have government health coverage (Medicaid) and are treated within specialized hospitals, many of which are part of large clinical trial consortia, thus affording them ready access to HSCT if required.

Specific aims:
- Determine the prevalence of pediatric ALL and AML using SEER data and estimate the proportion of patients who require HSCT.
- Determine the transplant rate of pediatric ALL and AML within the CIBMTR.
- Evaluate factors that are associated with the likelihood of receiving HSCT, in particular:
    - Patient related factors: including age, sex, race
    - Disease related factors: white blood count, CNS status (ALL), immunophenotype (ALL), cytogenetics and risk status (ALL and AML)
    - SES-related factors: payer status, regional income level/poverty level, distance to treating center
    - Other: year of transplant and region of the HSCT center

Scientific impact:
Disparities in access to HSCT among adult patients have been shown by multiple studies. Pediatric data is scant and generally has been the result of post-hoc sub-analysis within larger adult cohorts. Showing that access to HSCT is equitable in children, especially in a mixed-payer system such as the United States, would be a reassuring result to prove that children are not at a disadvantage due to socioeconomic and geographic factors. Equitable access to HSCT would be a strong testimony to the infrastructure in place surrounding children requiring HSCT, including the ongoing support of health funding and social support programs.

Scientific justification:
Hematopoietic stem cell transplantation (HSCT) is a costly procedure that is only offered at specialized centers in predominantly developed countries.[1] Differential access to HSCT has been reported in many countries and is affected by multiple variables including: disease-related factors, patient factors, donor availability, and socio-demographic, economic and geographic factors.[2-4] Disparities in access to HSCT have been described mostly in adults, citing differences by age, gender, race, and insurance status.[2,5-10] Among pediatric patients with acute leukemia (ALL and AML), the use of HSCT is typically reserved for those with high-risk features or relapsed disease, situations in which the expected outcomes of HSCT are superior when compared with chemotherapy alone.[11,12] The literature examining access to HSCT among children is scant and often the subject of subgroup analysis from larger adult studies.[5-7]

A large study linking the Surveillance, Epidemiology, and End Results (SEER) cancer registry and the Center for International Blood and Marrow Transplant Research (CIBMTR) registry showed that African Americans had lower rates of both autologous and allogeneic HSCT for treatment of leukemia, lymphoma and multiple myeloma.[7] Within this study, a sub-analysis among 2600 patients less than 20 years of age showed no difference in receipt of HSCT by race. Though this has been the largest study of children and adolescents, the manuscript did not provide a detailed analysis among this age group. Further, this study included patients from 1997-2002 and in the last 20 years, HSCT practices in pediatric ALL and AML has changed for several reasons, as follows: 1) during the time frame, autologous HSCT was being performed for pediatric AML and the analysis did not distinguish between allogeneic and autologous HSCT, 2) more intensive chemotherapy regimens have been developed meaning less patients will automatically be assigned to HSCT, 3) the advent of minimal residual disease has allowed better risk stratification such that those with persistent MRD are treated with HSCT and 4) the availability of CAR-T cells for treatment of ALL has changed the landscape of HSCT in the recent years. Two other studies have used SEER and CIBMTR linkage. Mehta et al. examined the effect of sex using HSCT cases from 1989-1999 and within the pediatric sub-analysis found that males were more likely to receive HSCT in in first remission but that no sex differences existed after relapse.[5] Paulson et al. examined geographic distance and poverty levels among US counties and found that patients from higher areas of poverty had lower access to HSCT, however, no disparity was seen in pediatric patients. [13] Though this study is contemporary (2000-2010), only patients with unrelated donors were included. A smaller study using hospital inpatient records at M.D. Anderson Cancer Center examined a pediatric subgroup under 18 years of age (n=324) and similarly found no difference in access to HSCT by sex, race, and payer status.[6]

In summary, there has been no large, contemporary studies examining access to HSCT in the pediatric population, including both ALL and AML and from all donor sources. Recently, population level data from the Cancer in Young People in Canada Registry showed that children with ALL had higher access to HSCT if they lived furthest from their treatment center and if they were diagnosed at a HSCT performing center (compared to centers that do not perform HSCT locally), but no effect due to race or income level.[14] The need for dedicated pediatric data from a large registry such as CIBMTR would greatly benefit the literature.

Patient eligibility population:

Pediatric patients with ALL and AML will be included. These are the most common pediatric malignancies requiring allogeneic HSCT, but unique differences between both will allow some worthy comparisons:

- Patients with ALL are generally treated with chemotherapy in CR1. Indications for HSCT include high-risk disease in CR1 or CR2
- Patients with AML are generally treated with chemotherapy in CR1. Indications for HSCT have evolved over the last 20 years, including the availability of a matched-related donor (regardless of disease risk), high risk disease and CR2.

Disease stages: all stages including primary refractory, CR1 and CR2 and beyond
Year of transplant: 2000 to present time.
Graft and donor types: all

Data requirements:

<u>CIBMTR data forms and elements:</u>

- Form 2400: Pre-Transplant Essential data: date of birth (month, year), sex, ethnicity, race, zip code, date of HCT, institution of HCT, donor information, product type

- Form 2010: AML Pre-HCT data
- Form 2011: ALL Pre-HCT data

To correlate with outcome in patients with:

- Form 2100: Post-HCT data
- ALL: Form 2111, Acute Lymphoblastic Leukemia Post-HCT Data
- AML: Form 2110, Acute Myelogenous Leukemia Post-HSCT Data

Sample requirements:
None required.

Study design:
This is a retrospective cohort registry-based study, looking at patients who received HSCT compared to those that did not.
HSCT will be described for the entire population and stratified by age, disease, conditioning regimen, donor type (MSD, MUD, haplo), graft source (marrow, PBSC, cord). Differential access will be compared to determine any relationship to HSCT outcomes such as engraftment failure, relapse and overall survival, will be determined by chi-square testing, regression models and survival analysis.

References:
1. Gratwohl A, Pasquini MC, Aljurf M, et al. One million haemopoietic stem-cell transplants: A retrospective observational study. Lancet Haematol. 2015;2(3):91.
2. Mitchell JM, Meehan KR, Kong J, Schulman KA. Access to bone marrow transplantation for leukemia and lymphoma: The role of sociodemographic factors. J Clin Oncol. 1997;15(7):2644-2651.
3. Morris TC, Velangi M, Jackson G, et al. Less than half of patients aged 65 years or under with myeloma proceed to transplantation: Results of a two region population-based survey. Br J Haematol. 2005;128(4):510-512.
4. Milone G, Sacchi N, Gallina A, et al. Access to alternative donor hematopoietic search and transplantation for acute leukemia in different macro-regions of Italy. A GITMO/IBMDR study. Bone Marrow Transplant. 2018;53(3):291-299.
5. Mehta P, Pollock BH, Nugent M, Horowitz M, Wingard JR. Access to stem cell transplantation: Do women fare as well as men? Am J Hematol. 2003;72(2):99-102.
6. Hwang JP, Lam TP, Cohen DS, Donato ML, Geraci JM. Hematopoietic stem cell transplantation among patients with leukemia of all ages in Texas. Cancer. 2004;101(10):2230-2238.
7. Joshua TV, Rizzo JD, Zhang MJ, et al. Access to hematopoietic stem cell transplantation: Effect of race and sex. Cancer. 2010;116(14):3469-3476.
8. Farnia S, Ganetsky A, Silver A, et al. Challenges around access to and cost of life-saving medications after allogeneic hematopoietic cell transplantation for medicare patients. Biol Blood Marrow Transplant. 2017;23(8):1387-1392.
9. Schriber JR, Hari PN, Ahn KW, et al. Hispanics have the lowest stem cell transplant utilization rate for autologous hematopoietic cell transplantation for multiple myeloma in the united states: A CIBMTR report. Cancer. 2017;123(16):3141-3149.
10. Jabo B, Morgan JW, Martinez ME, Ghamsary M, Wieduwilt MJ. Sociodemographic disparities in chemotherapy and hematopoietic cell transplantation utilization among adult acute lymphoblastic and acute myeloid leukemia patients. PLoS One. 2017;12(4):e0174760.
11. Pulsipher MA, Langholz B, Wall DA, et al. The addition of sirolimus to tacrolimus/methotrexate GVHD prophylaxis in children with ALL: A phase 3 children's oncology group/pediatric blood and marrow transplant consortium trial. Blood. 2014;123(13):2017-2025.

12. Peters C, Schrappe M, von Stackelberg A, et al. Stem-cell transplantation in children with acute lymphoblastic leukemia: A prospective international multicenter trial comparing sibling donors with matched unrelated donors-the ALL-SCT-BFM-2003 trial. J Clin Oncol. 2015;33(11):1265-1274.
13. Paulson K, Brazauskas R, He N, et al. Inferior access to allogeneic transplant in disadvantaged populations: A CIBMTR analysis. American Society of Hematology 58th Annual Meeting. 2016;128(22):842.
14. Truong TH, Pole JD, Bittencourt H, et al. Access to Hematopoietic Stem Cell Transplantation among Pediatric Patients with Acute Lymphoblastic Leukemia: A Population-based Analysis. Biol Blood Marrow Transplant. 2019 Feb 12. [Epub ahead of print]

Characteristics of pediatric patients who received first allogeneic transplants for AML or ALL in US between 2000 and 2019 reported to the CIBMTR (CRF)

Characteristic	AML	ALL
No. of patients	2252	2468
No. of centers	129	130
Age of recipient - no. (%)		
Median (min-max)	11.3 (0.2-21)	10.2 (0-21)
0 - 9	1032 (45.8)	1207 (48.9)
10 - 19	1075 (47.7)	1156 (46.8)
20 - 21	145 (6.4)	105 (4.3)
Sex - no. (%)		
Male	1215 (54)	1537 (62.3)
Female	1037 (46)	931 (37.7)
KPS - no. (%)		
<90	512 (22.7)	537 (21.8)
≥90	1496 (66.4)	1634 (66.2)
Missing	244 (10.8)	297 (12)
Race - no. (%)		
Caucasian	1714 (76.1)	1855 (75.2)
African-American	274 (12.2)	258 (10.5)
Asian	99 (4.4)	88 (3.6)
Pacific islander	9 (0.4)	7 (0.3)
Native American	20 (0.9)	17 (0.7)
Other	59 (2.6)	118 (4.8)
Unknown	77 (3.4)	125 (5.1)
Graft type - no. (%)		
Bone Marrow	976 (43.3)	1057 (42.8)
Peripheral Blood	455 (20.2)	477 (19.3)
Cord Blood	821 (36.5)	934 (37.8)
Donor type - no. (%)		
HLA-identical sibling	330 (14.7)	320 (13)
Other relative	177 (7.9)	172 (7)
Unrelated	1745 (77.5)	1976 (80.1)
Insurance type - no. (%)		
No insurance	25 (1.1)	39 (1.6)
Disability insurance +/-others	4 (0.2)	14 (0.6)
Private health insurance +/- others	839 (37.3)	860 (34.8)
Medicaid +/-others	855 (38)	888 (36)
Medicare +/-others	12 (0.5)	19 (0.8)
Others	159 (7.1)	187 (7.6)
Missing	358 (15.9)	461 (18.7)

Characteristic	AML	ALL
Zip code availability - no. (%)		
Zip code not available	321 (14.3)	393 (15.9)
Zip code available	1931 (85.7)	2075 (84.1)
Year of transplant - no. (%)		
2000 - 2004	624 (27.7)	806 (32.7)
2005 - 2009	751 (33.3)	851 (34.5)
2010 - 2014	516 (22.9)	418 (16.9)
2015 - 2019	361 (16)	393 (15.9)
Follow-up - median (min-max)	78.09 (2.99-223.39)	89.41 (3.19-222.17)

Proposal: 1911-79

Title:
Resource Intensity of End-of-Life Care in Children After Hematopoietic Stem Cell Transplant for Acute Leukemia: Rates and Disparities

Emily E Johnston, MD, MS; ejohnston@peds.uab.edu, The University of Alabama at Birmingham
Caitlin W. Elgarten, MD; elgartenc@email.chop.edu, The Children's Hospital of Philadelphia
Lena Winestone, MD, MPH; Lena.Winestone@ucsf.edu, University of California San Francisco Benioff Children's Hospital
Richard Aplenc, MD, PhD, MSCE; Aplenc@email.chop.edu, Perelman School of Medicine at the University of Pennsylvania/The Children's Hospital of Philadelphia

Hypothesis:
Among pediatric patients who undergo hematopoietic stem cell transplantation (HSCT) for acute leukemia, there is high resource utilization at the end-of-life with the highest resource utilization in minority patients, adolescents and young adults, and those who have not relapsed after transplant.

