Not for publication or presentation

A G E N D A
CIBMTR WORKING COMMITTEE FOR PEDIATRIC CANCER WORKING COMMITTEE
Honolulu, HI
Saturday, February 15, 2025, 1:00 – 3:00 PM HST

Co-Chair:	**Kirk R. Schultz, MD; The University of British Columbia, Vancouver, BC, Canada; Telephone: 604-875-2322; Email: kschultz@mail.ubc.ca**
Co-Chair:	**Akshay Sharma, MBBS; St. Jude Children's Research Hospital, Memphis, TN; Telephone: 901-595-2238; E-mail: Akshay.sharma@stjude.org**
Co-Chair:	**Parinda Mehta, MD; Cincinnati Children's Hospital, Cincinnati, OH; Telephone: 513-636-5917; E-mail: Parinda.mehta@cchmc.org**
Co-Chair:	**Christine Phillips, MD; Cincinnati Children's Hospital, Cincinnati, OH; Telephone: 513- 803-3216; E-mail: christine.phillips@cchmc.org**
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1. **Introduction**
   a. Minutes from February 2024 (Attachment 1)

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

3. **Presentations, Publications or Submitted papers**
   a. **PC19-03** Impact of Extramedullary Disease on the Outcomes after Allogeneic Hematopoietic Transplantation in Children and Young Adults with Acute Myeloid Leukemia – a CIBMTR Analysis. (K Rao/ H Rangarajan/ P Satwani/ D Chellapandian/ B Savani/ J Silva). ***Poster Presentation, ASH 2024.***
   b. **AC17-01** CD-19 chimeric antigen receptor T-cells with or without hematopoietic cell transplantation for treatment of refractory acute lymphocytic leukemia (M Perales/ J Park/ S Nikiforow). ***Submitted.***

c. **PC22-01** Impact of graft versus host disease following allogeneic hematopoietic cell transplantation on leukemia free survival in hematologic malignancies within the pediatric disease risk index risk stratification (A Bauchat/ M Qayed). ***Oral Presentation, Tandem 2025***

4. **Studies in progress** (Attachment 3)
   a. **PC19-02** Does mixed peripheral blood T Cell Chimerism predict relapse? (S Prockop/ J Boelens/ K Peggs). **Protocol Development**
   b. **PC19-03** The impact of pre-transplant extramedullary disease on the outcome of Allogeneic Hematopoietic Cell Transplantation for Acute Myeloid Leukemia in children (H Rangarajan/ P Satwani /D Chellapandian). **Manuscript Preparation.**
   c. **CT20-02** Resource utilization with chimeric antigen receptor T cells (M Battiwalla/ H Rangarajan/ C Scheckel). **Protocol Development.**
   d. **PC20-02** Germline genetics of pediatric Myelodysplastic Syndromes (J Poynter/ L Spector). **Data File Preparation.**
   e. **PC22-01** Impact of graft versus host disease following allogeneic hematopoietic cell transplantation on leukemia free survival in hematologic malignancies within the pediatric disease risk index risk stratification (A Bauchat/ M Qayed). **Manuscript Preparation**
   f. **PC22-02** Evaluating predictors of access and outcomes with hematopoietic cell transplantation in pediatric and adolescent patients with relapsed/refractory classical Hodgkin lymphoma after treatment on an initial cooperative group clinical trial (S Castellino/ J Kahn). **Protocol Development.**
   g. **PC23-01** Post-transplant cyclophosphamide vs. TCR αβ/CD19+ deplete approaches for haploidentical transplant in pediatric patients with acute leukemias and myelodysplastic syndrome: A CIBMTR/EBMT collaborative study (A Li/ H Rangarajan/ P Satwani). **Data File Preparation.**
   h. **PC23-02** Comparison of bone marrow and peripheral blood stem cells as graft source in children undergoing allogeneic hematopoietic stem cell transplantation for hematological malignancies with unmanipulated haploidentical grafts utilizing post-transplant cyclophosphamide as GvHD prophylaxis (A Srinivasan/ J Krueger). **Protocol Development**
   i. **PC24-01** Transplantation and cellular therapy for children and young adults with down's syndrome and acute leukemia (L Appell/ S Rotz). **Protocol development.**

5. **Future/proposed studies**
   a. **PROP 2410-40** Comparison of different TBI doses in relation to MRD status in pediatric acute lymphoblastic leukemia (T Takahashi/ A Keating) (Attachment 4)
   b. **PROP 2410-85** Is There an Optimal CD34+ Cell Dose In Pediatric Allogeneic Hematopoietic Cell Transplantation Performed for Malignant Diseases? (E Fraint/ T Knight) (Attachment 5)
   c. **PROP 2410-94** Effect of disease burden and pre-transplant therapy in pediatric patients with myelodysplastic syndrome in the current era (J Rossoff/ S Chaudhury) (Attachment 6)
   d. **PROP 2410-176** Comparison of Risk Factors Associated with Early and Late Disease Relapse Among Patients in Complete Remission at One Month after Tisagenlecleucel (Kymriah) therapy in Pediatric, Adolescent and Young Adult (AYA) Patients Treated for Relapsed or Refractory (r/r) B Cell Acute Lymphoblastic Leukemia (B Cell ALL) (L Davis/ P Satwani) (Attachment 7)
   e. **PROP 2410-182** Impact of Planned Post-Transplant Granulocyte Colony Stimulating Factor (G-CSF) on Transplant-Related Outcomes in Pediatric Patients with Malignant Disease Undergoing Haploidentical Hematopoietic Cell Transplant (HCT) with Post-Transplant Cyclophosphamide (ptCy) for Graft vs. Host Disease (GVHD) Prophylaxis (L Davis/ P Satwani) (Attachment 8)
   f. **PROP 2410-200** Hematopoietic Stem Cell Transplant Outcomes for Infant B-cell Acute Lymphoblastic Leukemia (N Lalefar/ H Rangarajan) (Attachment 9)

g. **PROP 2410-204** Transplantation Outcomes for Children with Hypodiploid Acute Lymphoblastic Leukemia in the Modern Era (A Bidgoli/ U Kapoor) (Attachment 10)

Proposed studies; not accepted for consideration at this time

h. **PROP 2408-14** Comparing the Progression-free Survival and Overall Survival of Autologous Stem Cell Transplantation and Allogeneic Stem Cell Transplantation in Refractory Langerhans Cell Histiocytosis (M Pamukcuoglu). ***Dropped due to small sample size.***
i. **PROP 2410-73** The impact of prior allogeneic HSCT on outcomes following subsequent CD**19**.CAR-T cell infusion for pediatric patients with relapsed/refractory B-cell ALL (S Naik/ M Pulsipher). ***Dropped due to overlap with current study/publication.***
j. **PROP 2410-136** Comparison of alternative donor options in pediatric AML with varying residual disease status (T Takahashi/ A Keating). ***Dropped due to overlap with published study***
k. **PROP 2410-207** The Impact of Hematopoietic Cell Transplantation in Complete Remission with Incomplete Count Recovery in Pediatric AML (E Krieger/ K Magee). ***Dropped due to supplemental data needed.***
l. **PROP 2410-211** Impact of KYMRIAH potency on incidence of relapse and cytokine release syndrome (U Kapoor/ P Satwani). ***Dropped due to supplemental data needed.***

6. Other business

MINUTES AND OVERVIEW PLAN
CIBMTR WORKING COMMITTEE FOR PEDIATRIC CANCER
San Antonio, TX
Thursday, February 22, 2024, 1:00 – 3:00 PM CT

Co-Chair:	**Muna Qayed, MD, MSc; Emory University School of Medicine, Atlanta, GA; Telephone: (404)785-1112; Email: muna.qayed@choa.org.**
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Co-Chair:	**Parinda Mehta, MD; Cincinnati Children's Hospital, Cincinnati, OH; Telephone: 513-636-5917; E-mail: Parinda.mehta@cchmc.org.**
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1. Introduction

The Pediatric Cancer Working Committee (PCWC) meeting was called at 1:02 pm CST on Thursday, February 22, 2024, by Dr. Amy Moskop. The chairs, statistical team, and SDs, Rachel Phelan & Amy Moskop, were present at the meeting. Attendees were asked to have their Tandem name badges scanned at the front gate for attendance purposes and to maintain the committee membership roster. Virtual attendees were reminded that they are part of the committee membership roster as well.
Dr. Moskop welcomed the attendees on behalf of the working committee leadership and introduced herself as the SD who is overseeing PCWC for this year's meeting and she introduced the current WC leadership. Dr. Moskop thanked the leaving chair, Dr. Muna Qayed, for her contribution to the PCWC and welcomed Dr. Parinda Mehta and Dr. Christine L. Phillips as incoming chairs. Dr. Moskop disclosed the WC leadership COI and funding disclosures. Then, Dr. Moskop welcomed Dr. Qayed as the next speaker.

Dr. Qayed provided an overview of HCT, CT, and PRO data available in the CIBMTR database. She also shared CIBMTR resources, programs, and WC materials. Dr. Qayed provided details for Publicly Available Research Dataset, Early Career Investigators program (ECI), and Tandem Collaborative session. Dr. Qayed introduced Dr. Schultz as the next speaker.

2. Accrual summary

Dr. Schultz introduced himself to the attendees and reminded them about WC participation, membership, and rules of authorship. He proceeded to take the attendees through the committee's goals, expectations, and limitations. He reminded the attendees of CIBMTR rules for authorship. Then he directed the attendees' attention to the accrual summaries included in the meeting materials. Dr. Schultz provided a concise summary of the pediatric data that is available in the CIBMTR database. Dr. Schultz introduced Dr. Sharma as the next speaker.

3. Presentations, Published or Submitted Papers

Dr. Sharma announced that PC20-01 was published as two papers. The first publication is a manuscript with focus on CNS Tumors; it was published in Bone Marrow Transplant. Second is a commentary with focus on Neuroblastoma which was published with TCT. He also announced that SC21-08 manuscript is under preparation after successful presentations at EBMT and ASPHO/PTCTC.

a. **PC20-01a** Knight TE, Ahn KW, Hebert KM, Atshan R, Wall DA, Chiengthong K, Rotz SJ, Fraint E, Rangarajan HG, Auletta JJ, Sharma A, Kitko CL, Hashem H, Williams KM, Wirk B, Dvorak CC, Myers KC, Pulsipher MA, Warwick AB, Lalefar NR, Schultz KR, Qayed M, Broglie L, Eapen M, Yanik GA. Effect of autograft CD34+ dose on outcome in pediatric patients undergoing autologous hematopoietic stem cell transplant for central nervous system tumors. **Transplantation and Cellular Therapy. 2023 Jun 1; 29(6):380.e1-380.e9. doi:10.1016/j.jtct.2023.03.024. Epub 2023 Mar 27. PMC10247464.**

b. **PC20-01b** Knight TE, Ahn KW, Hebert KM, Atshan R, Wall DA, Chiengthong K, Lund TC, Prestidge T, Rangarajan HG, Dvorak CC, Auletta JJ, Kent M, Hashem H, Talano JA, Rotz SJ, Fraint E, Myers KC, Leung W, Sharma A, Bhatt NS, Driscoll TA, Yu LC, Schultz KR, Qayed M, Broglie L, Eapen M, Yanik GA. No impact of CD34+ cell dose on outcome among children undergoing autologous hematopoietic stem cell transplant for high-risk neuroblastoma. **Bone Marrow Transplantation. 2023 Dec 1; 58(12):1390-1393. doi:10.1038/s41409-023-02092-3. Epub 2023 Sep 4**.

c. **SC21-08:** Optimizing Haploidentical Donor Selection for Pediatric HCT. (Liberio N/ Broglie L), **Presented at EBMT 2023 and ASPHO/PTCTC 2023. Manuscript in Preparation.**

4. Studies in Progress

Then, Dr. Sharma provided an overview of the WC portfolio of the active studies. Dr. Sharma introduced Dr. Mehta and Dr. Phillips as the next speakers for overview of studies in progress and Tandem proposal presentations.

a. **PC19-02:** Does mixed peripheral blood T Cell Chimerism predict relapse? (Prockop S/Boelens J/Peggs K), **Protocol Development.**
b. **PC19-03:** The impact of pre-transplant extramedullary disease on the outcome of Allogeneic Hematopoietic Cell Transplantation for Acute Myeloid Leukemia in Children. (Rangarajan H/ Satwani P/Chellapandian D), **Analysis.**
c. **PC20-02:** Germline genetics of pediatric Myelodysplastic Syndromes (MDS). (Poynter J/ Spector L), **Sample Typing.**
d. **PC22-01:** Impact of graft versus host disease following allogeneic hematopoietic cell transplantation on leukemia free survival in hematologic malignancies within the pediatric disease risk index risk stratification. (Bauchat A/Qayed M), **Protocol Development.**

e. **PC22-02:** Evaluating predictors of access and outcomes with hematopoietic cell transplantation in pediatric and adolescent patients with relapsed/refractory classical Hodgkin lymphoma after treatment on an initial cooperative group clinical trial. (Castellino S/Kahn J), **DUA and Protocol under Development.**
f. **SC21-08:** Optimizing Haploidentical Donor Selection for Pediatric HCT. (Liberio N/ Broglie L), **Manuscript in preparation.**
g. **PC23-01**: Post-transplant cyclophosphamide vs. TCR αβ/CD19+ deplete approaches for haploidentical transplant in pediatric patients with acute leukemias and myelodysplastic syndrome. (Li A/Rangarajan H/Satwani P), **Protocol Development.**
h. **PC23-02:** Comparison of Bone Marrow and Peripheral Blood Stem Cells as graft source in Children undergoing allogeneic Hematopoietic Stem Cell Transplantation for Hematological malignancies with unmanipulated haploidentical grafts utilizing post-transplant cyclophosphamide as GvHD prophylaxis. (Srinivasan A/ Krueger J), **Protocol Development.**

5. Future/Proposed Studies

Dr. Mehta welcomed the attendees and reminded them to remain involved in the PCWC ongoing studies. Then, she walked the attendees of the guidelines to submit Tandem proposals and the scoring logistics for the proposal presentations. She also reminded the presenters that each presentation duration is five minutes followed by five minutes for the Questions & Answers session. Dr. Mehta introduced Dr. Phillips as the next speaker to introduce each proposal title and the presenters to the audience in the following order.

a. **PROP 2310-91:** Evaluation of Allogeneic Hematopoietic Cell Transplantation Outcomes and Prognostic Factors in Acute Megakaryoblastic Leukemia: A CIBMTR and EBMT Joint Study, (Sharma A/ Bhatt N).

Dr. Bhatt presented the proposal on behalf of the group. The proposal hypothesizes that Allogeneic hematopoietic cell transplantation (Allo HCT) provides curative therapy for patients with Acute Megakaryoblastic Leukemia (AMKL), with improved outcomes in those who are transplanted in first complete remission.

<u>Comments from discussion:</u>

i. There was a question from the group about distinguishing between the patients diagnosed with Down Syndrome vs the patients that don't have Down Syndrome diagnosis. Dr. Bhatt replied that this is a great question, adding that the proposal was submitted a couple of years prior to this presentation. He also stated that there were 22 patients with Down Syndrome in the previous proposal cohort that looked at the years between 2000 and 2022; he also added that most of these patients had an HCT prior to 2010. If the proposal is selected, the study team will investigate the number of patients with this diagnosis to stratify the study population accordingly.
ii. An attendee suggested using the Pediatric disease risk index (DRI) score since the data is going to be more contemporary. There is a limitation since this study focus is AMKL but cytogenetics is an important factor for this population. The attendee added that in recent years she gained knowledge from her pathologist colleague that RAM phenotype AML can be classified as AMKL but CIBMTR doesn't have that level of data which one of the study limitations. Dr. Bhatt added that CIBMTR doesn't have granular cytogenetics data on TED retrieval; NUP 98, or CBFA2T3 – GLIS2 mutations are important but something to consider for the study population. Then the attendee added to consider that EBMT classification for cytogenetics is different than CIBMTR and EBMT doesn't use Pediatric DRI. Dr. Bhatt thanked the attendee for her input.

b. **PROP 2310-60:** Transplantation and Cellular Therapy for Children and Young Adults with Down's Syndrome and Acute Leukemia, (Appell L/ Rotz S).

Dr. Appell presented the proposal on behalf of the group. The proposal hypothesizes that children and adolescent and young adult (AYA) patients with Down syndrome (DS) and Acute Leukemia will have improved hematopoietic cell transplantation (HCT) outcomes in the more recent era. Further, it hypothesizes that children and AYA with DS and relapsed/refractory Acute Lymphoblastic Leukemia (ALL) undergoing CAR T-cell therapies will have improved outcomes compared to those who underwent HCT.

<u>Comments from discussion:</u>

i. *A question if the patients who received both CAR-T and HCT are going to excluded from the study population. Dr. Appell replied that the goal is to compare CAR-T to HCT; but the study team will investigate the patients that had HCT after CAR-T treatment. The attendee asked if the team will look at patients who had HCT before and after CAR-T. Dr. Appell replied that one of the proposed study limitation is investigating many objectives. She added that one of these objectives is to investigate the patient who had HCT as a cohort and investigate the patients who had CAR-T as a cohort then compare the two cohorts. She added another objective of the study is looking at patients who are getting consolidative HCT. The attendee asked if the number of patients who received CAR-T before or after CAR-T is sufficient for a study (N= 37), Dr. Appell replied that she thinks there are enough cases but we will have statistical input regarding these analyses.*
ii. *There was a comment about the poor forecasted outcomes of leukemia patients with Down Syndrome which can result in difficult decision making in regards HCT vs CAR-T treatments. He added this study will answer an important question to improve supportive case for the patients.*
iii. *There was a comment about including both AML & ALL in the study and how the outcomes are too different to compare. The attendee added that CAR-T and Allo HCT are not comparable since these two treatments & their outcomes are different. She added that CAR-T is used to treat B ALL, but the real question is how to treat Down Syndrome patients using Allo-HCT.*
iv. *An attendee agreed with the previous point by stating that the study should not compare All HCT and CAR-T at all. Stating that CAR-T is considered for many patients; sometimes before and others after Allo HCT. He added that some centers still treat patients with good outcomes with HCT while other centers are treating them with CAR-T first. He suggested investigating sequential cases (CAR T to HCT, HCT to CAR T); if a patient relapsed to focus on the order of treatments, and subsequent outcomes. He added that including patients with only CAR-T will be a limitation for the study population. Dr. Appell stated that this will be this study's focus due to the lack of literature on the topic to support decision making for health care providers. The attendee added including as many MRD cases in the study as possible.*
v. *A comment that Pediatric Real World CAR-T Consortium's Holly Pacenta collected data for 50 patients with Down Syndrome and he suggested that this study team should consider collaborating the two studies to avoid redundant work. The attendee added that in Chromosome 21, 4 of the 6 interferon receptors are present, hence, Down Syndrome is being reconsidered as interferonopathy. He added to investigating the number of patients of samples associated with the interferonopathy; further investigating serum or peripheral blood. The attendee added that he is interested in collaborating with the study team to investigate these questions further.*
vi. *A comment that not all CAR-T data is reported to CIBMTR; This is another study limitation that the study team should consider when designing this study. Dr. Moskop addressed the comment by stating that 60-70% of CAR-T data is reported to CIBMTR.*

c. **PROP 2310-106:** Influence of Pre-Transplant Chemotherapy Cycles on Allogeneic Transplant Outcomes in Pediatric Acute Myeloid Leukemia Patients in Complete Remission, (Krieger E/ Hoover A).

Dr. Krieger presented the proposal on behalf of the group. The proposal hypothesizes that in pediatric AML patients undergoing HCT in CR1, ≥ 3 cycles of chemotherapy prior to HCT is associated with a decreased overall survival (OS) and higher treatment-related mortality (TRM) compared to patients who receive <3 chemotherapy cycles before HCT.