Specific aims:
Aim 1: Compare the clinical and sociodemographic characteristics of patients that received a HSCT at a PHIS hospital and, subsequently, died in a PHIS hospital with those who died outside of a PHIS hospital.

Aim 2: Describe the utilization of end-of-life resources during the 30 days before death among children who died in a PHIS hospital after receiving a HSCT at a PHIS hospital.

Aim 3: Determine the proportion of patients with a resource intense phenotype in the last 30 days of life among children who died in a PHIS hospital after receiving a HSCT at a PHIS hospital.

Aim 4: Determine the clinical and sociodemographic characteristics associated with a resource intense phenotype among children who died in a PHIS hospital after receiving a HSCT at a PHIS hospital.

Scientific impact:
Understanding end-of-life care after Hematopoietic Stem Cell Transplant (HSCT) is essential to ensure that patients are receiving goal concordant care and to better allocate resources. In particular, there is a lack of information about end-of-life care for children dying after HSCT. We have previously shown adolescents (15-21 year olds) who die after receiving HSCT are more likely die in the hospital and receive medically aggressive end-of-life care than their older or younger counterparts.[1] However, studies of end-of-life care of children after HSCT have been hampered by insufficient power in single institution studies and lack of granular clinical details (such as post-transplant relapse) in larger data sources such as claims and administrative data. Therefore, it is essential that we examine end-of-life care patterns and disparities in a data source that combines power and fine clinical details (such as CIBMTR merged with an administration data set, the Pediatric Health Information System (PHIS)). This will allow us to examine how the patterns and disparities align with patient and family goals in future studies.
Care for children at the end-of-life is resource intense. In particular, children with malignancies who died in the hospital spent an average of 14 days in the hospital in their last year of life (IQR: 4-36).[2] This corresponds to approximately $71,000 in hospital costs in the last year of life. In particular, of children who died in the hospital 53% were mechanically ventilated during their terminal admission, 35% underwent surgery during their terminal admission, and 4.1% had a new medical technology (eg.

Gastrostomy Tube or Tracheostomy placement).[2] Therefore, children with cancer who die at PHIS hospitals are receiving medically invasive end-of-life care and are high resource utilizers. Better understanding their resource utilization will help us better allocate resources and monitor how new therapies (eg. Immunotherapy) and interventions (e.g. palliative care for all children receiving a HSCT) affect end-of-life care for these children.

Scientific justification:

Children dying of cancer deserve high quality end-of-life care. However, it appears that many children with cancer are suffering at the end-of-life and may not be receiving goal-concordant end-of-life care. In particular, 58% of children dying of cancer are in pain in their final weeks.[3] Additionally, over 60% of children dying of cancer die in the hospital and over 20% are admitted to the Intensive Care Unit (ICU) at end-of-life.[4] Intensity of EOL care (e.g., medically-intense interventions [intubation, hemodialysis] and lack of hospice use) receives much attention in adult oncology due to concerns that it may not be consistent with patient goals, is associated with worse caregiver outcomes, and is expensive. The majority of older adults who know they are dying do not want life-extending measures.[5,6] Among adult caregivers of dying patients, more intense EOL care and hospital death are associated with worse caregiver outcomes (major depression, post-traumatic stress, and prolonged grief disorder).[7,8] There is growing evidence that parents of children who died of cancer would also prefer their child to die at home. Of 140 parents who lost a child due to cancer in one study, 88 parents were able to choose where their child died – 72% of these had their child die at home.[9] We also conducted interviews with bereaved families whose child died of cancer about their end-of-life experiences – they endorsed a desire for home death (which was frequently prevented by lack of home care resources that serve children) and a desire to stay out of the ICU at end-of-life. Therefore, it is essential to better understand medical intensity at end-of-life in children with cancer, particularly those undergoing HSCT.

Children with hematologic malignancies are more likely to die in the hospital and have medically intense end-of-life care at end-of-life than children with solid tumors.[4,10] In fact, over 60% of children with cancer die in the hospital, with the highest rates in children with hematologic malignancies.[4] This is most likely partially driven by high rates of medical intensity in children who die after HSCT.[1] However, population-based studies of end-of-life care of children with cancer have been hampered by their inability to differentiate between disease-related and treatment-related deaths. This will is particularly true in children dying after HSCT as transplant has higher treatment-related mortality than conventional chemotherapy. Therefore, it is essential to consider disease status and GVHD when examining end-of-life care for children after HSCT. We, therefore propose this study to examine end-of-life care amongst a cohort of children with HSCT for hematologic malignancies who died in the hospital.

Children with hematologic malignancies are not the only children with cancer receiving medically aggressive end-of-life care. Children <5, adolescents 15-21, and minorities are more likely to die in the hospital and receive medically aggressive end-of-life care.[4] Such age and racial/ethnic disparities have also been found in location of death for children with complex chronic conditions.[11] However, without disease status it is difficult to know if these disparities are differences in disease state, parental preferences, or other systemic factors such as palliative care access.

No single database exists that contains extensive information on transplantation outcomes including death and post-transplant disease status as well as healthcare resource and pharmacy utilization. The Pediatric Health Information System (PHIS) database is a pediatric database that includes clinical and resource utilization data for inpatient, emergency department and observation unit patient encounters for over 45 freestanding pediatric hospitals across the United States, including 19 transplant centers. Data elements in the PHIS database include demographics, dates of admission and discharge, discharge diagnosis and procedures codes, and length of stay. The PHIS data also contain billing data corresponding to specific resources utilized including inpatient pharmaceutical agents with medication

name and route of administration. Dr. Aplenc's research group, who is collaborating on this proposed work, has extensive experience with the PHIS database and has previously explored resource utilization in pediatric oncology patients.[10-17] The group has also successfully merged this data with other databases,[18-21] including data from the Center for International Blood and Marrow Transplant Research (CIBMTR), the most comprehensive database of clinical information on transplanted patients (HS14-01). CIBMTR and PHIS have previously merged to examine children who were transplanted due to leukemia at PHIS hospitals (GV17-01). Patients who died in that dataset will form the basis of this analysis and do not require a separate data merge. The use of PHIS and CIBMTR in concert can be leveraged to more accurately explore resource utilization and disparities in end-of-life care for children who die after HSCT given the additional disease and transplant information available in CIBMTR that would not be available in PHIS alone.

Patient eligibility population (FROM GV17-01):
This cohort will include patients who received an allogeneic HSCT at the ages of 1-21 years for treatment of acute leukemia (ALL or AML) from 2004-2017 and died within 5 years of HSCT. The GV17-01 study population included 2847 PHIS transplants who were matched to a CIBMTR transplant record (using the following linkage parameters: within 5 days of the date of transplant, within 3 days of date of birth of recipient, and matching recipient sex, transplanted due to AML or ALL, and had complete data records (see Table 1). The 5-year survival of that cohort is approximately 53%, which would give us approximately **1300** deceased patients in the cohort.

Table 1: GV17-01 Cohort		**Excluded**	**N**
PHIS transplant record sent to CIBMTR			5414
Matched to a CIBMTR record in TED retrieval • Date of HCT (+/- 5 days) • Date of birth of recipient (+/- 3 days) • Recipient sex		518	4896
First allogeneic HCT		440	4456
Recipient age between 1-21 years old	< 1 year old (n=132) ≥ 22 years old (n=82)	214	4242
Transplant performed for AML, ALL, according to CIBMTR records	CML (n=147) Other acute leukemia (n=107) MDS (n=97) MPS (n=84)* Other leukemia (n=12) NHL (n=52) HD (n=2) Other malignancies (n=21) Inherited abnormalities of erythrocyte differentiation or function (n=13) Severe aplastic anemia (n=5) SCID & other immune system disorders (n=6) Histiocytic disorders (n=9)	560	3682

Inherited disorders of metabolism (n=2) Other (n=3)		
Research consent	182	3500
Exclude embargoed centers	78	3422
Additional exclusions		
Exclude donor groups	161	3261
Exclude missing GVHD prophylaxis	31	3230
Exclude advanced disease status	300	2930
Exclude missing disease status	15	2915
Exclude ≤ 6/8-matched unrelated donor	68	**2847**

Data requirements:

We propose to use data elements from the following forms in the CIBMTR database:

- Recipient Baseline and 100-day follow-up data (2000, 2100)
- AML pre- and post-transplant forms (2010, 2110)
- ALL pre- and post-transplant forms (2011, 2111)

Data elements from these forms will be used to compile outcome data including:

- Presence or absence of aGVHD, including type of GVHD (e.g skin, gut, liver), maximum grade of aGVHD, date of aGVHD onset and date of maximum GVHD grade
- Relapse including date of relapse
- Mortality including cause and date of death

We will also collect the following covariates for potential inclusion in a multivariable regression model:

- Demographic information: Age at transplant and death and sex
- Diagnostic information: Indication for transplant and date of diagnosis
- Transplant-related variables: Date of transplant

Study design:

This will be a retrospective analysis of pediatric leukemia patients who underwent HSCT at centers that contribute to both CIBMTR and PHIS databases who died within 5 years of transplant using the previously merged PHIS/CIBMTR dataset from study **GV17-01**. This cohort was established i using a probabilistic merge strategy based on institutional codes, date of birth, and date of transplant.

Exposure:

Resource intense end-of-life care in the last 30 days of life or during their terminal admission: 1 or more of the following

- Invasive Mechanical Ventilation
- Hemodialysis (Fitzgerald) or periteonal dialysis
- CPR
- ECMO
- Invasive monitoring AND a Vasoactive Infusion
    - Arterial blood gas
    - PA wedge monitoring
    - Pulmonary artery pressure monitoring

- Systemic arterial pressure monitoring
- Arterial catheterization
- Insertion of implantable pressure lead
- Arterial catheter insertion
- Arterial line monitoring
- Swan-ganz catheter insertion
- PA line monitoring

Covariates:
Demographic, diagnostic variables (AML versus ALL), year of death, time between diagnosis and death, time between HSCT and death, and treatment related variables (time since HSCT, relapse after HSCT, degree of GVHD) will be abstracted from CIBMTR. Additional covariates will be abstracted from PHIS for inclusion in the multivariable model including:

- Insurance
- Race
- % of household in poverty based on zip code (SES)
- Region of US for terminal hospital
- Presence of Trisomy 21

Outcomes:

- Resource intense end-of-life care (as described above)

Statistical considerations:

- Descriptive statistics will be calculated for each exposure, covariate, and outcome as the exposure and covariate rates in this population have not been described
- T-tests and Chi Squared analysis will be used to compare the children who had a transplant at a PHIS center and died at the same PHIS center with children who had their transplant at a PHIS center and died elsewhere
- Univariate analysis will be performed to assess the association between each covariate and resource intense end-of-life care
- We will construct a multivariable regression model that incorporates our primary exposure data and aforementioned covariates to assess the association between the covariates and resource intense end-of-life care (Aim 4)
    - Sensitivity analysis will remove items to try to assess those who are most likely to have died from their underlying disease rather than treatment-related morality
        - those that did not have Grade 3 or 4 GVHD
        - those that did not have relapsed disease post-transplant
        - those that died within 100 days of transplant

Limitations:
This study will examine children who received a transplant at a PHIS center and then, subsequently died at a PHIS center. We will be missing children who 1) died at a non-PHIS hospital or 2) died at home. Unfortunately, current datasets do not allow us to distinguish these two from each-other. Therefore, in Aim 1 we will compare those children who died at a PHIS hospital to those that die in another center to see how our cohort compares to the larger cohort of children who died. Additionally, this will allows us to determine patterns of cares and disparities but it will not allow us to determine if these patterns are

consistent with patient and family wishes (goal concordant care). However, this will give us the preliminary population level data necessary for such follow-up studies.