<u>Comments from discussion:</u>

i. *There was a comment to the study team about considering the effect of conditioning regimen since the study population is large. The attendee added the study team should consider Busulfan, Cytoxan, Treosulfan, vs others. He also suggested looking at TBI conditioning regimen and the number of chemotherapy cycles given to a patient before the disease status is complete remission. Dr. Krieger replied that the study team is trying to keep the study focused on a specific question, but the study team will propose these questions during protocol development. The attendee added that answering the proposed questions will help with patients' treatment and care.*
ii. *There was a comment about TACL team investigating a study similar to the proposed study that looks at the number of chemotherapy cycles to achieve complete remission. The attendee stated that this proposal is slightly different and he requested more details on the proposed study: He asked if the study team is proposing that 5% of patients were in complete remission? Dr. Krieger replied that the study population was stratified based on their remission and MRD status. The attendee added that these are primary refractory patients defined by the second cycle of chemotherapy. Dr. Krieger replied that these patients' disease status is CR1. The attendee replied that these cases are CR1 meaning a good percentage of these patients will be refractory and some will be cytogenetics driven. Dr. Krieger replied that the patient with high-risk cytogenetics will be excluded from the study population with a focus on patients who are in CR after 1 or 2 inductions. The attendee suggested that the study team investigate the cytogenetics risks.*
iii. *There was a comment about the practical importance of this study's question regarding COG protocol. These protocols are requesting that patients continue with chemotherapy while in CR and are otherwise ready for HCT. There is sometimes a need to remove these patients from COG protocol to move to HCT. If the proposed study results supports that these patients don't need to continue with chemotherapy therapy treatment will be helpful for the community.*
iv. *An attendee agreed with the pervious comment. He also recommended that the study team review and use COG high risk criteria to help guild the practice. Dr. Krieger stated that the study team assumed that the study population consist of patient in early CR, but the group will consider expanding the study population.*
v. *A comment that there is bias in the proposed study making it hard to change practice. The attendee added that she doesn't consider giving an extra cycle of chemotherapy for a patient who is MRD- and has a donor since there are infection or relapse concerns. She added that the study will not capture these patients since the study population consists of patients who proceeded to HCT. Dr. Krieger replied that answering the question about the patients who lack organ function needed for HCT requires collaboration between CIBMTR and COG. Dr. Krieger added that she isn't aware of such collaboration. The PCWC statistician replied by stating that there's an ongoing study that requires linkage between CIBMT and COG data. Dr. Krieger expressed her enthusiasm for such a study, adding the study she is proposing will consider patients that were treated at a COG centers and non-COG centers.*

vi. A question about the treatment for FLT3 mutation. He also asked about the effect of TKI duration on the outcomes. Dr. Krieger replied that the study team didn't consider FLT3 in the study design but that is a great question to consider.

vii. An attendee announced that there is an ongoing study with PTCTC similar to the proposed study and the possibility of future collaboration between CIBMTR and PTCTC.

d. **PROP 2310-170:** Comparison of total body irradiation vs chemotherapy-based conditioning regimens for infants with high risk KMT2A-rearranged infantile acute lymphoblastic leukemia undergoing allogenic stem cell transplantation, (Lake A/ Duncan C).

Dr. Lake presented the proposal on behalf of the group. The proposal hypothesizes that Chemotherapy-based conditioning regimens are non-inferior in survival and transplant related mortality compared with TBI-based regimens in infants with high risk (HR) KMT2A-rearranged (KMT2Ar) Infantile Acute Lymphoblastic Leukemia (ALL).

<u>Comments from discussion:</u>

i. There was a question if the study population includes AML and ALL cases. Dr. Lake replied that this study population consist of ALL cases only.

ii. There was a question about the data granularity relating to neurological issues like seizures, neuro cognitive delays, developmental delays. Dr. Lake replied that looking at neurological issues, besides seizures, will be difficult since CIBMTR doesn't collect this data. Dr. Lake added that there are studies looking into Neuro cognitive looking at TBI for infants but not through CIBMTR. PCWC SD added that CIBMTR recently started collecting seizure data on the CRF forms totaling 50 cases from this proposal cohort but this remains limited.

iii. There was a question if the study objective is to show that TBI is a better approach for infants. Dr. Lake replied that it is potentially a reasonable treatment to present to the patient's parents, providing the parents with more treatment options. Dr. Lake added that the study result may prove that TBI is superior to chemotherapy followed by HCT. He added that the relapse rate is high for the patients who received chemotherapy followed by HCT.

iv. There was a comment about the FORUM trial study resulted in a shift to give TBI to patients older than 4 years rather than at 2 years old. The attendee added that the study showed that patients between 2 and 4 years old had a significant decrease in overall survival rate. He added that the physicians are hesitant to use TBI especially for an infant, less than 1 or 2 years old. He expressed that the proposed study will be interesting, but he emphasized that if TBI is used then there is a reason for using it; adding such as the patients was high risk.

v. There was a comment about the proposed study's impact on the field. MRD is one of the main driving factors for HCT. If the proposed study outcomes show the impact of non-radiation conditioning regimen for patients who are MRD-. The attendee addressed the pervious comment stating that the age at diagnosis in the proposed study and FORUM study is very similar between the two study populations.

vi. There was a comment to agree with the previous two points adding that using TBI for infants is limited in practice to extreme cases. The attendee added if the proposed study results are favorable, there is a still a need for alternative chemotherapy agents. She added that it is difficult to retrieve neurological complications data from CIBMTR retrieval. This is a study limitation that can mislead the study results.

vii. There was a question about factoring CAR-T for the proposed study population. Dr. Lake informed the attendee that CAR-T isn't factored in this population. The attendee

added that care providers would choose CAR-T treatment when appropriate for a patient so it is important. Then, the attendee added that there's always a compelling reason for treating patients with TBI. She added that most providers follow recommendations from Japanese or BuFlu Thiotepa.

viii. *There was a comment about one third of patients in CR1 received TBI and TBI for patients in CR2 but that can be related to high-risk disease.*

e. **PROP 2310-233:** Transplant outcomes in pediatric, adolescent, and young adult patients with hypoplastic myelodysplastic syndrome.

Dr. Chakravarthy presented the proposal on behalf of the group. The proposal hypothesizes that certain patients with hypoplastic MDS may not require a myeloablative conditioning (MAC) regimen prior to hematopoietic cell transplant (HCT) and may receive a reduced intensity conditioning (RIC) with overall similar outcomes with less toxicities.

<u>Comments from discussion:</u>

i. *A question about disease biology regarding patients' ages; the attendee suggested restricting the study population to pediatrics patients. Dr. Chakravarthy agreed with the attendees.*
ii. *A comment from an attendee, a SD from CIBMTR, about the ongoing CIBMTR study that investigates AML and MDS for AYA, adolescent and young adult, which includes patients up to age 39 years old.*
iii. *An attendee expressed her concerns about the population's small size. Dr. Chakravarthy replied that this is a valid concern; adding that the presented table included data between 2013 and 2021; and the study team will consider expanding the years of HCT to 2008 to 2022, which should increase the population size.*
iv. *One of the PCWC leadership chairs expressed the possibility of collaborating with EBMT to complete compelling studies to benefit the field. He added that this collaboration will help with a study that has a small sample size but this does require more complexity in protocol development.*
v. *One of the PCWC leadership chairs addressed the question about combining adults and pediatrics in the proposed study population. Adding that not all adults diagnosed with MDS receive an HCT. She also added that including adults will address the population size concern, but the study team have to investigate how similar the adults/AYA patients and pediatric patients are, which may require an input from an AYA/adult provider.*
vi. *A comment about remaining cautious about combining pediatrics with AYA since young adults' biology can be similar to adults' biology. There is concern that there may be some patients (AYAs) with certain syndromes that were not previously captured in older CIBMTR data.*
vii. *A question about excluding patients who had a second HCT. Dr. Chakravarthy replied these patients are excluded due to the impact of second HCT on toxicity and type of conditioning regimen the patient would receive. The attendee asked if this would miss a relapse, graft failure or other endpoint from the first transplant. Dr. Chakravarthy replied with a yes.*
viii. *An attendee pointed out that the study population exclude patients with bone marrow failure disorders starting in 2008. He added that there is no certainty that these patients with bone marrow failure would be excluded from the study population due to how these data were collected in the past.*
ix. *An attendee announced that UCSF, Oakland is developing and MDS registry if the study team would like to explore this registry and possible collaboration.*

6. Dropped proposed studies

The committee received the following additional studies proposal, but these proposals were not selected for presentation at the Tandem meeting, for the reason outlined below.

a. **Prop 2309-18:** Determining the Optimal CD34+ Cell Dose and TNC Content in Pediatric Allogeneic Hematopoietic Cell Transplantation Performed for Malignant Diseases.
Dropped due to feasibility (few patients with both TNC and CD34 available).
b. **PROP 2310-43:** Risk Factors Associated with Late Disease Relapse Among Patients in Complete Remission at One Year after Tisagenlecleucel (Kymriah) therapy in Pediatric, Adolescent and Young Adult (AYA) Patients Treated for Relapsed or Refractory (r/r) B Cell Acute Lymphoblastic Leukemia (B Cell ALL).
Dropped due to feasibility (too few patients and events for analysis at this time).
c. **PROP 2310-68:** Does Augmenting Total Body Irradiation with a Cranial or Craniospinal Boost before Stem Cell Transplantation Protect Against Post-Transplant Central Nervous System Relapse in Pediatric Patients with Acute Lymphoblastic Leukemia?
Dropped due to feasibility (all times when radiation given is not collected).
d. **PROP 2310-81:** Validating the Disease Risk Stratification System (DRSS) in Pediatric Patients: A collaborative study between CIBMTR and EBMT.
Dropped due to overlap with a published study.
e. **PROP 2310-129:** Does radiation-based preparation improve transplant outcomes in pediatric AML patients with CNS involvement?
Dropped due to overlap with ongoing study.
f. **PROP 2310-131:** Post HCT outcomes for pediatric AML in remission with incomplete hematologic recovery prior to conditioning.
Dropped due to feasibility (data not collected by CIBMTR).
g. **PROP 2310-144:** Evaluating the Efficacy of Consolidative Allogeneic Hematopoietic Stem Cell Transplantation in Pediatric Pre B-ALL Patients Achieving CR with Tisagenlecleucel CAR T-cell Therapy.
Dropped due to overlap with ongoing study.
h. **PROP 2310-214:** Outcomes of autologous stem cell transplant for relapsed/refractory germ cell tumors in women**.**
Dropped due to feasibility (ovarian germ cell tumors are not currently collected as disease indication, forms to be updated).

7. Concluding Notes

The meeting was adjourned at 2:28 p.m. After the new proposals were presented, each attendee had the opportunity to vote using the Tandem mobile application or Tandem website. Based on the voting results, current scientific merit, and impact of the studies on the field, the PCWC leadership will determine which studies will move forward as the committee's research portfolio for the upcoming year.

Working Committee Overview Plan 2024-2025		
Study Number and Title	**Current Status**	**Chairs Priority**
PC19-02: Does mixed peripheral blood T cell chimerism predict relapse?	Protocol development/ Data file preparation	2
PC19-03: The impact of pre-transplant extramedullary disease on the outcome of allogeneic hematopoietic cell transplantation for Acute Myeloid Leukemia in Children- A combined CIBMTR and EBMT analysis.	Analysis/ Manuscript preparation	1
PC20-02: Germline genetics of pediatric myelodysplastic syndromes.	Sample Typing/ Analysis	3
PC22-01: Impact of Graft Versus Host Disease following Allogeneic Hematopoietic Cell Transplantation on Leukemia free survival in Hematologic Malignancies within the pediatric disease Risk Index Risk Stratification.	Protocol development/ Datafile preparation	4
PC22-02: Evaluating predictors of access and outcomes with Hematopoietic Cell Transplantation (HCT) in pediatric and adolescent patients with relapsed/refractory classical Hodgkin Lymphoma (cHL) after treatment on an initial cooperative group clinical trial.	Protocol development/ DUA development	7
PC23-01: Post-transplant Cyclophosphamide vs. TCR αβ/CD19+ deplete approaches for Haploidentical Transplant in pediatric patients with Acute Leukemias and Myelodysplastic Syndrome: A CIBMTR/EBMT collaborative study.	Protocol pending	5
PC23-02: Comparison of bone marrow and peripheral blood stem cells as graft source in Children undergoing Allogeneic Hematopoietic Stem Cell Transplantation for Hematological malignancies with unmanipulated haploidentical grafts utilizing post-transplant Cyclophosphamide as GvHD prophylaxis.	Protocol pending	6

Not for publication or presentation

Working Assignments for Working Committee Leadership (March 2024)	
Kirk Schultz	**PC19-02:** Does mixed peripheral blood T cell chimerism predict relapse? **PC19-03:** The impact of pre-transplant extramedullary disease on the outcome of allogeneic hematopoietic cell transplantation for Acute Myeloid Leukemia in Children – A combined CIBMTR and EBMT analysis. **PC23-01:** Post-transplant Cyclophosphamide vs. TCR αβ/CD19+ deplete approaches for Haploidentical Transplant in pediatric patients with Acute Leukemias and Myelodysplastic Syndrome: A CIBMTR/EBMT collaborative study.
Akshay Sharma	**PC20-02:** Germline genetics of pediatric myelodysplastic syndromes. **PC23-01:** Post-transplant Cyclophosphamide vs. TCR αβ/CD19+ deplete approaches for Haploidentical Transplant in pediatric patients with Acute Leukemias and Myelodysplastic Syndrome: A CIBMTR/EBMT collaborative study.
Parinda Mehta	**PC22-01:** Impact of Graft Versus Host Disease following Allogeneic Hematopoietic Cell Transplantation on Leukemia free survival in Hematologic Malignancies within the pediatric disease Risk Index Risk Stratification. **PC23-02:** Comparison of bone marrow and peripheral blood stem cells as graft source in Children undergoing Allogeneic Hematopoietic Stem Cell Transplantation for Hematological malignancies with unmanipulated haploidentical grafts utilizing post-transplant Cyclophosphamide as GvHD prophylaxis.
Christine Phillips	**PC22-02:** Evaluating predictors of access and outcomes with Hematopoietic Cell Transplantation (HCT) in pediatric and adolescent patients with relapsed/refractory classical Hodgkin Lymphoma (cHL) after treatment on an initial cooperative group clinical trial.

Characteristics of patients aged <= 18 years transplanted between 2008 - 2024, and reported to the CIBMTR

Table 1: PCWC 2025 accruals: Allogeneic Transplants

Characteristic	TED, N (%)	CRF, N (%)	Total
Primary disease - no. (%)			
AML	4814 (34.5)	1793 (38.4)	6607 (35.5)
ALL	6196 (44.4)	1853 (39.7)	8049 (43.2)
Other Acute Leukemia	427 (3.1)	130 (2.8)	557 (3.0)
CML	377 (2.7)	101 (2.2)	478 (2.6)
Other Leukemia	37 (0.3)	8 (0.2)	45 (0.2)
MDS	1396 (10.0)	548 (11.7)	1944 (10.4)
NHL	476 (3.4)	147 (3.2)	623 (3.3)
HD	122 (0.9)	66 (1.4)	188 (1.0)
Plasma cell disorder	2 (0.0)	3 (0.1)	5 (0.0)
Solid Tumor	119 (0.9)	15 (0.3)	134 (0.7)
Donor type - no. (%)			
HLA-identical sibling	4084 (29.2)	599 (12.8)	4683 (25.1)
Other related	3249 (23.3)	830 (17.8)	4079 (21.9)
8/8 matched URD	2938 (21.0)	734 (15.7)	3672 (19.7)
7/8 mismatched URD	947 (6.8)	318 (6.8)	1265 (6.8)
<= 6/8 mismatched URD	44 (0.3)	26 (0.6)	70 (0.4)
Multi-donor	116 (0.8)	52 (1.1)	168 (0.9)
Unrelated (matching TBD)	1182 (8.5)	108 (2.3)	1290 (6.9)
Cord blood	1404 (10.1)	1997 (42.8)	3401 (18.3)
Not reported	2 (0.0)	0 (0.0)	2 (0.0)
Graft Type - no. (%)			
Bone marrow	7826 (56.0)	1684 (36.1)	9510 (51.0)
Peripheral blood	4691 (33.6)	970 (20.8)	5661 (30.4)
Cord blood	1391 (10.0)	1984 (42.5)	3375 (18.1)
Not Reported	58 (0.4)	26 (0.6)	84 (0.5)
Conditioning Regimen Intensity - no. (%)			
MAC	10702 (76.6)	3722 (79.8)	14424 (77.4)
RIC	1446 (10.4)	323 (6.9)	1769 (9.5)
NMA	491 (3.5)	142 (3.0)	633 (3.4)
Needs Review	1327 (9.5)	477 (10.2)	1804 (9.7)
GVHD prophylaxis - no. (%)			
None	213 (1.5)	245 (5.3)	458 (2.5)
Ex-vivo T-cell depletion	862 (6.2)	187 (4.0)	1049 (5.6)
CD34 selection	398 (2.8)	127 (2.7)	525 (2.8)

Characteristic	TED, N (%)	CRF, N (%)	Total
PtCy + other(s)	1992 (14.3)	465 (10.0)	2457 (13.2)
PtCy alone	44 (0.3)	5 (0.1)	49 (0.3)
TAC + MMF +- other(s) (except PtCy)	967 (6.9)	416 (8.9)	1383 (7.4)
TAC + MTX +- other(s) (except MMF, PtCy)	2693 (19.3)	736 (15.8)	3429 (18.4)
TAC + other(s) (except MMF, MTX, PtCy)	111 (0.8)	39 (0.8)	150 (0.8)
TAC alone	195 (1.4)	41 (0.9)	236 (1.3)
CSA + MMF +- other(s) (except PtCy,TAC)	1302 (9.3)	1079 (23.1)	2381 (12.8)
CSA + MTX +- other(s) (except PtCy,TAC,MMF)	4004 (28.7)	773 (16.6)	4777 (25.6)
CSA + other(s) (except PtCy,TAC,MMF,MTX)	204 (1.5)	311 (6.7)	515 (2.8)
CSA alone	683 (4.9)	148 (3.2)	831 (4.5)
Other(s)	216 (1.5)	63 (1.4)	279 (1.5)
Not Reported	82 (0.6)	29 (0.6)	111 (0.6)

Table 2: PCWC 2025 accruals: Autologous Transplants

Characteristic	TED, N (%)	CRF, N (%)	Total
Primary disease - no. (%)			
AML	75 (0.6)	11 (0.7)	86 (0.6)
ALL	8 (0.1)	0 (0.0)	8 (0.1)
Other Acute Leukemia	1 (0.0)	0 (0.0)	1 (0.0)
MDS	1 (0.0)	1 (0.1)	2 (0.0)
NHL	286 (2.2)	47 (3.1)	333 (2.3)
HD	1011 (7.7)	115 (7.6)	1126 (7.7)
Plasma cell disorder	7 (0.1)	3 (0.2)	10 (0.1)
Solid Tumor	11676 (89.4)	1328 (88.2)	13004 (89.3)
Sarcoma (osteosarcoma, rhabdomyosarcoma, Ewings, PNET and other sarcoma)	363 (2.8)	30 (2.0)	393 (2.7)
Wilm's Tumor	188 (1.4)	15 (1.0)	203 (1.4)
Testicular	80 (0.6)	6 (0.4)	86 (0.6)
Other gonadal tumors	44 (0.3)	8 (0.5)	52 (0.4)
Extragonadal germ cell tumors	308 (2.4)	33 (2.2)	341 (2.3)
Neuroblastoma	5735 (43.9)	549 (36.5)	6284 (43.1)
Other solid tumor	801 (6.1)	91 (6.0)	892 (6.1)
Medulloblastoma	2127 (16.3)	338 (22.5)	2465 (16.9)
Retinoblastoma	145 (1.1)	8 (0.5)	153 (1.1)
Other CNS tumor	1885 (14.4)	250 (16.6)	2135 (14.7)
Graft Type - no. (%)			
Bone marrow	284 (2.2)	25 (1.7)	309 (2.1)
Peripheral blood	12775 (97.8)	1474 (97.9)	14249 (97.8)
Cord blood	4 (0.0)	6 (0.4)	10 (0.1)
Not reported	2 (0.0)	0 (0.0)	2 (0.0)
Conditioning Regimen Intensity - no. (%)			
MAC	2998 (22.9)	257 (17.1)	3255 (22.3)
RIC	948 (7.3)	118 (7.8)	1066 (7.3)
NMA	40 (0.3)	2 (0.1)	42 (0.3)
Need Review	9079 (69.5)	1128 (75.0)	10207 (70.1)

Table 3: PCWC 2025 accruals: Biorepository CIBMTR

Unrelated Donor HCT Research Sample Inventory - Summary for First Allogeneic Transplants in CRF and TED with biospecimens available through the CIBMTR Repository stratified by availability of paired samples, recipient only samples and donor only samples, Biospecimens include: whole blood, serum/plasma and limited quantities of viable cells and cell lines (collected prior to 2006), Specific inventory queries available upon request through the CIBMTR Immunobiology Research Program