Non-CIBMTR data source:
This data set allows us to supplement the clinical information available through CIBMTR with granular data regarding resource utilization at the time of death to critically examine end-of-life care for children who died after HSCT.

Conflicts of interest:
I have no conflicts of interest pertinent to this proposal.

References:
1. Johnston EE, Muffly L, Alvarez E, et al. End-of-Life Care Intensity in Allogeneic Hematopoietic Cell Transplant Recipients: A Population Level Analysis. *J Clin Oncol*. 2018; 36(30): 3023-3030.
2. Ananth P, Melvin P, Feudtner C, Wolfe J, Berry JG. Hospital Use in the Last Year of Life for Children With Life-Threatening Complex Chronic Conditions. *Pediatrics*. 2015;136(5):938-946.
3. Wolfe J, Grier HE, Klar N, et al. Symptoms and suffering at the end of life in children with cancer. *N Engl J Med*. 2000;342(5):326–333.
4. Johnston EE, Alvarez E, Saynina O, Sanders L, Bhatia S, Chamberlain LJ. Disparities in the Intensity of End-of-Life Care for Children With Cancer. *Pediatrics*. 2017;140(4):e20170671.
5. Weeks JC, Cook EF, O'Day SJ, et al. Relationship between cancer patients' predictions of prognosis and their treatment preferences. *JAMA*. 1998;279(21):1709-1714.
6. McCarthy EP, Phillips RS, Zhong Z, Drews RE, Lynn J. Dying with cancer: patients' function, symptoms, and care preferences as death approaches. *J Am Geriatr Soc*. 2000;48(5 Suppl):S110-121.
7. Wright AA, Zhang B, Ray A, et al. ASsociations between end-of-life discussions, patient mental health, medical care near death, and caregiver bereavement adjustment. *JAMA*. 2008;300(14):1665-1673.
8. Wright AA, Keating NL, Balboni TA, Matulonis UA, Block SD, Prigerson HG. Place of death: correlations with quality of life of patients with cancer and predictors of bereaved caregivers' mental health. *J Clin Oncol Off J Am Soc Clin Oncol*. 2010;28(29):4457-4464.
9. Dussel V, Kreicbergs U, Hilden JM, et al. Looking beyond where children die: determinants and effects of planning a child's location of death. *J Pain Symptom Manage*. 2009;37(1):33-43.
10. Kassam A, Sutradhar R, Widger K, et al. Predictors of and Trends in High-Intensity End-of-Life Care Among Children With Cancer: A Population-Based Study Using Health Services Data. *J Clin Oncol*. 2017;35(2):236-242.
11. Feudtner C, Silveira MJ, Christakis DA. Where do children with complex chronic conditions die? Patterns in Washington State, 1980–1998. *Pediatrics*. 2002;109(4):656–660.

Characteristic of pediatric leukemia patients who underwent HSCT at centers that contribute to both CIBMTR and PHIS databases who died within 5 years of transplant using the previously merged PHIS/CIBMTR dataset from study **GV17-01**

Characteristic	
No. of patients	1049
Age at transplant, years - no. (%)	
Median (min-max)	11.4 (1-21.8)
1-2	134 (12.8)
3-10	365 (34.8)
11-15	305 (29.1)
16-21	245 (23.4)
CRF or TED track - no. (%)	
TED	551 (52.5)
CRF	498 (47.5)
Sex - no. (%)	
Male	614 (58.5)
Female	435 (41.5)
Race - no. (%)	
Caucasian	779 (74.3)
Non-Caucasian	175 (16.7)
Missing	95 (9.1)
Karnofsky performance score prior to transplant - no. (%)	
< 90	154 (14.7)
≥ 90	748 (71.3)
Missing	147 (14)
Disease - no. (%)	
AML	451 (43)
ALL	598 (57)
Donor type - no. (%)	
HLA-identical sibling	251 (23.9)
Haploidentical (mismatched other relative)	60 (5.7)
8/8-matched unrelated	281 (26.8)
7/8-matched unrelated	175 (16.7)
6/6-matched UCB	29 (2.8)
5/6-matched UCB	113 (10.8)
≤4/6-matched UCB	80 (7.6)
UCB missing HLA	25 (2.4)
UCB missing number of units	35 (3.3)
Graft type - no. (%)	
BM	576 (54.9)
PB	191 (18.2)

Characteristic	
UCB	282 (26.9)
Conditioning regimen intensity (TED-as reported by center) & TBI use - no. (%)	
MA-TBI	655 (62.4)
MA-no TBI	270 (25.7)
RIC/NMA-TBI	46 (4.4)
RIC/NMA-no TBI	46 (4.4)
Missing	32 (3.1)
GVHD prophylaxis - no. (%)	
Ex-vivo T-cell depletion	38 (3.6)
CD34 selection	29 (2.8)
Post-transplant Cy	15 (1.4)
CNI + MMF	289 (27.6)
CNI + MTX	536 (51.1)
CNI alone	108 (10.3)
Others	34 (3.2)
Year of transplant - no. (%)	
2004-2006	184 (17.5)
2007-2009	246 (23.5)
2010-2013	334 (31.8)
2014-2017	285 (27.2)

Proposal: 1911-160

Title:
Predictors of Cost of Initial Hospitalization for Pediatric Allogeneic Hematopoietic Cell Transplantation.

Hemalatha Rangarajan MD, Hemalatha.Rangarajan@nationwidechildrens.org, Nationwide Children's Hospital
Prakash Satwani, MD, ps2087@columbia.edu, Columbia University Medical Center

Research hypothesis:
A merger of CIBMTR and Pediatric Health Information System (PHIS) database will be able to provide enough number of patients to create and validate a predictive model of cost for the transplant admission for patients ≤ 21 years of age undergoing alloHCT for malignant and non-malignant disease.

Specific aims:
Aim 1:
To determine the cost associated with first admission for children undergoing allogeneic hematopoietic cell transplant (alloHCT) for malignant and non-malignant diseases from 2010-2019.

Aim 2:
To validate and test a predictive model of cost for the transplant admission for patients ≤ 21 years of age undergoing alloHCT for malignant and non-malignant disease. This model will only include pre-alloHCT characteristics.

Background:
Healthcare utilization and cost is at the forefront of the national debate in the US. In this setting having accurate information regarding the costs associated with treatment is crucial for making informed decisions in our healthcare system. In United States according to an Agency for Health Care Research and Quality Report [1], overall hospital costs grew by 6.3% to $344 billion from 2004 to 2007. HCT accounted for the most rapid increase in total hospital costs with a growth rate of 84.9%. A total of 1.3 billion US dollars were spent in 2007, due to the increased number of transplants and increased lengths of hospitalization (LOH).[1]AlloHCT a curative therapy for children with malignant and nonmalignant diseases, is a highly specialized, resource intensive and costly medical procedure. The financial burden and subsequent bankruptcy are known complications experienced by HCT recipients and families. In adults, this financial toxicity can lead to non-compliance and hesitancy in accepting medical care.[2,3]. Further, as we embark on newer treatment modalities such as gene therapy, it would be imperative that we understand the cost of current standard of care in order to compare cost-effectiveness of newer treatment modalities.
Costs have been well described in adult patients undergoing alloHCT (in most cases for leukemia) with reported cost range from $96,000-$204,000 for the first year post-transplant.[3] **Within the first year post-transplant, 84% of costs were generated within the first 100 days and 94% of these costs were incurred as an inpatient**.[4] Thus, examination of inpatient costs especially first admission is a reasonable assessment of the major drivers of transplant related cost for the first year post-transplant. Important drivers of cost include pre-transplant factors such as use of alternative donors, intensity of conditioning regimen, comorbidities and most post-transplant complications such as infections, organ toxicity and graft versus host disease.[4-7]In a study of cost associated with first transplant admit at our center [8], 240 children underwent alloHCT from 2005-2016. Median cost of hospitalization was $158,896 (range 13,126-1,471,698). Variables associated with higher cost (>$150,000) of initial hospitalization included use of alternative donors (OR 2.978, 95% CI 1.447-6.131, p=0.003), cord blood grafts(OR 7.676, 95% CI 2.856-20.6, p<0.001, reference bone marrow), myeloablative

conditioning (OR 2.487, 95% CI 1.182-5.231, p=0.016), and positive CMV status (OR 2.067, 95% CI 1.03-4.133, p=0.040). In a subset analysis of costs only in 131 unrelated donors[9], we found that median cost per day survived (through day +365) was lowest for patients receiving PBSC with CD34 selection $926 (322–5316) as compared to UCB $1918 (491–107,93), unmanipulated PBSC $1516 (630–27,516), and BM $1205 (506–11,181) (p = 0.010). For non-malignant alloHCT, UCB had the highest costs per day survived $1530 (491–793) and PBSC with CD34 selection had the lowest at $482 (322–3092) (p < 0.001). In a multivariable model for costs per day survived, high-risk disease (p = 0.009) and graft failure (p < 0.001) were significantly associated with higher cost and alloHCT between 2010 and 2015 as compared to 2005 and 2009 (p = 0.017) was significantly associated with lower cost per day survived. This study illustrated the important differences in cost and healthcare utilization among the different donor sources used for unrelated alloHCT. Similarly, in a PHIS based multicenter study conducted by us [10] we found that 80% of costs were incurred during the initial transplant admission. In this study, we compared alloHCT related costs in adolescent and young adults (15-39 years) with children (< 15 years) with acute leukemias and myelodysplastic syndromes. We observed that although LOH was similar between AYA and children, AYA incurred greater median adjusted costs (338,458 versus $275,723; *P* < .001) and costs per hospital day ($7122 versus $5838; *P* < .001) In a multivariable analysis increasing age at HCT, use of cord blood, unrelated donors, occurrence of any GVHD, infection, use of dialysis or mechanical ventilation were significant drivers of costs in AYA recipients than in children. As the data for this study was extracted only using the PHIS database, it was limited by lack of information on pre-transplant characteristics, the intensity of the conditioning regimens administered and their impact on initial transplant admit costs. Therefore, our studies were either limited to a single center or lacked the detailed level of granularity on pretransplant variables in a multicenter cohort.

Scientific justification:
In pediatrics more detailed understanding of costs for alloHCT would provide important information to enable sensible resource allocation and cost containment. Therefore, we propose merging data from PHIS with that of the CIBMTR for the purpose of this study. This will enable us to capture a multicenter data with the detailed level of granularity that is required for a study of this nature. Furthermore, a model of cost for the transplant admission individualized based on patient characteristics could allow for more accurate payment allocation for this costly procedure. The results from this study could lead to policy changes and renegotiation of contracts for transplant admission based on the contemporary data and cost could be adjudicated based on pre-transplant characteristics and donor source. Cost data from this study could also be utilized for cost effectiveness comparisons with gene therapy treatment for malignant and non-malignant diseases.

Study design:
We will conduct a retrospective study of a multi-center, national cohort of pediatric patients undergoing alloHCT for malignant and non-malignant disease during the period from 1/1/2010 to 12/31/2019.

Patient eligibility:
This study will include all patients who were ≤ 21 years of age at the time of alloHCT from 1/1/2010 to 12/31/2019. To be included in study, patient must be represented in both CIBMTR & PHIS databases.

CIBMTR data requirements:
Pre-transplant characteristics to be included are described in the table below (will be obtained from pre-**Transplant Essential Data (TED) forms.**

Malignant disease	Non-malignant disease
Age	Age
Sex	Sex
Weight	Weight

BMI%	BMI%
Race	Race
Disease risk	
• Early /Intermediate/Advanced	
Donor type	Donor type
• Matched sibling/Alternative donor	• Matched Sibling/Alternative donor
Cell Source	Cell Source
• Bone marrow	• Bone marrow
• Other	• Other
HLA Match	HLA Match
• Mismatch	• Mismatch
• Full match	• Full match
Conditioning	Conditioning
• Myeloablative	• Myeloablative
• Reduced Intensity	• Reduced Intensity
Pre-transplant CMV status	Pre-transplant CMV status
• Negative	• Negative
• Positive	• Positive
HCT-Comorbidity Index	HCT-Comorbidity Index
• HCT-CI 0-2	• HCT-CI 0-2
• HCT-CI ≥3	• HCT-CI ≥3
Performance status	Performance status
• 90-100	• 90-100
• <90	• <90

PHIS database:

Inpatient charges will be obtained from the Pediatric Health Information System Database (PHIS).[11] 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. Health care utilization will be assessed by hospital length of stay and intensive care unit admission. 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 2018 dollars.

Merging and validating:

Patients in PHIS database who received alloHCT will be identified using DRG code (014). 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.[12,13] Once linked, merge accuracy will be assessed with institution level validation at Columbia University Medical Center (CUMC) and Nationwide Children's hospital (NCH). This process will be similar to our recently published study. [13,14]

Feasibility:

We the PIs have extensive experience in working with the PHIS database[10,15,16].[9] We have independently extracted data from PHIS database for several published studies. 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[14] . In projects as mentioned above we merged the robust data from our center with that from the PHIS database[9]. 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[14] and HS 14-01[17]).

Statistical methods:

Pre-transplant characteristics that will be included in the model are: be age, weight, body mass index, gender, race, disease, donor type, stem cell source, degree of HLA match, CMV risk, HCT-comorbidity index (HCT-CI), performance status, and conditioning regimen. We expect the costs to be positively skewed and so regression will be performed on a transformed scale of the costs with the transformation being identified by the Box-Cox transformation approach. Univariable linear regression will be used to identify potential predictors to be incorporated in the multivariable model. The univariable analysis will be conducted in a randomly selected 50% sample. The threshold for the significance in univariable regression analysis will be set at 0.05. The multivariable model will be created based on the initial screening in the same 50% sample. In order to be included in the final model, predictors must meet the level of significance of 0.05. The model will then be validated in the other remaining 50% of the sample. The validation model includes only those predictors meeting the above criteria. The final model contains only those variables that maintained the significance <0.05 in the validation model.

References:

1. Stranges ETR, Russo CTR, Friedman BA. Procedures with the Most Rapidly Increasing Hospital Costs, 2004-2007: HCUP Statistical Brief #82. In: Healthcare Cost and Utilization Project (HCUP) Statistical Briefs. Rockville (MD): Agency for Healthcare Research and Quality (US); December 2009.
2. Khera N, Chang YH, Hashmi S, et al. Financial burden in recipients of allogeneic hematopoietic cell transplantation. Biol Blood Marrow Transplant. 2014;20(9):1375-1381.
3. Khera N, Zeliadt SB, Lee SJ. Economics of hematopoietic cell transplantation. Blood. 2012;120(8):1545-1551.
4. Saito AM, Cutler C, Zahrieh D, et al. Costs of allogeneic hematopoietic cell transplantation with high-dose regimens. Biol Blood Marrow Transplant. 2008;14(2):197-207.
5. Majhail NS, Mothukuri JM, Brunstein CG, Weisdorf DJ. Costs of hematopoietic cell transplantation: comparison of umbilical cord blood and matched related donor transplantation and the impact of posttransplant complications. Biol Blood Marrow Transplant. 2009;15(5):564-573.
6. Majhail NS, Mothukuri JM, Macmillan ML, et al. Costs of pediatric allogeneic hematopoietic-cell transplantation. Pediatr Blood Cancer. 2010;54(1):138-143.
7. Blommestein HM, Verelst SG, Huijgens PC, Blijlevens NM, Cornelissen JJ, Uyl-de Groot CA. Real-world costs of autologous and allogeneic stem cell transplantations for haematological diseases: a multicentre study. Ann Hematol. 2012;91(12):1945-1952.
8. Larisa Broglie ZJ, Prakash Satwani. Pre-Transplant Predictors of Cost of First Hospitalization for Pediatric Allogeneic Hematopoietic Cell Transplantation (alloHCT). Biology of Blood and Marrow Transplantation. 2019;25(3):S306.
9. Bourgeois W, Ricci A, Jin Z, et al. Health care utilization and cost among pediatric patients receiving unrelated donor allogeneic hematopoietic cell transplantation. Bone Marrow Transplant. 2018.
10. Rangarajan HG, Smith LC, Stanek JR, 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):1031-1038.
11. 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.).
12. Arnold SD, Brazauskas R, He N, et al. Clinical risks and healthcare utilization of haematopoietic cell transplantation for sickle cell disease in the U.S. using merged databases. Haematologica. 2017.
13. Berry JG, Hall DE, Kuo DZ, et al. Hospital utilization and characteristics of patients experiencing recurrent readmissions within children's hospitals. Jama. 2011;305(7):682-690.
14. Arnold SD, Brazauskas R, He N, 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):1823-1832.
15. Ricci A, Jin Z, Broglie L, et al. Healthcare utilization and financial impact of acute-graft-versus host disease among children undergoing allogeneic hematopoietic cell transplantation. Bone Marrow Transplant. 2019.
16. Rangarajan HG, Stanek JR, Abu-Arja R, et al. Venous Thromboembolism in Pediatric Hematopoietic Cell Transplant: A Multicenter Cohort Study. Biol Blood Marrow Transplant. 2018;24(2):337-342.
17. Staci D Arnold RB, Naya He, Yimei Li, Prakash Satwani, Michael A Pulsipher, Matt Hall, Yoshiko Atsuta, Jignesh Dalal, Theresa Hahn, Carmem Bonfim, Nandita Khera, Richard Aplenc and Wael Saber. Role of Donor Source on Clinical Outcomes and Inpatient Resource Utilization for Hematopoietic Cell Transplantation in Children with Acute Leukemia. Blood. 2016: 128:3575.

Characteristic of pediatric patients who underwent first allogeneic transplants at centers that contribute to both CIBMTR and PHIS databases from 2010 to 2019 registered in the CIBMTR (**TED**)

Characteristic	Malignant Diseases	Non-malignant disease
No. of patients	3647	3262
No. of centers	37	36
Recipient age at HCT, years - no. (%)		
Median (min-max)	11.2 (0.4-21)	5.9 (0-21)
<10	1639 (44.9)	2215 (67.9)
10-17	1536 (42.1)	850 (26.1)
18-19	337 (9.2)	155 (4.8)
20-29	135 (3.7)	42 (1.3)
Gender- no. (%)		
Male	2124 (58.2)	1967 (60.3)
Female	1523 (41.8)	1295 (39.7)
KPS - no. (%)		
<90	569 (15.6)	429 (13.2)
≥90	3028 (83)	2647 (81.1)
Missing	50 (1.4)	186 (5.7)
Race - no. (%)		
Caucasian	2802 (76.8)	2082 (63.8)
African-American	358 (9.8)	709 (21.7)
Asian	149 (4.1)	185 (5.7)
Pacific islander	11 (0.3)	12 (0.4)
Native American	33 (0.9)	25 (0.8)
Unknown	294 (8.1)	249 (7.6)
Disease - no. (%)		
Acute myelogenous leukemia	1311 (35.9)	0
Acute lymphoblastic leukemia	1571 (43.1)	0
Other leukemia	3 (0.1)	0
Chronic myelogenous leukemia	96 (2.6)	0
Myelodysplastic/myeloproliferative disorders	380 (10.4)	0
Other acute leukemia	112 (3.1)	0
Non-Hodgkin lymphoma	127 (3.5)	0
Hodgkin lymphoma	34 (0.9)	0
Other Malignancies	13 (0.4)	0
Severe aplastic anemia	0	659 (20.2)
Inherited abnormalities erythrocyte differentiation or function	0	1045 (32)
SCID and other immune system disorders	0	906 (27.8)
Inherited abnormalities of platelets	0	45 (1.4)
Inherited disorders of metabolism	0	246 (7.5)

Characteristic	Malignant Diseases	Non-malignant disease
Histiocytic disorders	0	306 (9.4)
Autoimmune Diseases	0	28 (0.9)
Other diseases	0	27 (0.8)
Graft type - no. (%)		
Bone Marrow	2165 (59.4)	2252 (69)
Peripheral Blood	711 (19.5)	434 (13.3)
Cord Blood	771 (21.1)	576 (17.7)
Donor type - no. (%)		
HLA-identical sibling	879 (24.1)	1082 (33.2)
Identical twin	3 (0.1)	8 (0.2)
Other relative	420 (11.5)	280 (8.6)
Unrelated	2345 (64.3)	1891 (58)
Missing	0	1 (0)
Year of transplant - no. (%)		
2010 - 2014	1864 (51.1)	1551 (47.5)
2015 - 2019	1783 (48.9)	1711 (52.5)
Follow-up - median (min-max)	43.95 (2.43-112.93)	36.88 (1.02-105.23)

Proposal: 1911-215

Title:
Access to Allogeneic Hematopoietic Cell Transplant in the United States After Implementation of the Affordable Care Act

Neel S Bhatt, MBBS, MPH, nbhatt@fredhutch.org, Fred Hutchinson Cancer Center
Akshay Sharma, MBBS, Akshay.sharma@stjude.org, St. Jude Children's Research Hospital
Navneet Majhail, MD, MS, majhain@ccf.org, Cleveland Clinic
Theresa Hahn, PhD, Theresa.hahn@roswellpark.org, Rowell Park Comprehensive Cancer Center

Hypothesis:
We hypothesize that access to allogeneic hematopoietic cell transplant (HCT) for patients who have been previously identified as having lower access has increased since the implementation of Affordable Care Act (ACA) Medicaid expansion.

Specific aims:
Primary:

- To assess the association between Affordable Care Act (ACA) Medicaid expansion and the rate of allogeneic HCT in females in the states which expanded coverage on January 1, 2014
- To assess the association between Affordable Care Act (ACA) Medicaid expansion and the rate of allogeneic HCT in African American population in the states which expanded coverage on January 1, 2014
- To study the association between ACA Medicaid expansion and the rate of allogeneic HCT for these living in high poverty areas in the states which expanded coverage on January 1, 2014

Secondary:

- To assess the association between ACA Medicaid expansion and the rates of uninsured patients undergoing allogeneic HCT in the states which expanded coverage on January 1, 2014

Scientific impact:
The Patient Protection and Affordable Care Act, also known as the Affordable Care Act (ACA) was signed into law on March 23, 2010. While several changes occurred immediately after its implementation (e.g. cost-free preventive services), the primary components such as Medicaid expansion and subsidized coverage were implemented on January 1, 2014. Several studies have shown reduction in healthcare access disparities secondary to socioeconomic status and race since the implementation of ACA[1,2], however, its impact on access to HCT is unknown. Results of this proposed study will provide the crucial information for future efforts focusing on healthcare policy and advocacy.