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Number of patients	4632	1431	1714
Source of data			
CRF	2749 (59)	712 (50)	1033 (60)
TED	1883 (41)	719 (50)	681 (40)
Number of centers	163	124	201
Disease at transplant			
AML	1393 (30)	493 (34)	522 (30)
ALL	2009 (43)	574 (40)	759 (44)
Other leukemia	30 (1)	5 (<1)	10 (1)
CML	276 (6)	90 (6)	132 (8)
MDS	571 (12)	157 (11)	207 (12)
Other acute leukemia	117 (3)	47 (3)	26 (2)
NHL	176 (4)	45 (3)	38 (2)
Hodgkin Lymphoma	46 (1)	8 (1)	14 (1)
MPN	14 (<1)	12 (1)	6 (<1)
AML Disease status at transplant			
CR1	612 (44)	236 (48)	212 (41)
CR2	448 (32)	146 (30)	133 (25)
CR3+	33 (2)	11 (2)	16 (3)
Advanced or active disease	278 (20)	95 (19)	136 (26)
Missing	22 (2)	5 (1)	25 (5)
ALL Disease status at transplant			
CR1	604 (30)	157 (27)	191 (25)
CR2	862 (43)	272 (47)	309 (41)
CR3+	336 (17)	96 (17)	123 (16)
Advanced or active disease	171 (9)	41 (7)	74 (10)
Missing	36 (2)	8 (1)	62 (8)
MDS Disease status at transplant			
Early	184 (32)	39 (25)	37 (18)
Advanced	179 (31)	69 (44)	55 (27)
Missing	208 (36)	49 (31)	115 (56)
NHL Disease status at transplant			
CR1	33 (19)	9 (20)	11 (29)
CR2	47 (27)	21 (47)	9 (24)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
CR3+	18 (10)	1 (2)	1 (3)
PR	14 (8)	2 (4)	1 (3)
Advanced	60 (34)	12 (27)	9 (24)
Missing	4 (2)	0	7 (18)
Recipient age at transplant			
0-9 years	2220 (48)	680 (48)	826 (48)
10-17 years	2412 (52)	751 (52)	888 (52)
Median (Range)	10 (0-18)	11 (0-18)	10 (0-18)
Recipient race			
White	3654 (86)	1127 (85)	1199 (82)
Black or African American	334 (8)	94 (7)	136 (9)
Asian	150 (4)	52 (4)	81 (6)
Native Hawaiian or other Pacific Islander	12 (<1)	2 (<1)	11 (1)
American Indian or Alaska Native	34 (1)	14 (1)	10 (1)
Other	17 (<1)	10 (1)	8 (1)
More than one race	72 (2)	30 (2)	20 (1)
Unknown	359 (N/A)	102 (N/A)	249 (N/A)
Recipient ethnicity			
Hispanic or Latino	862 (25)	235 (22)	294 (25)
Non Hispanic or non-Latino	2479 (71)	802 (74)	570 (48)
Non-resident of the U.S.	145 (4)	53 (5)	330 (28)
Unknown	1146 (N/A)	341 (N/A)	520 (N/A)
Recipient sex			
Male	2730 (59)	854 (60)	1005 (59)
Female	1902 (41)	577 (40)	709 (41)
Karnofsky score			
10-80	708 (15)	256 (18)	300 (18)
90-100	3743 (81)	1122 (78)	1309 (76)
Missing	181 (4)	53 (4)	105 (6)
HLA-A B DRB1 groups - low resolution			
<=3/6	3 (<1)	4 (<1)	1 (<1)
4/6	64 (1)	8 (1)	6 (<1)
5/6	1016 (22)	261 (20)	336 (22)
6/6	3452 (76)	1036 (79)	1199 (78)
Unknown	97 (N/A)	122 (N/A)	172 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	216 (5)	6 (1)	26 (3)
6/8	379 (8)	31 (3)	53 (6)
7/8	1204 (27)	226 (25)	289 (30)
8/8	2681 (60)	632 (71)	583 (61)
Unknown	152 (N/A)	536 (N/A)	763 (N/A)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
HLA-DPB1 Match			
Double allele mismatch	1258 (31)	139 (27)	148 (26)
Single allele mismatch	2183 (53)	276 (53)	302 (54)
Full allele matched	670 (16)	109 (21)	109 (19)
Unknown	521 (N/A)	907 (N/A)	1155 (N/A)
High resolution release score			
No	839 (18)	1423 (99)	1552 (91)
Yes	3793 (82)	8 (1)	162 (9)
KIR typing available			
No	3480 (75)	1429 (>99)	1698 (99)
Yes	1152 (25)	2 (<1)	16 (1)
Graft type			
Marrow	3677 (79)	1140 (80)	1309 (76)
PBSC	951 (21)	280 (20)	402 (23)
BM+PBSC	2 (<1)	2 (<1)	1 (<1)
PBSC+UCB	0	5 (<1)	1 (<1)
Others	2 (<1)	4 (<1)	1 (<1)
Number of cord units			
Unknown	4632 (N/A)	1431 (N/A)	1714 (N/A)
Conditioning regimen			
Myeloablative	4293 (93)	1347 (94)	1593 (93)
RIC/Nonmyeloablative	314 (7)	79 (6)	96 (6)
TBD	25 (1)	5 (<1)	25 (1)
Donor age at donation			
To Be Determined/NA	54 (1)	49 (3)	36 (2)
0-9 years	2 (<1)	2 (<1)	0
10-17 years	1 (<1)	0	1 (<1)
18-29 years	2043 (44)	673 (47)	677 (39)
30-39 years	1421 (31)	445 (31)	566 (33)
40-49 years	912 (20)	212 (15)	338 (20)
50+ years	199 (4)	50 (3)	96 (6)
Median (Range)	32 (3-61)	30 (4-61)	32 (17-61)
Donor/Recipient CMV serostatus			
+/+	1038 (22)	412 (29)	369 (22)
+/-	751 (16)	192 (13)	291 (17)
-/+	1276 (28)	355 (25)	436 (25)
-/-	1476 (32)	403 (28)	529 (31)
CB - recipient +	0	5 (<1)	1 (<1)
CB - recipient -	0	3 (<1)	0
CB - recipient CMV unknown	0	1 (<1)	0
Missing	91 (2)	60 (4)	88 (5)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
GvHD Prophylaxis			
No GvHD Prophylaxis	13 (<1)	3 (<1)	7 (<1)
TDEPLETION alone	44 (1)	8 (1)	24 (1)
TDEPLETION +- other	276 (6)	80 (6)	136 (8)
CD34 select alone	29 (1)	12 (1)	9 (1)
CD34 select +- other	57 (1)	21 (1)	27 (2)
Cyclophosphamide alone	8 (<1)	2 (<1)	3 (<1)
Cyclophosphamide +- others	65 (1)	47 (3)	39 (2)
FK506 + MMF +- others	253 (5)	78 (5)	58 (3)
FK506 + MTX +- others(not MMF)	1373 (30)	487 (34)	295 (17)
FK506 +- others(not MMF,MTX)	97 (2)	12 (1)	18 (1)
FK506 alone	55 (1)	16 (1)	12 (1)
CSA + MMF +- others(not FK506)	234 (5)	60 (4)	61 (4)
CSA + MTX +- others(not MMF,FK506)	1638 (35)	458 (32)	777 (45)
CSA +- others(not FK506,MMF,MTX)	202 (4)	60 (4)	96 (6)
CSA alone	148 (3)	48 (3)	89 (5)
Other GVHD Prophylaxis	107 (2)	27 (2)	34 (2)
Missing	33 (1)	12 (1)	29 (2)
Donor/Recipient sex match			
Male-Male	1747 (38)	531 (37)	600 (35)
Male-Female	1063 (23)	308 (22)	361 (21)
Female-Male	964 (21)	314 (22)	390 (23)
Female-Female	829 (18)	253 (18)	337 (20)
CB - recipient M	0	3 (<1)	1 (<1)
CB - recipient F	0	6 (<1)	0
Missing	29 (1)	16 (1)	25 (1)
Year of transplant			
1986-1990	73 (2)	9 (1)	30 (2)
1991-1995	436 (9)	107 (7)	203 (12)
1996-2000	579 (13)	212 (15)	331 (19)
2001-2005	704 (15)	153 (11)	325 (19)
2006-2010	855 (18)	154 (11)	188 (11)
2011-2015	1005 (22)	215 (15)	243 (14)
2016-2020	675 (15)	339 (24)	238 (14)
2021-2024	305 (7)	242 (17)	156 (9)
Follow-up among survivors, Months			
N Eval	2424	776	861
Median (Range)	72 (0-353)	37 (0-295)	57 (0-385)

Unrelated cord Donor HCT Research Sample Inventory - Summary for First Allogeneic Transplants in CRF and TED with biospecimens available through the CIBMTR Repository stratified by availability of paired samples, recipient only samples and donor only samples, Biospecimens include: whole blood, serum/plasma and limited quantities of viable cells and cell lines (collected prior to 2006), Specific inventory queries available upon request through the CIBMTR Immunobiology Research Program

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Number of patients	1555	502	628
Source of data			
CRF	1137 (73)	331 (66)	339 (54)
TED	418 (27)	171 (34)	289 (46)
Number of centers	89	76	120
Disease at transplant			
AML	618 (40)	186 (37)	227 (36)
ALL	654 (42)	237 (47)	280 (45)
Other leukemia	10 (1)	1 (<1)	4 (1)
CML	18 (1)	5 (1)	9 (1)
MDS	158 (10)	46 (9)	68 (11)
Other acute leukemia	44 (3)	14 (3)	23 (4)
NHL	46 (3)	13 (3)	12 (2)
Hodgkin Lymphoma	5 (<1)	0	4 (1)
MPN	2 (<1)	0	1 (<1)
AML Disease status at transplant			
CR1	292 (47)	99 (53)	100 (44)
CR2	215 (35)	53 (28)	70 (31)
CR3+	13 (2)	0	5 (2)
Advanced or active disease	97 (16)	34 (18)	47 (21)
Missing	1 (<1)	0	5 (2)
ALL Disease status at transplant			
CR1	224 (34)	78 (33)	105 (38)
CR2	309 (47)	110 (46)	111 (40)
CR3+	98 (15)	35 (15)	46 (16)
Advanced or active disease	22 (3)	13 (5)	18 (6)
Missing	1 (<1)	1 (<1)	0
MDS Disease status at transplant			
Early	61 (39)	15 (33)	36 (53)
Advanced	54 (34)	22 (48)	16 (24)
Missing	43 (27)	9 (20)	16 (24)
NHL Disease status at transplant			
CR1	11 (24)	2 (15)	1 (8)
CR2	18 (39)	8 (62)	7 (58)
CR3+	5 (11)	1 (8)	0

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
PR	3 (7)	0	1 (8)
Advanced	9 (20)	2 (15)	3 (25)
Recipient age at transplant			
0-9 years	1003 (65)	350 (70)	399 (64)
10-17 years	552 (35)	152 (30)	229 (36)
Median (Range)	7 (0-18)	7 (0-18)	8 (0-18)
Recipient race			
White	1077 (74)	355 (75)	393 (72)
Black or African American	221 (15)	71 (15)	71 (13)
Asian	72 (5)	21 (4)	44 (8)
Native Hawaiian or other Pacific Islander	5 (<1)	2 (<1)	10 (2)
American Indian or Alaska Native	19 (1)	5 (1)	6 (1)
Other	0	0	1 (<1)
More than one race	63 (4)	18 (4)	21 (4)
Unknown	98 (N/A)	30 (N/A)	82 (N/A)
Recipient ethnicity			
Hispanic or Latino	470 (31)	134 (27)	123 (20)
Non Hispanic or non-Latino	1040 (68)	347 (71)	323 (53)
Non-resident of the U.S.	15 (1)	10 (2)	160 (26)
Unknown	30 (N/A)	11 (N/A)	22 (N/A)
Recipient sex			
Male	904 (58)	276 (55)	357 (57)
Female	651 (42)	226 (45)	271 (43)
Karnofsky score			
10-80	249 (16)	84 (17)	101 (16)
90-100	1259 (81)	391 (78)	476 (76)
Missing	47 (3)	27 (5)	51 (8)
HLA-A B DRB1 groups - low resolution			
<=3/6	12 (1)	4 (1)	3 (1)
4/6	435 (29)	138 (30)	150 (26)
5/6	757 (51)	232 (50)	303 (52)
6/6	272 (18)	92 (20)	128 (22)
Unknown	79 (N/A)	36 (N/A)	44 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	564 (43)	128 (36)	176 (40)
6/8	379 (29)	113 (32)	119 (27)
7/8	240 (18)	71 (20)	91 (21)
8/8	141 (11)	40 (11)	53 (12)
Unknown	231 (N/A)	150 (N/A)	189 (N/A)
HLA-DPB1 Match			
Double allele mismatch	262 (39)	47 (35)	56 (36)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Single allele mismatch	339 (51)	77 (57)	79 (50)
Full allele matched	66 (10)	12 (9)	22 (14)
Unknown	888 (N/A)	366 (N/A)	471 (N/A)
High resolution release score			
No	1016 (65)	471 (94)	616 (98)
Yes	539 (35)	31 (6)	12 (2)
KIR typing available			
No	1114 (72)	497 (99)	619 (99)
Yes	441 (28)	5 (1)	9 (1)
Graft type			
UCB	1535 (99)	493 (98)	618 (98)
PBSC+UCB	8 (1)	5 (1)	7 (1)
Others	12 (1)	4 (1)	3 (<1)
Number of cord units			
1	1447 (93)	0	583 (93)
2	108 (7)	0	45 (7)
Unknown	0 (N/A)	502 (N/A)	0 (N/A)
Conditioning regimen			
Myeloablative	1472 (95)	474 (94)	578 (92)
RIC/Nonmyeloablative	82 (5)	28 (6)	48 (8)
TBD	1 (<1)	0	2 (<1)
Donor/Recipient CMV serostatus			
CB - recipient +	941 (61)	319 (64)	376 (60)
CB - recipient -	590 (38)	172 (34)	224 (36)
CB - recipient CMV unknown	24 (2)	11 (2)	28 (4)
GvHD Prophylaxis			
No GvHD Prophylaxis	5 (<1)	3 (1)	3 (<1)
TDEPLETION alone	1 (<1)	0	0
TDEPLETION +- other	6 (<1)	4 (1)	3 (<1)
CD34 select alone	0	1 (<1)	0
CD34 select +- other	6 (<1)	1 (<1)	3 (<1)
Cyclophosphamide +- others	5 (<1)	0	3 (<1)
FK506 + MMF +- others	321 (21)	144 (29)	105 (17)
FK506 + MTX +- others(not MMF)	106 (7)	27 (5)	39 (6)
FK506 +- others(not MMF,MTX)	32 (2)	16 (3)	14 (2)
FK506 alone	9 (1)	7 (1)	5 (1)
CSA + MMF +- others(not FK506)	821 (53)	223 (44)	283 (45)
CSA + MTX +- others(not MMF,FK506)	49 (3)	11 (2)	22 (4)
CSA +- others(not FK506,MMF,MTX)	161 (10)	54 (11)	115 (18)
CSA alone	23 (1)	6 (1)	23 (4)
Other GVHD Prophylaxis	8 (1)	4 (1)	7 (1)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Missing	2 (<1)	1 (<1)	3 (<1)
Donor/Recipient sex match			
CB - recipient M	904 (58)	276 (55)	356 (57)
CB - recipient F	651 (42)	226 (45)	271 (43)
CB - recipient sex unknown	0	0	1 (<1)
Year of transplant			
1996-2000	0	0	2 (<1)
2001-2005	46 (3)	39 (8)	14 (2)
2006-2010	563 (36)	124 (25)	205 (33)
2011-2015	549 (35)	128 (25)	227 (36)
2016-2020	287 (18)	131 (26)	103 (16)
2021-2024	110 (7)	80 (16)	77 (12)
Follow-up among survivors, Months			
N Eval	904	312	343
Median (Range)	68 (0-196)	45 (0-213)	48 (0-186)

Related Donor HCT Research Sample Inventory - Summary for First Allogeneic Transplants in CRF and TED with biospecimens available through the CIBMTR Repository stratified by availability of paired samples, recipient only samples and donor only samples, Biospecimens include: whole blood, serum/plasma and limited quantities of viable cells and cell lines (collected prior to 2006), Specific inventory queries available upon request through the CIBMTR Immunobiology Research Program

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Number of patients	1326	201	92
Source of data			
CRF	278 (21)	43 (21)	15 (16)
TED	1048 (79)	158 (79)	77 (84)
Number of centers	54	44	37
Disease at transplant			
AML	454 (34)	63 (31)	36 (39)
ALL	611 (46)	99 (49)	45 (49)
Other leukemia	3 (<1)	0	0
CML	38 (3)	1 (<1)	2 (2)
MDS	104 (8)	20 (10)	8 (9)
Other acute leukemia	50 (4)	3 (1)	1 (1)
NHL	52 (4)	13 (6)	0
Hodgkin Lymphoma	11 (1)	2 (1)	0
MPN	3 (<1)	0	0
AML Disease status at transplant			
CR1	287 (63)	43 (68)	21 (58)
CR2	112 (25)	16 (25)	9 (25)
CR3+	6 (1)	1 (2)	1 (3)
Advanced or active disease	47 (10)	1 (2)	5 (14)
Missing	2 (<1)	2 (3)	0
ALL Disease status at transplant			
CR1	219 (36)	37 (37)	18 (40)
CR2	305 (50)	49 (49)	20 (44)
CR3+	75 (12)	11 (11)	5 (11)
Advanced or active disease	12 (2)	2 (2)	2 (4)
MDS Disease status at transplant			
Early	22 (21)	4 (20)	2 (25)
Advanced	67 (64)	10 (50)	2 (25)
Missing	15 (14)	6 (30)	4 (50)
NHL Disease status at transplant			
CR1	16 (31)	4 (31)	
CR2	20 (38)	2 (15)	
CR3+	2 (4)	0	

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Advanced	13 (25)	7 (54)	
Missing	1 (2)	0	
Recipient age at transplant			
0-9 years	560 (42)	95 (47)	40 (43)
10-17 years	766 (58)	106 (53)	52 (57)
Median (Range)	12 (0-18)	11 (1-18)	11 (1-18)
Recipient race			
White	894 (75)	134 (76)	59 (77)
Black or African American	151 (13)	24 (14)	4 (5)
Asian	66 (6)	11 (6)	7 (9)
Native Hawaiian or other Pacific Islander	6 (1)	3 (2)	1 (1)
American Indian or Alaska Native	17 (1)	2 (1)	1 (1)
More than one race	51 (4)	2 (1)	5 (6)
Unknown	141 (N/A)	25 (N/A)	15 (N/A)
Recipient ethnicity			
Hispanic or Latino	467 (36)	82 (42)	24 (28)
Non Hispanic or non-Latino	801 (62)	108 (56)	59 (68)
Non-resident of the U.S.	24 (2)	4 (2)	4 (5)
Unknown	34 (N/A)	7 (N/A)	5 (N/A)
Recipient sex			
Male	763 (58)	97 (48)	60 (65)
Female	563 (42)	104 (52)	32 (35)
Karnofsky score			
10-80	243 (18)	40 (20)	17 (18)
90-100	1048 (79)	155 (77)	70 (76)
Missing	35 (3)	6 (3)	5 (5)
HLA-A B DRB1 groups - low resolution			
<=3/6	373 (31)	57 (33)	25 (37)
4/6	115 (10)	15 (9)	9 (13)
5/6	35 (3)	8 (5)	4 (6)
6/6	685 (57)	95 (54)	30 (44)
Unknown	118 (N/A)	26 (N/A)	24 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	468 (40)	72 (42)	33 (49)
6/8	20 (2)	5 (3)	0
7/8	24 (2)	2 (1)	4 (6)
8/8	672 (57)	93 (54)	30 (45)
Unknown	142 (N/A)	29 (N/A)	25 (N/A)
HLA-DPB1 Match			
Double allele mismatch	1 (<1)	0	1 (2)
Single allele mismatch	381 (35)	43 (36)	22 (47)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Full allele matched	708 (65)	76 (64)	24 (51)
Unknown	236 (N/A)	82 (N/A)	45 (N/A)
High resolution release score			
No	733 (55)	195 (97)	92 (100)
Yes	593 (45)	6 (3)	0
Graft type			
Marrow	961 (72)	111 (55)	63 (68)
PBSC	336 (25)	80 (40)	28 (30)
UCB	1 (<1)	8 (4)	0
BM+PBSC	3 (<1)	0	1 (1)
BM+UCB	3 (<1)	2 (1)	0
Others	22 (2)	0	0
Number of cord units			
Unknown	1326 (N/A)	201 (N/A)	92 (N/A)
Conditioning regimen			
Myeloablative	1233 (93)	189 (94)	85 (92)
RIC/Nonmyeloablative	90 (7)	9 (4)	5 (5)
TBD	3 (<1)	3 (1)	2 (2)
Donor age at donation			
To Be Determined/NA	3 (<1)	3 (1)	0
0-9 years	347 (26)	51 (25)	21 (23)
10-17 years	347 (26)	54 (27)	21 (23)
18-29 years	269 (20)	38 (19)	24 (26)
30-39 years	205 (15)	37 (18)	20 (22)
40-49 years	129 (10)	11 (5)	4 (4)
50+ years	26 (2)	7 (3)	2 (2)
Median (Range)	17 (0-61)	17 (0-61)	19 (1-53)
Donor/Recipient CMV serostatus			
+/+	508 (38)	87 (43)	37 (40)
+/-	150 (11)	16 (8)	11 (12)
-/+	355 (27)	45 (22)	23 (25)
-/-	295 (22)	40 (20)	19 (21)
CB - recipient +	4 (<1)	6 (3)	0
CB - recipient -	0	4 (2)	0
Missing	14 (1)	3 (1)	2 (2)
GvHD Prophylaxis			
No GvHD Prophylaxis	33 (2)	4 (2)	0
TDEPLETION alone	72 (5)	27 (13)	10 (11)
TDEPLETION +- other	32 (2)	11 (5)	3 (3)
CD34 select alone	12 (1)	0	1 (1)
CD34 select +- other	16 (1)	7 (3)	2 (2)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Cyclophosphamide alone	3 (<1)	1 (<1)	0
Cyclophosphamide +- others	407 (31)	40 (20)	27 (29)
FK506 + MMF +- others	93 (7)	12 (6)	5 (5)
FK506 + MTX +- others(not MMF)	391 (29)	49 (24)	22 (24)
FK506 +- others(not MMF,MTX)	2 (<1)	1 (<1)	1 (1)
FK506 alone	8 (1)	2 (1)	1 (1)
CSA + MMF +- others(not FK506)	35 (3)	6 (3)	2 (2)
CSA + MTX +- others(not MMF,FK506)	187 (14)	27 (13)	16 (17)
CSA +- others(not FK506,MMF,MTX)	1 (<1)	2 (1)	0
CSA alone	28 (2)	8 (4)	1 (1)
Other GVHD Prophylaxis	4 (<1)	1 (<1)	1 (1)
Missing	2 (<1)	3 (1)	0
Donor/Recipient sex match			
Male-Male	448 (34)	48 (24)	31 (34)
Male-Female	264 (20)	49 (24)	15 (16)
Female-Male	312 (24)	43 (21)	29 (32)
Female-Female	298 (22)	50 (25)	17 (18)
CB - recipient M	3 (<1)	5 (2)	0
CB - recipient F	1 (<1)	5 (2)	0
Missing	0	1 (<1)	0
Year of transplant			
2006-2010	35 (3)	3 (1)	0
2011-2015	270 (20)	30 (15)	16 (17)
2016-2020	550 (41)	88 (44)	34 (37)
2021-2024	471 (36)	80 (40)	42 (46)
Follow-up among survivors, Months			
N Eval	1005	160	58
Median (Range)	24 (0-142)	24 (0-147)	13 (0-97)