Scientific justification:
Allogeneic hematopoietic cell transplant (HCT) is a curative treatment option for patients with malignant and non-malignant hematopoietic disorders. Increasing use of HCT is evident from the number of transplants performed in the United States which has doubled in last two decades.[3] However, it is important to note that there are significant disparities in access to HCT which are thought to be related to availability of donor, recipients' social (race/ ethnicity) and economic (socioeconomic status, education, employment status, insurance coverage) status, provider (referral, provider expertise,

attitude), and health-care system (infrastructure, workforce, number of HCT centers) factors.[4] Two prior studies using the Center for International Blood and Marrow Transplant Research (CIBMTR) and Surveillance, Epidemiology, and End Results (SEER) data have assessed the impact of recipients' sex, race, and socioeconomic status on their access to HCT. Joshua et al. studied the effect of recipient race and sex on access to HCT for patients undergoing HCT from 1997 to 2002 and found that the likelihood of undergoing HCT was significantly higher in Caucasians compared to African Americans (Odds ratio [OR] 1.40; 95% confidence interval [CI] 1.34-1.46) and in males compared to females (OR 1.07; 95% CI 1.05-1.1).[5] Another recent CIBMTR analysis by Paulson et al. studied patients diagnosed with AML, ALL, and MDS from 2000 to 2009 and showed that patients from areas with high poverty were less likely to undergo unrelated donor HCT.[6]

HCT is a resource-intensive and expensive procedure[7] and patients without insurance are less likely to undergo HCT.[8,9] It is also known that racial/ ethnic minorities are more likely to be uninsured.[10] In 2010, the Affordable Care Act (ACA) was implemented which aimed to expand insurance coverage while controlling costs and thereby improve equity in healthcare access and outcomes. Since implementation of ACA, the percentage of uninsured population in the United States has declined from 15% in 2011 to 9% in 2017.[11] A recent analysis showed that Medicaid expansion implemented by the ACA improved time to cancer care in African American patients (Adamson BJS et al. ASCO 2019). Current literature lacks data on the impact of ACA Medicaid expansion on access to HCT, especially for the population which has been shown to have lower access prior to ACA.

In this study using data from the CIBMTR, we will be studying the variations in rates of HCT after the implementation of ACA using recipients' sex, race/ ethnicity, geographical location, and socioeconomic status.

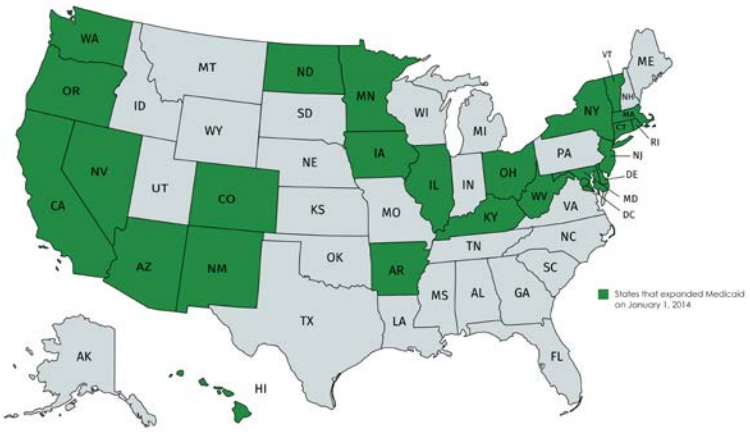
Patient eligibility population:

- Patients who underwent allogeneic HCT between January 1, 2008 and December 31, 2019
- Residing in the states which expanded Medicaid coverage on January 1, 2014 (Figure 1)

Following CIBMTR forms will be used:

2400	Pre-Transplant Essential Data
2402	Pre-Transplant Disease Classification
2000	Recipient Baseline Data (For secondary aim only)

Figure 1: Medicaid Expansion Coverage Map



Data Requirements:

Patient-related:

- Age at HCT: in 10-year increment
- Gender: male vs female
- Race/ ethnicity: Caucasian vs African American
- Zip code
- Insurance status (for secondary aim): insured vs. uninsured

Disease-related:

- Disease diagnosis

Donor-related:

- Donor type: HLA-identical, unrelated, cord blood

Transplant-related:

- Year of transplant: 2008-13 vs. 2014-19

Outcome:

- Number of allogeneic HCT

Sample requirements:

Not applicable

Study design:

This study will be a retrospective cohort study comparing the rates of allogeneic HCT according to the recipient sex, race/ ethnicity, and geographical location. The CIBMTR database will be used to identify all patients between January 1, 2008 and December 31, 2019 who underwent allogeneic HCT. Zip codes will be used to determine patient residence. The US Census Data will be used to determine the sociodemographic makeup of county including zip codes in order to identify the population size and median income of the county. Poverty will be determined in accordance with the previous CIBMTR study.[6]

Given the implementation of ACA Medicaid expansion varied by states, the rates of HCT will be compared before and after the Medicaid expansion within selected states that implemented Medicaid expansion on 1/1/2014 (25 states including District of Columbia, Figure 1).

Descriptive statistics will be presented for the patient-, disease- and transplant- related variables and will be compared between patients transplanted before and after the ACA Medicaid expansion.

Primary aims:

Univariate and multivariate regression analyses will be performed to study the association between ACA Medicaid expansion (year of HCT as a covariate: 2014-19 vs. 2008-13) and the rates of HCT by patient sex, race/ ethnicity, and geographical location (% population below poverty) after adjusting for age at HCT. Depending on the numbers, we may stratify for the disease diagnoses and donor types. Odds ratios (OR) and 95% confidence intervals (CI) will be provided for the likelihood of HCT for females, African Americans, and patients living in high poverty areas. TED level data will be used for this analysis.

Secondary aim:
Univariate and multivariate regression analyses will be performed to study the association between ACA Medicaid expansion (year of HCT as a covariate: 2014-19 vs. 2008-13) and the rates of uninsured population after adjusting for age at HCT and race/ ethnicity. OR and 95% CI will be provided for the likelihood of uninsured status. This analysis will be limited to a population subset due to the availability of insurance variable only at CRF level.
P value < 0.05 will be considered statistically significant. SAS 9.4 (SAS Inc., Cary, NC) will be used for all analyses.

Non-CIBMTR data source:
Not applicable

References:
1. Buchmueller TC, Levinson ZM, Levy HG, et al: Effect of the Affordable Care Act on Racial and Ethnic Disparities in Health Insurance Coverage. Am J Public Health 106:1416-21, 2016
2. Griffith K, Evans L, Bor J: The Affordable Care Act Reduced Socioeconomic Disparities In Health Care Access. Health Aff (Millwood), 2017
3. D'Souza A FC: urrent Uses and Outcomes of Hematopoietic Cell Transplantation (HCT): CIBMTR Summary Slides. 2018
4. Majhail NS, Omondi NA, Denzen E, et al: Access to hematopoietic cell transplantation in the United States. Biol Blood Marrow Transplant 16:1070-5, 2010
5. Joshua TV, Rizzo JD, Zhang MJ, et al: Access to hematopoietic stem cell transplantation: effect of race and sex. Cancer 116:3469-76, 2010
6. Paulson K, Brazauskas R, Khera N, et al: Inferior Access to Allogeneic Transplant in Disadvantaged Populations: A Center for International Blood and Marrow Transplant Research Analysis. Biol Blood Marrow Transplant 25:2086-2090, 2019
7. Majhail NS, Mau LW, Denzen EM, et al: Costs of autologous and allogeneic hematopoietic cell transplantation in the United States: a study using a large national private claims database. Bone Marrow Transplant 48:294-300, 2013
8. Mitchell JM, Meehan KR, Kong J, et al: Access to bone marrow transplantation for leukemia and lymphoma: the role of sociodemographic factors. J Clin Oncol 15:2644-51, 1997
9. Cho C: Factors affecting stem cell transplantation for leukemia and lymphoma, Georgetown University, 2006
10. Ward E, Jemal A, Cokkinides V, et al: Cancer disparities by race/ethnicity and socioeconomic status. CA Cancer J Clin 54:78-93, 2004
11. KAISER FAMILY FOUNDATION: Health Insurance Coverage of the Total Population. Available at https://www.kff.org/other/state-indicator/total-population/?currentTimeframe=0&sortModel=%7B%22colId%22:%22Location%22,%22sort%22:%22asc%22%7D. Accessed on December 17, 2018,

Characteristics of patients who received first allogeneic transplants between 2008 and 2019 in US reported to the CIBMTR (**CRF**)

Characteristic	**2008 - 2013**	**2014 - 2019**
No. of patients	11561	13540
No. of centers	160	165
Age of recipient - no. (%)		
Median (min-max)	47.9 (0-82.3)	55.1 (0-87.8)
0 - 9	1475 (12.8)	1377 (10.2)
10 - 19	1017 (8.8)	1085 (8)
20 - 29	994 (8.6)	981 (7.2)
30 - 39	1078 (9.3)	911 (6.7)
40 - 49	1670 (14.4)	1347 (9.9)
50 - 59	2689 (23.3)	2512 (18.6)
60 - 69	2330 (20.2)	4183 (30.9)
70+	308 (2.7)	1144 (8.4)
Sex - no. (%)		
Male	6705 (58)	7970 (58.9)
Female	4856 (42)	5570 (41.1)
KPS - no. (%)		
<90	3611 (31.2)	5458 (40.3)
≥90	7645 (66.1)	7815 (57.7)
Missing	305 (2.6)	267 (2)
Race - no. (%)		
Caucasian	9754 (84.4)	10342 (76.4)
African-American	958 (8.3)	1749 (12.9)
Asian	456 (3.9)	739 (5.5)
Pacific islander	35 (0.3)	49 (0.4)
Native American	66 (0.6)	98 (0.7)
Unknown	292 (2.5)	563 (4.2)
Disease - no. (%)		
Acute myelogenous leukemia	4541 (39.3)	4209 (31.1)
Acute lymphoblastic leukemia	1575 (13.6)	1713 (12.7)
Other leukemia	428 (3.7)	293 (2.2)
Chronic myelogenous leukemia	449 (3.9)	268 (2)
Myelodysplastic/myeloproliferative disorders	2407 (20.8)	4269 (31.5)

Characteristic	2008 - 2013	2014 - 2019
Other acute leukemia	127 (1.1)	122 (0.9)
Non-Hodgkin lymphoma	772 (6.7)	672 (5)
Hodgkin lymphoma	44 (0.4)	88 (0.6)
Plasma cell disorder/Multiple Myeloma	49 (0.4)	38 (0.3)
Other Malignancies	5 (0)	9 (0.1)
Severe aplastic anemia	400 (3.5)	710 (5.2)
Inherited abnormalities erythrocyte differentiation or function	278 (2.4)	597 (4.4)
SCID and other immune system disorders	365 (3.2)	484 (3.6)
Inherited abnormalities of platelets	0	1 (0)
Inherited disorders of metabolism	115 (1)	62 (0.5)
Histiocytic disorders	5 (0)	5 (0)
Autoimmune Diseases	1 (0)	0
Graft type - no. (%)		
Bone Marrow	2092 (18.1)	3257 (24.1)
Peripheral Blood	6706 (58)	8565 (63.3)
Cord Blood	2763 (23.9)	1718 (12.7)
Donor type - no. (%)		
HLA-identical sibling	2995 (25.9)	3032 (22.4)
Other relative	683 (5.9)	2671 (19.7)
Unrelated	7883 (68.2)	7837 (57.9)
Insurance type - no. (%)		
No insurance	147 (1.3)	135 (1)
Disability insurance +/-others	230 (2)	298 (2.2)
Private health insurance +/- others	6773 (58.6)	6751 (49.9)
Medicaid +/-others	2361 (20.4)	2658 (19.6)
Medicare +/-others	1412 (12.2)	3143 (23.2)
Others	500 (4.3)	424 (3.1)
Missing	138 (1.2)	131 (1)
Zip code availability - no. (%)		
Zip code not available	378 (3.3)	1165 (8.6)
Zip code available	11183 (96.7)	12375 (91.4)
Follow-up - median (min-max)	86.41 (2.66-131.41)	25.56 (0.92-65.56)

Proposal: 1911-253

Title:
Impact of seasons on outcomes of allogenic hematopoietic cell transplantation (HCT) in North America

Pierre Teira, MD, MSc, pierre.teira.hsj@ssss.gouv.qc.ca, Sainte Justine Hospital/University of Montreal

Hypothesis:
Seasons may have an impact on outcomes of HCT due to seasonal epidemic infections and seasonal variations in the human circadian rhythms.