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A RESEARCH COLLABORATION BETWEEN THE MEDICAL COLLEGE OF WISCONSIN AND NMDP

TO: Pediatric Cancer Working Committee Members

FROM: Larisa Broglie, MD MS; Scientific Director for the Pediatric Cancer Working Committee

RE: 2024-2025 Studies in Progress Summary

PC19-02 Does mixed peripheral blood T Cell Chimerism predict relapse? (A Lake / S Prockop / J Boelens / K Peggs). This study aims to study the effect of mixed T-cell chimerism on relapse, hypothesizing that it is not associated with post-transplant relapse. There has been an extensive review of the available chimerism data and discussion with our statistical team to select an appropriate analysis plant. Ultimately, the objectives of this study are 1) to determine the incidence of short term mixed chimerism and determine if is associated with relapse and 2) to determine the incidence of persistent mixed chimerism and determine if it is associated with relapse. The demographics tables will be prepared with a contemporary cohort and protocol shared with the Working Committee soon.
Status: Demographics table preparation and Protocol Development.

PC19-03 The impact of pre-transplant extramedullary disease on the outcome of Allogeneic Hematopoietic Cell Transplantation for Acute Myeloid Leukemia in children (H Rangarajan/ P Satwani /D Chellapandian). The objective of this study is to determine whether the presence of extramedullary disease in pediatric patients with AML prior to transplant impacts overall survival and disease-free survival. The study has been completed and was presented as a poster presentation at ASH in December 2024.
Status: A manuscript draft is currently being prepared for publication.

CT20-02 Resource utilization with chimeric antigen receptor T cells (M Battiwalla/ H Rangarajan/ C Scheckel). The objective of this study is to:

1. Determine “real world” costs and HCRU incurred during CAR-T therapy for in pediatric ALL patients.
2. Identify patient, disease, and cellular therapy related factors associated with increased HCRU and costs
3. Compare the HCRU and costs incurred by Kymriah treated pediatric (≤21 years) patients with that of pediatric patients who underwent allo HCT between September 2017- June 30 2021.
4. Identify impact of increased HCRU and costs on CART on 1 year LFS, 1 year OS.

Status: Protocol Development

PC20-02 Germline genetics of pediatric Myelodysplastic Syndromes (J Poynter/ L Spector). The objective of this study is to identify genetic susceptibility variants for pediatric patients with MDS in an unselected cohort of pediatric patients. Genotyping will be conducted using the Illumina Global Screening array and controls will include > 2000 DNA samples that have been genotyped for other childhood cancer studies. To improve power, we will focus on regions of the genome expressed in myeloid cells as determined by ATAC-seq in primary MDS cell cultures. The study is currently in sample typing, with demographics dataset shared with PIs.

Status: Updating the datafile to include select outcomes so analysis can be completed by PIs

PC22-01 Impact of graft versus host disease following allogeneic hematopoietic cell transplantation on leukemia free survival in hematologic malignancies within the pediatric disease risk index risk stratification (A Bauchat/ M Qayed). The primary objective of this study is to determine the impact of development of grade I and II acute graft versus host disease (aGVHD) on relapse and leukemia-free survival in children undergoing hematopoietic cell transplant (HCT) for ALL and AML, with the hypothesis that mild to moderate aGVHD is associated with improved Leukaemia-free survival in children with favourable risk disease by pediatric DRI classification. The study analysis has been completed and
Status: The results will be presented at Tandem on ***Saturday February 15 (Oral Abstract - Session J - Relapse, 10am-12:30pm).*** *Manuscript Preparation.*

PC22-02 Evaluating predictors of access and outcomes with hematopoietic cell transplantation in pediatric and adolescent patients with relapsed/refractory classical Hodgkin lymphoma after treatment on an initial cooperative group clinical trial (S Castellino/ J Kahn). The objective of this study is primary to use a novel data linkage between the Children's Oncology Group (COG) and the CIBMTR to: 1) evaluate the receipt of HCT in a contemporary cohort of children and adolescents with r/r HL; to determine patient- and disease-related factors associated with receipt of HCT including age at initial diagnosis, race/ethnicity, insurance type, and location of care during COG therapy; 2) to evaluate post-transplant survival outcomes (PFS, TRM, OS) in the above transplanted cohort.
Status: Protocol draft in place. Working through the data sharing and data linkage agreements between COG and CIBMTR.

PC23-01 Post-transplant cyclophosphamide vs. TCR αβ/CD19+ deplete approaches for haploidentical transplant in pediatric patients with acute leukemias and myelodysplastic syndrome: A CIBMTR/EBMT collaborative study (A Li/ H Rangarajan/ P Satwani). The primary objective of the study is to compare the 2-year leukemia free survival (LFS) between patients who received TCR αβ/CD19+ depletion versus PTCY for GVHD prophylaxis for haploidentical transplant. The initial plan was to collaborate with EBMT, however, we will not combine our data with EBMT but instead have 2 parallel studies and potentially a joint commentary. The datafile has been prepared and will be shared with the Working Committee soon.
Status: Datafile preparation.

PC23-02 Comparison of bone marrow and peripheral blood stem cells as graft source in children undergoing allogeneic hematopoietic stem cell transplantation for hematological malignancies with unmanipulated haploidentical grafts utilizing post-transplant cyclophosphamide as GvHD prophylaxis (A Srinivasan/ J Krueger). The hypothesis of this study is that 1-yr chronic GvHD free relapse free survival (CRFS) is similar between recipients of peripheral blood stem cell and bone marrow haploidentical grafts utilizing PT-Cy GvHD prophylaxis. The protocol has been completed
Status: The protocol is being finalized and demographics tables prepared.

PC24-01 Transplantation and cellular therapy for children and young adults with down's syndrome and acute leukemia (L Appell/ S Rotz). This study is a collaboration between CIBMTR and EBMT. The primary objective will be to evaluate overall survival in children with Down's Syndrome with AML who receive allo-transplant and ALL with CART or HCT. We have met with EBMT and finalized a protocol. The demographics tables are being prepared.
Status: *Protocol in Development with EBMT and demographics tables being prepare*

Field	Response
Proposal Number	2410-40-TAKAHASHI
Proposal Title	Comparison of different TBI doses in relation to MRD status in pediatric acute lymphoblastic leukemia
Key Words	ALL, TBI, CNS
Principal Investigator #1: - First and last name, degree(s)	Takuto Takahashi, MD, PhD
Principal Investigator #1: - Email address	takuto.takahashi@childrens.harvard.edu
Principal Investigator #1: - Institution name	Boston Children's Hospital, Dana-Farber Cancer Institute
Principal Investigator #1: - Academic rank	Assistant Professor
Junior investigator status (defined as ≤5 years from fellowship)	Yes
Do you identify as an underrepresented/minority?	No
Principal Investigator #2 (If applicable): - First and last name, degree(s):	Amy Keating
Principal Investigator #2 (If applicable): - Email address:)	-
Principal Investigator #2 (If applicable): - Institution name:	-
Principal Investigator #2 (If applicable): - Academic rank:	-
Junior investigator status (defined as ≤5 years from fellowship)	No
Do you identify as an underrepresented/minority?	No
We encourage a maximum of two Principal Investigators per study. If more than one author is listed, please indicate who will be identified as the corresponding PI below:	-
If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:	-
Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.	-
Do any of the PI(s) within this proposal have a CIBMTR WC study in manuscript preparation >6 months?	No
PROPOSED WORKING COMMITTEE:	Pediatric Cancer
Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.	No
If you have already spoken with a scientific director or working committee chair regarding this study, then please specify who:	-
RESEARCH QUESTION:	Does a higher TBI dose result in better outcomes in pediatric ALL post HCT? Does measurable disease status (MRD) prior to HCT correlate with the TBI effects?
RESEARCH HYPOTHESIS:	We hypothesize that TBI of 12 Gy is noninferior to higher TBI doses in both children with no measurable disease prior to HCT and with residual disease.

Field	Response
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	Primary: 3-year disease free survival Secondary: 3-year OS, TRM, relapse, GRFS, chronic GVHD; 100-day acute GVHD Exploratory: Cataracts, gonadal dysfunction, growth hormone deficiency/short stature, hypothyroidism, secondary malignancy
SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.	This study will assess whether 12 Gy of TBI is noninferior to higher-dose, more resource-demanding and potentially more toxic TBI in pediatric ALL, using contemporary data that includes MRD status. If the use of 12 Gy proves equally effective, this could reduce the logistical demands of TBI and limit unnecessary radiation exposure, decreasing sedation occasions in younger children and potentially decreasing long-term toxicities. The findings will help optimize TBI use, improve resource allocation and potentially patient outcomes, supporting safer, evidence-based conditioning strategies in HCT.