Specific aims:
To assess the impact of the season where the transplantation is done on disease relapse, incidence of acute and chronic graft versus host disease (GVHD), non-relapse mortality (NRM), event-free survival (EFS) and overall survival (OS) in patients receiving allogeneic hematopoietic cell transplantation (HCT) in North America.

Scientific justification:
While yearly seasonal incidence and outbreaks of many viruses are very well described and while the potential negative impact of those viruses for immunocompromised patients is very well known[1-5], there is a near complete lack of studies systematically analyzing the potential influence of seasons on HCT outcomes. Among viruses with life threatening potential in immunocompromised patients, the majority is epidemic in winter and springs (influenza and parainfluenza viruses, adenovirus, RSV, metapneumovirus, rotavirus, norovirus, coronavirus) and a minority is encountered in summer (enterovirus, West Nil virus). Moreover, bacterial infections of the upper and lower respiratory tract as well as digestive infection like Clostridium difficile, have also a seasonal distribution and may come as secondary complications of viral infections.
Besides seasonal infectious outbreaks, several physiologic circadian rhythms are modulated by seasonal changes such as external temperature or daily light exposure[6]. Notably, winter season is associated with immunologic and endocrine changes leading to a pro-inflammatory state[7]. Moreover, seasonal affective disorders, typically presenting as depressive mood in winter[8], may disturb adherence to medication and to appointment for follow-up after HCT.

Patient eligibility population:
All patients receiving a first allogeneic transplantation, in USA (except Hawai) and Canada, between 2005 and 2015, for any disease, from any donor, with any conditioning intensity and reported to the CIBMTR are included.

Data requirements:.
<u>Patient related:</u>
- Age: < 16y vs 16 to 40 vs ≥40y.
- Gender: Male vs Female
- Race (White vs. Hispanic vs. Black vs. Other)
- Karnofsky performance score at transplant: < 90 vs. 90-100
- Disease: malignant vs non malignant disease
- CMV serostatus of donor and recipient

Transplant related:

- ASBMT RFI disease risk category: Low vs Intermediate vs High
- Year of transplant: 2005 – 2010 vs 2010 – 2015
- HCT type: autologous vs allogeneic
- Graft type: Bone marrow vs peripheral blood vs cord blood
- Donor Type: Related vs Unrelated
- Donor/Recipient HLA match: HLA-identical related vs non HLA-identical related vs HLA matched unrelated vs mismatched unrelated
- Conditioning intensity: Myeloablative (MA) vs RIC/Non MA
- TBI-based conditioning: Yes vs No
- T-cell depletion: Yes (in vivo/ex vivo) vs No
- GVHD prophylaxis: CSA/Tac + MMF ± Other (not MTX) vs CSA/Tac + MTX ± Other (Not MMF) vs CSA/Tac ± Other (not MTX/MMF) vs TCD vs Other
- Acute GVHD: grade 0-1 vs. 2-4 (as time-dependent variable)
- Chronic GVHD: limited vs extensive vs none (as a time-dependent variable)

Study design:

This study aims to determine whether the season of HCT impacts on the main outcomes of relapse, NRM, GVHD, EFS and OS.

Patients will be split in 4 seasons according to the dates of meteorological seasons: Winter (December 1 to February 28 or 29), Springs (March 1 to May 31), Summer (June 1 to August 31) and Fall (September 1 to November 30). Meteorological seasons appears more adequate than astronomical seasons based on dates of equinox and solstice to describe weather and environmental changes. If methodologically too complex, the 4 seasons could be merged in 2 seasons (Winter+Springs vs Summer+Fall).

In a second analysis, patients will be split within 9 groups according to the state where the transplantation was performed. These 9 groups are based on the 9 climatically consistent regions within the contiguous United States as defined by the National Centers for Environmental Information from the National Oceanic and Atmospheric Administration (NOAA)[9]. These regions are Northwest (WA, OR, ID), West (CA, NY), Northern rockies and plains (MT, WY, ND, SD, NE), Southwest (UT, AZ, NM, CO), South (KS, OK, TX, AR, LA, MS), Upper Midwest (MN, IA, WI, MI), Ohio Valley (MO, IL, IN, OH, WV, KY, TN), Northeast (PA, MD, DE, NJ, CT, RI, MA, NY, VT, NH, ME), Southeast (AL, FL, GA, SC, NC, VA).

Adults (16 years-old and more) and children (less than 16 years-old) will be analyzed separately. The age limit of 16 years-old which is usually the upper limit of age for the end of puberty appears more accurate than the legal definition of 18 years-old to differentiate adults and children on a biologic and physiologic basis. Moreover, in many studies looking at the age as a risk factors for outcomes, the turning point of poorer outcomes is about 14 to 16 years-old.

Median time from HCT to each outcome will also be analyzed for each group and will be compared between groups in order to determine if complications occurs with the same timeframe depending on season of HCT or climatically consistent regions. Causes of death will also be compared among groups.

A subset analysis will be conducted for nonmalignant diseases. A difference of outcome depending on seasons or climate for these diseases may help to decide the best time to perform the transplantation. Indeed, for some nonmalignant diseases, such as hemoglobinopathies or bone marrow failure syndromes, HCT may not be an emergency treatment and patients could beneficiate to be transplanted in a more favorable season.

Outcomes:

Patients will be analyzed for:

- Overall survival: time to death. Death from any cause will be considered an event. Surviving patients will be censored at time of last follow-up.
- Disease Free survival: time to relapse or death from any cause.
- Non-relapse mortality: death without evidence of disease relapse. Relapse is the competing risk.
- Cause of death
- Relapse of malignant disease: NRM is the competing risk.
- aGVHD grade 2 – 4: Death is the competing risk. Patients are to be censored after relapse.
- cGVHD, any severity: Death is the competing risk. Patients are to be censored after relapse.

Statistical methodology:

Patient-, disease-, and transplant – related factors will be compared between groups using the Pearson chi-square test for discrete variables and the Kruskal-Wallis test for continuous variables. Probabilities of disease-free and overall survival will be calculated using the Kaplan Meier estimator. Values for other endpoints will be generated using cumulative incidence estimates to account for competing risks.
In multivariable analyses of seasons, the proportional hazard assumption will be examined. If violated, it will be included as a time-dependent covariate. A stepwise selection procedure will be used. Interactions between the main effect and significant covariates will be examined.

Conflicts of interest:

None

References:

1. Kmeid J, Vanichanan J, Shah DP, et al. Outcomes of Influenza Infections in Hematopoietic Cell Transplant Recipients: Application of an Immunodeficiency Scoring Index. Biology of blood and marrow transplantation : journal of the American Society for Blood and Marrow Transplantation 2016;22:542-8.
2. Choi SM, Boudreault AA, Xie H, Englund JA, Corey L, Boeckh M. Differences in clinical outcomes after 2009 influenza A/H1N1 and seasonal influenza among hematopoietic cell transplant recipients. Blood 2011;117:5050-6.
3. Ogimi C, Waghmare AA, Kuypers JM, et al. Clinical Significance of Human Coronavirus in Bronchoalveolar Lavage Samples From Hematopoietic Cell Transplant Recipients and Patients With Hematologic Malignancies. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America 2017;64:1532-9.
4. Seo S, Campbell AP, Xie H, et al. Outcome of respiratory syncytial virus lower respiratory tract disease in hematopoietic cell transplant recipients receiving aerosolized ribavirin: significance of stem cell source and oxygen requirement. Biology of blood and marrow transplantation : journal of the American Society for Blood and Marrow Transplantation 2013;19:589-96.
5. Seo S, Xie H, Leisenring WM, et al. Risk Factors for Parainfluenza Virus Lower Respiratory Tract Disease after Hematopoietic Cell Transplantation. Biology of blood and marrow transplantation : journal of the American Society for Blood and Marrow Transplantation 2018.
6. Grant WB, Bhattoa HP, Boucher BJ. Seasonal variations of U.S. mortality rates: Roles of solar ultraviolet-B doses, vitamin D, gene exp ression, and infections. The Journal of steroid biochemistry and molecular biology 2017;173:5-12.
7. Pierre K, Schlesinger N, Androulakis IP. The role of the hypothalamic-pituitary-adrenal axis in modulating seasonal changes in immunity. Physiological genomics 2016;48:719-38.

8. Menculini G, Verdolini N, Murru A, et al. Depressive mood and circadian rhythms disturbances as outcomes of seasonal affective disorder treatment: A systematic review. Journal of affective disorders 2018;241:608-26.
9. Thomas R. Karl and Walter James Koss. "Regional and National Monthly, Seasonal, and Annual Temperature Weighted by Area, 1895-1983." Historical Climatology Series 4-3 National Climatic Data Center, Asheville, NC, 38 pp 1984.

Characteristics of patients who received first allogeneic transplants in US between 2005 and 2015 reported to the CIBMTR (**CRF**)

Characteristic	Spring	Summer	Fall	Winter
No. of patients	6967	6912	6523	6320
No. of centers	183	174	177	181
Age of recipient - no. (%)				
Median (min-max)	46 (0-82.6)	45.4 (0-81.1)	46.8 (0-80.6)	46.9 (0-79.1)
0 - 9	976 (14)	1057 (15.3)	973 (14.9)	961 (15.2)
10 - 19	672 (9.6)	754 (10.9)	634 (9.7)	606 (9.6)
20 - 29	651 (9.3)	615 (8.9)	552 (8.5)	514 (8.1)
30 - 39	653 (9.4)	583 (8.4)	579 (8.9)	533 (8.4)
40 - 49	995 (14.3)	938 (13.6)	867 (13.3)	858 (13.6)
50 - 59	1503 (21.6)	1513 (21.9)	1422 (21.8)	1397 (22.1)
60 - 69	1311 (18.8)	1246 (18)	1297 (19.9)	1259 (19.9)
70+	206 (3)	206 (3)	199 (3.1)	192 (3)
Sex - no. (%)				
Male	4011 (57.6)	4067 (58.8)	3774 (57.9)	3689 (58.4)
Female	2956 (42.4)	2845 (41.2)	2749 (42.1)	2631 (41.6)
Karnofsky score prior to HCT - no. (%)				
90-100%	4458 (64)	4511 (65.3)	4131 (63.3)	4020 (63.6)
< 90%	2168 (31.1)	2060 (29.8)	2092 (32.1)	2027 (32.1)
Missing	341 (4.9)	341 (4.9)	300 (4.6)	273 (4.3)
Race - no. (%)				
Caucasian	5766 (82.8)	5722 (82.8)	5374 (82.4)	5243 (83)
African-American	578 (8.3)	618 (8.9)	585 (9)	540 (8.5)
Asian/Pacific islander	321 (4.6)	281 (4.1)	279 (4.3)	264 (4.2)
Native American	41 (0.6)	44 (0.6)	42 (0.6)	39 (0.6)
Other	33 (0.5)	28 (0.4)	28 (0.4)	33 (0.5)
Missing	228 (3.3)	219 (3.2)	215 (3.3)	201 (3.2)
Disease - no. (%)				
Acute myelogenous leukemia	2545 (36.5)	2411 (34.9)	2410 (36.9)	2272 (35.9)
Acute lymphoblastic leukemia	1031 (14.8)	959 (13.9)	912 (14)	916 (14.5)
Other leukemia	235 (3.4)	266 (3.8)	254 (3.9)	230 (3.6)
Chronic myelogenous leukemia	289 (4.1)	284 (4.1)	232 (3.6)	270 (4.3)
Myelodysplastic/myeloproliferative disorders	1285 (18.4)	1295 (18.7)	1258 (19.3)	1220 (19.3)
Other acute leukemia	66 (0.9)	65 (0.9)	68 (1)	67 (1.1)
Non-Hodgkin lymphoma	539 (7.7)	505 (7.3)	423 (6.5)	490 (7.8)
Hodgkin lymphoma	43 (0.6)	36 (0.5)	28 (0.4)	27 (0.4)
Plasma cell disorder/Multiple Myeloma	53 (0.8)	42 (0.6)	37 (0.6)	35 (0.6)

Characteristic	Spring	Summer	Fall	Winter
Other Malignancies	12 (0.2)	10 (0.1)	9 (0.1)	12 (0.2)
Breast Cancer	0	1 (0)	2 (0)	0
Severe aplastic anemia	270 (3.9)	296 (4.3)	264 (4)	238 (3.8)
Inherited abnormalities erythrocyte differentiation or function	184 (2.6)	301 (4.4)	191 (2.9)	145 (2.3)
SCID and other immune system disorders	206 (3)	241 (3.5)	213 (3.3)	198 (3.1)
Inherited abnormalities of platelets	9 (0.1)	10 (0.1)	9 (0.1)	7 (0.1)
Inherited disorders of metabolism	112 (1.6)	100 (1.4)	117 (1.8)	110 (1.7)
Histiocytic disorders	72 (1)	74 (1.1)	86 (1.3)	69 (1.1)
Autoimmune Diseases	4 (0.1)	6 (0.1)	4 (0.1)	6 (0.1)
Other diseases	12 (0.2)	10 (0.1)	6 (0.1)	8 (0.1)
Stem cell source - no. (%)				
Bone Marrow	1487 (21.3)	1634 (23.6)	1401 (21.5)	1367 (21.6)
Peripheral Blood	4093 (58.7)	3968 (57.4)	3862 (59.2)	3713 (58.8)
Cord Blood	1381 (19.8)	1299 (18.8)	1255 (19.2)	1238 (19.6)
Missing or Other	6 (0.1)	11 (0.2)	5 (0.1)	2 (0)
Donor type - no. (%)				
HLA-identical sibling	1696 (24.3)	1677 (24.3)	1457 (22.3)	1519 (24)
Identical twin	63 (0.9)	60 (0.9)	38 (0.6)	41 (0.6)
Other relative	441 (6.3)	448 (6.5)	441 (6.8)	387 (6.1)
Unrelated	4752 (68.2)	4707 (68.1)	4499 (69)	4350 (68.8)
Missing	15 (0.2)	20 (0.3)	88 (1.3)	23 (0.4)
Zip code availability - no. (%)				
No	980 (14.1)	943 (13.6)	785 (12)	840 (13.3)
Yes	5987 (85.9)	5969 (86.4)	5738 (88)	5480 (86.7)
Year of transplant - no. (%)				
2005-2009	3687 (52.9)	3699 (53.5)	3211 (49.2)	3256 (51.5)
2010-2015	3280 (47.1)	3213 (46.5)	3312 (50.8)	3064 (48.5)
Follow-up - median (min-max)	87.86 (1.61-174.01)	75.13 (2.66-171.25)	71.84 (0-168.06)	74.67 (1.55-175.1)

Proposal: 1911-265

Title:
Assessing Top Barriers to Participate in Transplant Clinical Trials for Multiple Myeloma Patients

Ehsan Malek, MD, Ehsan.Malek@UHhospitals.org, Case Western Reserve University
Leland, Metheny, MD, Leland.Metheny@uhhospitals.org, Case Western Reserve University

Research hypothesis:
There is statistically significant difference between age, racial composition and renal function of enrolled patients on STAMINA (BMT CTN 0702) trial and patients on CIBMTR registry underwent auto-transplant.

Specific aims:
Aim#1:
To assess the difference in age, racial composition and renal function between enrolled patients on STAMINA trial and patients on CIBMTR registry.

Aim#2:
To determine the rate of patients in CIBMTR registry who do not meet eligibility criteria for BMT CTN 0702.

Aim#3:
To assess the significance of each eligibility criteria lead to potential exclusion from BMT CTN 0702 trial.

Scientific impact:
Only 3% of patients participate in oncology trials in the United States [12], while the UK is at the other end of the spectrum with 35% of MM patients participating in research [13]. Older patients, those with more organ dysfunction, and patients from certain race or lower socioeconomic background are under- represented in trials [14]. This study aims to map eligibility criteria of one of the most recent and largest transplant trials, STAMINA or BMT CTN 0702 trial, in the context of CIBMTR registry. This study has potential to define top demographics barriers to recruit on transplant clinical trials in MM space; also may lead to modification of eligibility criteria that can increase or balance the enrollment in future transplant trials for MM patients.

Scientific justification:
Clinical trials are imperative for testing novel cancer therapies, advancing the science of cancer care, and determining the best treatment strategies to enhance outcomes for patients with cancer. However, barriers to clinical trial enrollment contribute to low participation in cancer clinical trials. Many factors play a role in the persistently low rates of trial participation, including financial barriers, logistical concerns, and the lack of resources for patients and clinicians to support clinical trial enrollment and retention. Furthermore, restrictive eligibility criteria often result in the exclusion of certain patient populations, which thus adds to the widening disparities seen between patients who enroll in trials and those treated in routine practice.
Real-world populations may have substantially different patient/disease characteristics compared with clinical trial cohorts. In a recent analysis of the CONNECT-MM registry, it was reported that up to 40% of patients treated in routine care would be ineligible for enrollment to randomized controlled trials in newly diagnosed MM due to common stringent eligibility criteria [1]. Importantly, this analysis showed that trial-ineligible patients had a significantly lower 3-year survival rate (63%) compared with trial-eligible patients (70%, p-value = 0.0392). Broadening eligibility criteria to increase the generalizability of clinical trial results is

a recognized need towards more informed treatment decision-making [1] [2]. Similarly, other studies reported a deep gap between clinical trial standards and real world data [3]. As a more specific example, continuous or long-term therapy, a key in MM therapy design, may have limitations in routine clinical practice, associated with toxicity burden, patient burden, and other factors such as cost [4] [5] [6]. Furthermore, given higher incidence of MM among African-Americans and the known role of socio-geo-demographic factors in enrollment on clinical trials the enrolled patients on clinical trials can be racially skewed [7][8].
Strict patient selection criteria in clinical trials is an important aspect and is the subject of a recent American Society of Clinical Oncology initiative to broaden clinical trial eligibility criteria to be more representative of patient populations [2]. Determination of the appropriate regimen for MM patients in clinical practice requires individualized assessment of various patient-related, disease-related, and treatment-related characteristics. The gap between efficacy detected in trial setting and the effectiveness in real world is also associated with toxicity and comorbidity burden, patient and physician motivation, different distributions of academic versus community centers at which patients receive their treatment, strict protocol-enforced surveillance, treatment access issues, and other determinants contributing to premature discontinuation of treatment regimens outside of clinical studies.
Here, we would compare STMINA (BMT CTN 0702) trial as a landmark auto-transplant trial to CIBMTR registry trial to define potential barriers on enrolment.

Patient eligibility population:
Inclusion:
CIBMTR database: All MM patients received Auto-transplant after 2008 and were under 70 years old at the time of diagnosis
STAMINA trial: All enrolled patients

Exclusion:
CIBMTR database: Allogeneic stem cell transplant

Study design:
The STAMINA trial was a phase III randomized trial (n= 758) that enrolled transplant-eligible MM pts within 12 months of initiating therapy and randomly assigned them 1:1:1 into 3 cohorts of 1) single autologous transplant 2) tandem autologous transplants 2) single autologous transplant plus consolidation therapy. It enrolled patients younger than 70 years old who achieved adequate autologous graft with adequate organ function (i.e., cardiac, renal, hepatic and pulmonary). It excludes non-secretory myeloma, plasma cell leukemia and patient with neuropathy greater than grade II or prior malignancy or recent heart attack 16.
Data to be collected from STAMINA (BMT CTN 0702) trial: Our group at Case Comprehensive Cancer Center analyzing the inflammatory/metabolic cytokine signature for the enrolled patients on this trial to assess the possible impact on post-transplant clinical outcome (i.e., one of the secondary endpoint of the trial). As an immediate step before launching the offered project the BMT CTN 0702 Principal Investigators will be consulted.

Data to be collected from CIBMTR:
- Geographical
- Race
- Age
- Renal impairment
- Disease subtype
- Disease stage
- Prior therapy
- Prior malignancy

- Pre-transplant disease response.
- Post- transplant therapy
- PFS
- OS

Non-CIBMTR data source:
Please see *Study Design* section under *Data to be collected from BMT CTN 0702 trial*

Conflicts of Interest:
No

References:
1. Shah, J. J. *et al.* Analysis of common eligibility criteria of randomized controlled trials in newly diagnosed multiple myeloma patients and extrapolating outcomes. *Clin. Lymphoma Myeloma Leuk.* **17**, 575–583 (2017).
2. Kim, E. S. *et al.* Broadening eligibility criteria to make clinical trials more representative: American Society of Clinical Oncology and Friends of Cancer Research Joint Research Statement. *J. Clin. Oncol.* **35**, 3737–3744 (2017).
3. Klausen, T. W. *et al.* The majority of newly diagnosed myeloma patients do not fulfill the inclusion criteria in clinical phase III trials. *Leukemia* 1 (2018).
4. Guglielmelli, T. & Palumbo, A. Multiple myeloma: is a shift toward continuous therapy needed to move forward? (2015).
5. Baz, R. *et al.* Development of a conceptual model to illustrate the impact of multiple myeloma and its treatment on health-related quality of life. *Support. Care Cancer* **23**, 2789–2797 (2015).
6. Rajkumar, S. V. & Harousseau, J. L. Next-generation multiple myeloma treatment: a pharmacoeconomic perspective. *Blood* **128**, 2757–2764 (2016).
7. Waxman, A. J. *et al.* Racial disparities in incidence and outcome in multiple myeloma: a population-based study. *Blood* blood-2010 (2010).
8. Albain, K. S., Unger, J. M., Crowley, J. J., Coltman, C. A. & Hershman, D. L. Racial disparities in cancer survival among randomized clinical trials patients of the Southwest Oncology Group. *JNCI J. Natl. Cancer Inst.* **101**, 984–992 (2009).
9. van Beurden-Tan, C. H., Franken, M., Blommestein, H., Uyl-de Groot, C. & Sonneveld, P. Systematic Literature Review and Network Meta-Analysis of Treatments for Relapsed/Refractory Multiple Myeloma Patients. *Clin. Lymphoma Myeloma Leuk.* **17**, e144 (2017).
10. Li, T., Puhan, M. A., Vedula, S. S., Singh, S. & Dickersin, K. Network meta-analysis-highly attractive but more methodological research is needed. *BMC Med.* **9**, 79 (2011).
11. Sherman, R. E. *et al.* Real-world evidence—what is it and what can it tell us. *N Engl J Med* **375**, 2293–2297 (2016).
12. Combest, A. J., Reitsma, D. J., Moseley, A., Steele, S. D. & Bonneterre, M.-E. A. Adult participation in oncology clinical trials by indication, race, and age. (2013).
13. Bird, J. *et al.* UK Myeloma Forum (UKMF) and Nordic Myeloma Study Group (NMSG): guidelines for the investigation of newly detected M-proteins and the management of monoclonal gammopathy of undetermined significance (MGUS). *Br. J. Haematol.* **147**, 22–42 (2009).
14. Booth, C. & Tannock, I. Randomised controlled trials and population-based observational research: partners in the evolution of medical evidence. *Br. J. Cancer* **110**, 551 (2014).
15. Palumbo, A. *et al.* Geriatric assessment predicts survival and toxicities in elderly myeloma: an International Myeloma Working Group report. *Blood* blood-2014 (2015).

Characteristics of patients who underwent the first autologous transplants for multiple myeloma from 2010 to 2013 in US from centers who participated in CTN0702 registered in the CIBMTR (**TED**)

Characteristic	CTN0702	All other patients
No. of patients	757	8482
No. of centers	57	53
Age of recipient - no. (%)		
Median (min-max)	56.9 (20.2-71)	59.8 (18.7-70)
thru 19	0	1 (0)
thru 29	3 (0.4)	17 (0.2)
thru 39	42 (5.5)	169 (2)
thru 49	136 (18)	1107 (13.1)
thru 59	317 (41.9)	3042 (35.9)
thru 69	253 (33.4)	4146 (48.9)
thru high	6 (0.8)	0
Sex - no. (%)		
Male	454 (60)	4775 (56.3)
Female	303 (40)	3707 (43.7)
Karnofsky score prior to HCT - no. (%)		
90-100%	514 (67.9)	4861 (57.3)
< 90%	226 (29.9)	3417 (40.3)
Missing	17 (2.2)	204 (2.4)
Stem cell source - no. (%)		
Bone Marrow	0	7 (0.1)
Peripheral Blood	757	8475 (99.9)
Race - no. (%)		
Caucasian	589 (77.8)	6672 (78.7)
African-American	133 (17.6)	1403 (16.5)
Asian	20 (2.6)	199 (2.3)
Pacific islander	1 (0.1)	21 (0.2)
Native American	2 (0.3)	30 (0.4)
Unknown	12 (1.6)	157 (1.9)
Disease status at transplant - no. (%)		
CR	130 (17.2)	1246 (14.7)
Very good partial response	275 (36.3)	2663 (31.4)
Partial response	310 (41)	3717 (43.8)
Stable disease	36 (4.8)	530 (6.2)
Progressive disease/Relapse	6 (0.8)	299 (3.5)
Missing	0	27 (0.3)
TED or CRF track - no. (%)		
TED	4 (0.5)	8147 (96.1)
CRF	753 (99.5)	335 (3.9)
Zip code availability - no. (%)		

Characteristic	CTN0702	All other patients
Zip code not available	17 (2.2)	5934 (70)
Zip code available	740 (97.8)	2548 (30)
Year of transplant - no. (%)		
2010	73 (9.6)	1952 (23)
2011	220 (29.1)	1994 (23.5)
2012	247 (32.6)	2221 (26.2)
2013	217 (28.7)	2315 (27.3)
Follow-up - median (min-max)	72.83 (3.82-104.67)	72.5 (0.43-114.41)

Selection Criteria		Removed	Remained
Inclusion	First Auto, MM, in US		
	2010-2013		
	age<70		15967
Exclusion	No Consent	146	15821
	Centers embargoed	1057	14764

Proposal: 1912-06

Title:
Understanding the costs of cellular immunotherapy for cancer

J Douglas Rizzo, MD, drizzo@mcw.edu, Medical College of Wisconsin

Research hypothesis:
There are significant patient, disease and Cellular Therapy factors which can be used to predict the cost of patient care within the first 100 days of receipt cellular immunotherapy for cancer

Specific aims:
- To describe the costs of care within the first 100 days of receipt of cellular immunotherapy for cancer
- To evaluate patient, disease and treatment characteristics that affect costs of care
- To determine how post-treatment complications, particularly cytokine release syndrome (CRS) and immune-effector cell associated neurotoxicity syndrome (ICANS), impact costs of care
- To describe the site of infusion (IP or OP) and impact on costs of care

Scientific impact:
Limited previous studies have described costs of care for cellular immunotherapy for cancer, however no multivariate analysis have been performed to better define clinical and treatment characteristics that affect those costs.

Scientific justification:
Chimeric antigen receptor (CAR) T-cells are a novel therapeutic approach for the treatment of cancer (1-3). These autologous cellular therapies involve genetic modification, most commonly using a viral vector which, after insertion in the cellular genome, leads to the expression of a chimeric protein. These proteins are designed to be expressed across the cellular membrane, including an extracellular single-chain variable fragment (scFv) that recognizes a target protein expressed in the cancer cell, and several intracellular costimulatory domains (4). The therapeutic use of these cellular products involves a multi-step process of collection, manufacturing, lymphodepleting chemotherapy and infusion. After three pivotal clinical trials in acute lymphoblastic leukemia (ALL) and diffuse large B-cell lymphoma (DLBCL) demonstrating impressive results in a population of patients with dismal prognoses (5-7), two CAR T-cells that target CD-19 were approved by the US Food and Drug Administration (FDA) and are currently in clinical use (8-10).
Use of cellular immunotherapy to treat cancer has rapidly expanded in the last 3 years. Patients have received treatment in clinical trials, and currently 2 products are available for commercial use in the US for patients with B cell malignancies. A third product for use in patients with plasma cell disorders is likely to be approved for commercial use before the end of 2019.
These therapies are very expensive, with product costs alone ranging between $373,000 and $475,000 to commercial payers. Patients treated with cellular immunotherapy generally have a high burden of disease, and complications of treatment, especially cytokine release syndrome (CRS) and immune-effector cell associated neurotoxicity syndrome (ICANS), can be life-threatening and require prolonged hospitalization and expensive treatment to manage complications. Additionally, these therapies are often used in the setting of transplantation – either to set up a consolidative HCT, or to salvage patients who have relapsed after HCT.

Patient eligibility population:
All patients who have received cellular immunotherapy for cancer at centers participating in Vizient CDB and CIBMTR between 2016 and 2018. All types of cellular therapy will be included, as available in the CDB and CIBMTR databases, including commercially available and investigational.

Data requirements:
No CIBMTR supplemental data will be required. This study will require merging clinical data from CIBMTR and encounter data from Vizient CDB. The cost "perspective" will be that of a health system encounter expenses.

Sample requirements:
No samples required

Study design:
Standard descriptive statistics, and prognostic factor analysis. Data will be included for commercially approved products, as well investigational products. Because reported expenses for investigational products may differ from commercially available products, the data will be explored to determine whether these two categories should be analyzed separately.

Non-CIBMTR data source:
We will link clinical data from CIBMTR with available data from Vizient participating centers to establish the study dataset. This will provide necessary encounter data to understand the costs of treatment. Data elements used to link include Center name and number, dates of treatment, patient sex and date of birth, disease. These procedures have led to high percentage of patient matching for HCT. Once the merged dataset is complete, a de-identified dataset will be used for analyses.
Currently, only a few centers have agreed to data sharing between Vizient and CIBMTR. This study will be initiated once enough centers have agreed to participate.

Conflicts of interest:
Corporate support of the CIBMTR

References:
1. Sadelain M. CAR therapy: the CD19 paradigm. J Clin Invest. 2015;125(9):3392-400.
2. June CH, Riddell SR, Schumacher TN. Adoptive cellular therapy: a race to the finish line. Sci Transl Med. 2015;7(280):280ps7.
3. Porter DL, Levine BL, Kalos M, Bagg A, June CH. Chimeric antigen receptor-modified T cells in chronic lymphoid leukemia. N Engl J Med. 2011;365(8):725-33.
4. Batlevi CL, Matsuki E, Brentjens RJ, Younes A. Novel immunotherapies in lymphoid malignancies. Nat Rev Clin Oncol. 2016;13(1):25-40.
5. Kochenderfer JN, Dudley ME, Kassim SH, Somerville RP, Carpenter RO, Stetler-Stevenson M, et al. Chemotherapy-refractory diffuse large B-cell lymphoma and indolent B-cell malignancies can be effectively treated with autologous T cells expressing an anti-CD19 chimeric antigen receptor. J Clin Oncol. 2015;33(6):540-9.
6. Sadelain M, Brentjens R, Riviere I, Park J. CD19 CAR Therapy for Acute Lymphoblastic Leukemia. Am Soc Clin Oncol Educ Book. 2015:e360-3.
7. Turtle CJ, Riddell SR, Maloney DG. CD19-Targeted chimeric antigen receptor-modified T-cell immunotherapy for B-cell malignancies. Clin Pharmacol Ther. 2016;100(3):252-8.

8. Maude SL, Laetsch TW, Buechner J, Rives S, Boyer M, Bittencourt H, et al. Tisagenlecleucel in Children and Young Adults with B-Cell Lymphoblastic Leukemia. N Engl J Med. 2018;378(5):439-48.
9. Neelapu SS, Locke FL, Bartlett NL, Lekakis LJ, Miklos DB, Jacobson CA, et al. Axicabtagene Ciloleucel CAR T-Cell Therapy in Refractory Large B-Cell Lymphoma. N Engl J Med. 2017;377(26):2531-44.
10. Schuster SJ, Bishop MR, Tam CS, Waller EK, Borchmann P, McGuirk JP, et al. Tisagenlecleucel in Adult Relapsed or Refractory Diffuse Large B-Cell Lymphoma. N Engl J Med. 2019;380(1):45-56.

Table 1. Characteristics of CAR-T immunotherapy reported to CIBMTR from centers participating in Vizient clinical database in 2020

Characteristic	Investigational	Commercial
No. of patients	277	1083
No. of centers	42	68
Age at CT - no. (%)		
Median (min-max)	58 (2-80)	61 (0-91)
<10	6 (2)	41 (4)
10-17	6 (2)	31 (3)
18-29	24 (9)	72 (7)
30-39	16 (6)	47 (4)
40-49	37 (13)	101 (9)
50-59	63 (23)	222 (20)
60-69	89 (32)	353 (33)
>=70	36 (13)	216 (20)
Sex - no. (%)		
Male	165 (60)	694 (64)
Female	110 (40)	389 (36)
Missing	2 (1)	0
Disease - no. (%)		
AML	5 (2)	0
ALL	46 (17)	115 (11)
CLL/PLL	2 (1)	0
NHL	102 (37)	952 (88)
HD	9 (3)	0
PCD/MM	103 (37)	0
Other malignancies	2 (1)	0
Missing	8 (3)	16 (1)
Indication for CT - no. (%)		
Relapsed, persistent or progressive disease	43 (16)	0
Suboptimal donor chimerism	1 (0)	0
Prevent disease relapse	14 (5)	1 (0)
Solid tumor	2 (1)	0
Malignant hematologic disorder	216 (78)	1082 (100)
Other indication	1 (0)	0
Year of CT - no. (%)		
2016	52 (19)	0

Characteristic	Investigational	Commercial
2017	59 (21)	15 (1)
2018	100 (36)	513 (47)
2019	66 (24)	555 (51)
Among patients with follow-up form		
No. of patients	226	799
Cytokine Release Syndrome - no. (%)		
No	111 (49)	191 (24)
Yes	114 (50)	607 (76)
Missing	1 (0)	1 (0)
Neurotoxicity - no. (%)		
No	165 (73)	415 (52)
Yes	61 (27)	383 (48)
Missing	0	1 (0)