SCIENTIFIC JUSTIFICATION: Provide a background summary of previous related research and their strengths and weaknesses, justification of your research and why your research is still necessary.	Total body irradiation (TBI) has long been a key component of hematopoietic cell transplantation (HCT) conditioning, particularly for pediatric acute lymphoblastic leukemia (ALL). TBI provides uniform cytotoxicity, targeting sanctuary sites like the central nervous system and testes, which are often less accessible to chemotherapy. It also induces strong immunosuppression, facilitating engraftment and reducing graft rejection. Clinically, TBI has shown to outperform chemotherapy-based conditioning, with the recent FORUM study confirming its superior outcomes in pediatric ALL1. However, the optimal TBI dose has not been established to date. Despite these benefits, increasing TBI dose presents logistical challenges and potentilly increased late adverse effects. Myeloablative TBI is typically delivered at doses between 12-14 Gy, delivered in fractionated doses over several days with repeated sedations in younger children. Given the resource demands and the restriction of TBI to non-holiday weekdays, increased radiation doses that require additional fractions/days of TBI can delay transplantation and limit flexibility in HCT planning, may negatively affecting patient outcomes. In addition, an early study from the CIBMTR (1964 to 1992) reported a dose-dependent risk of secondary malignancy by fractionated TBI (p<0.001). Most of this cohort consists of myeloablative HCT for hematologic malignancy (60% the fractionated TBI was dosed at ≥12 and <14 Gy)2. This dose dependency within the myeloablative TBI range was not observed in later studies including more recent patients3,4. In contrast, the clinical advantage of higher TBI doses (>12 Gy) remains uncertain with no definitive evidence supporting increased efficacy at higher doses. Previous studies have explored optimal TBI dosing using the CIBMTR database. Tracey et al. analyzed pediatric ALL data from the CIBMTR in the years 1998-20075. A higher TBI dose (≥13 Gy), compared to a lower dose (<12 Gy), revealed no significant difference in relapse (hazard risk [HR]: 1.13, p = 0.41), transplant-related mortality (TRM) (HR: 0.73, p = 0.06) or overall mortality (HR: 0.87, p = 0.23)5. On the contrary, Sabloff et al. reported significant clinical effects of varying TBI doses ranging from 12-14 Gy in adults with hematologic malignancies from the CIBMTR data (2001-2013)6. Compared to TBI at 12 Gy, TBI 13-13.75 Gy showed higher TRM (HR 1.25, p = 0.007) but comparable relapse (HR 0.92, p = 0.29), and overall survival (HR: 1.06, p = 0.36). However, further increases in TBI dose to14 Gy reduced relapse (HR 0.69, p = 0.002) and also similarly increased TRM (HR 1.25, p = 0.03), leading to comparable overall survival (HR: 0.89, p = 0.17). Importantly, neither of these retrospective studies nor the prospective European FORUM study incorporated measurable

Field	Response
	residual disease (MRD) status, which is now recognized as a key prognostic factor for relapse and overall outcomes in leukemia. To address this gap in understanding, we propose using contemporary CIBMTR data, which includes MRD status, to assess the comparative efficacy of different TBI doses in pediatric ALL. This analysis will provide critical insights into whether higher doses of TBI offer additional benefit or if 12 Gy is a noninferior standard in both patients with no MRD and with residual disease.
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	This proposed CIBMTR study will include patients with ALL diagnosis of ages <30 years in the CIBMTR database with the evaluable MRD data from 2008 onward. The rationale for the study cohort selection includes 1) age up to 30 years are often treated at pediatric HCT centers, 2) MRD data was available for the years 2008-2017 in previous studies (Qayed et al, Blood 20217), and 3) the main changes in HCT regimens in pediatric ALL over this period can be captured in the dataset and accounted for in the study (e.g., posttransplantation cyclophosphamide). We plan to enrich the sample size to capture smaller differences and account for confounders statistically (e.g., include the age and HCT year as variables in multivariable models). [Inclusion] - Patients aged <30 years at the time of HCT - Diagnosis of ALL (including both B-cell and T-cell ALL) - Received an allogeneic HCT with myeloablative TBI [Required data elements] 1. TBI information (dose, shielding, fractionations) 2. MRD status (blasts in bone marrow <5.0%) by flow cytometry or molecular testing
Does this study include pediatric patients?	Yes
If this study does not include pediatric patients, please provide justification:	-

Field	Response
DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion- variables to be considered in the multivariate analyses. Outline any supplementary data required.	1. Pre-TED (Form 2400 R9.0) 1-1) Recipient data: Age, sex, weight, height 1-2) Donor information: Product type (BM/PBSC/single UCB/other), donor type (related/unrelated), HLA match, donor age, donor sex, CD34+ cell dose, CMV status 1-3) Product processing/manipulation T-cell depletion (Yes/No) 1-4) Clinical Status of Recipient Prior to the conditioning Karnofsky/Lansky scale, Recipient CMV-antibodies 1-5) Pre-HSCT preparative regimen: Conditioning regimen (myeloablative/non-myeloablative/reduced intensity conditioning), drug used, TBI (Yes/No), TBI dose, total number of fractions 1-6) GVHD prophylaxis: (Yes/No) to [ATG, corticosteroids, cyclosporine, cyclophosphamide, tacrolimus, methotrexate, mycophenolate, sirolimus, alemtuzumab] 2. Post-TED (Form 2450) 2-1) Survival Dead/alive, Date, Primary cause of death 2-2) Subsequent transplant Subsequent HCT (Yes/No) 2-3) Initial ANC recovery Evidence of initial hematopoietic recovery (yes, no, N/A, previously reported), Date, late graft failure (Yes/No) 2-4) Initial Platelet recovery Evidence of initial platelet recovery (yes, no, N/A, previously reported), Date 2-5) Acute GVHD Yes/No, Date of onset, Maximum grade, Maximum stages by organ 2-6) Chronic GVHD Yes/No, Date of onset, Maximum grade, Limited/extensive 3. ALL Pre-HSCT data (Form 2011) 3-1) MRD status* 3-2) Blasts in bone marrow (%) at the last evaluation prior to preparative regimen - By any method for earlier years (e.g., molecular markers) - By flow cytometry for recent years *Positive MRD status will be determined by detectable bone marrow blasts at <5.0%. We will also refer to the data extraction methods of the study performed by Qayed, et al. on the disease-risk index development (Blood 2021, included CIBMTR data for 2008-20177). 3-2) CNS disease Yes/No, CNS leukemia at any time prior to the start of the preparative regimen 3-3) Radiation therapy Yes/No, Cranial, craniospinal, other sites 4. Recipient Baseline Data (Form 2000) 4-1) Additional radiation given to other sites within 21 days of the HCT Yes/No, dose of all sites 5. Post-Infusion Follow-Up (Form 2100) 5-1) Cataracts, gonadal dysfunction, growth hormone deficiency/short stature, hypothyroidism
Types of cellular therapy data this proposal includes:	Hematopoietic Cell Transplantation (HCT)
PATIENT REPORTED OUTCOME (PRO) REQUIREMENTS: If the study requires PRO data collected by CIBMTR, the proposal should include: 1) A detailed description of the PRO domains, timepoints, and proposed analysis of PROs; 2) A description of the hypothesis speci	N/A

Field	Response
MACHINE LEARNING: Please indicate if the study requires methodology related to machine-learning and clinical predictions.	N/A
SAMPLE REQUIREMENTS: If the study requires biologic samples from the CIBMTR Repository, the proposal should also include: 1) A detailed description of the proposed testing methodology and sample requirements; 2) A summary of the investigator's previous e	N/A
NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required.	N/A
REFERENCES:	1. Peters C, Dalle J-H, Locatelli F, et al. Total Body Irradiation or Chemotherapy Conditioning in Childhood ALL: A Multinational, Randomized, Noninferiority Phase III Study. Journal of Clinical Oncology. 2021;39(4):295-307. 2. Curtis RE, Rowlings PA, Deeg HJ, et al. Solid Cancers after Bone Marrow Transplantation. New England Journal of Medicine. 1997;336(13):897-904. 3. Rizzo JD, Curtis RE, Socié G, et al. Solid cancers after allogeneic hematopoietic cell transplantation. Blood. 2009;113(5):1175-1183. 4. Baker KS, Leisenring WM, Goodman PJ, et al. Total body irradiation dose and risk of subsequent neoplasms following allogeneic hematopoietic cell transplantation. Blood. 2019;133(26):2790-2799. 5. Tracey J, Zhang M-J, Thiel E, Sobocinski KA, Eapen M. Transplantation Conditioning Regimens and Outcomes after Allogeneic Hematopoietic Cell Transplantation in Children and Adolescents with Acute Lymphoblastic Leukemia. Biology of Blood and Marrow Transplantation. 2013;19(2):255-259. 6. Sabloff M, Chhabra S, Wang T, et al. Comparison of High Doses of Total Body Irradiation in Myeloablative Conditioning before Hematopoietic Cell Transplantation. Biol Blood Marrow Transplant. 2019;25(12):2398-2407. 7. Qayed M, Ahn KW, Kitko CL, et al. A validated pediatric disease risk index for allogeneic hematopoietic cell transplantation. Blood. 2021;137(7):983-993.
CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning?	No, I do not have any conflicts of interest pertinent to this proposal
If yes, provide detail on the nature of employment, name of organization, role, entity, ownership, type of financial transaction or legal proceeding and whether renumeration is >$5000 annually.	-

The below selection criteria were applied

Selection criteria	# excluded	N
Cases available in CIBMTR HCT Essentials Extract *		441766
First Allo HCT	246638	195128
Years of HCT: 2008-2022	23172	171956
Disease: ALL	145418	26538
Age at diagnosis: < 30 year	13487	13051
Conditioning Regimen Intensity: Myeloablative Conditioning	1796	11255
Conditioning Regimen: TBI	1556	9699
CRF Track	7582	2117
Patient Consented	116	2001
Follow-up present	66	1935
TBI Dose: >=8.0 GY and <132 GY	322	1613

**Data source: HCT Essentials Oct 2024*

Table 1: Patients that underwent first allogeneic HCT for ALL with TBI conditioning regimen Intensity between 2008-2022

Characteristic	9.0 - 9.9 GY	10.0 - 10.9 GY	11.0 - 11.9 GY	12.0 - 12.9 GY	13.0 -13.2 GY	>13.2 GY	Total
No. of patients	16	9	3	924	517	144	1613
No. of centers	11	6	2	144	84	35	174
Patient age - median (min-max)	19.3 (2.5-29.9)	20.0 (8.7-29.9)	24.3 (11.0-27.5)	14.5 (0.5-30.0)	14.3 (0.7-29.9)	15.0 (0.7-29.8)	14.5 (0.5-30.0)
Age Range - no. (%)							

Characteristic	9.0 - 9.9 GY	10.0 - 10.9 GY	11.0 - 11.9 GY	12.0 - 12.9 GY	13.0 -13.2 GY	>13.2 GY	Total
<2 years	0 (0.0)	0 (0.0)	0 (0.0)	23 (2.5)	7 (1.4)	4 (2.8)	34 (2.1)
2-10 years	5 (31.3)	1 (11.1)	0 (0.0)	330 (35.7)	198 (38.3)	49 (34.0)	583 (36.1)
11-28 years	3 (18.8)	3 (33.3)	1 (33.3)	251 (27.2)	149 (28.8)	38 (26.4)	445 (27.6)
19 -30 years	8 (50.0)	5 (55.6)	2 (66.7)	320 (34.6)	163 (31.5)	53 (36.8)	551 (34.2)
Donor type - no. (%)							
HLA-identical sibling	2 (12.5)	7 (77.8)	0 (0.0)	157 (17.0)	70 (13.5)	26 (18.1)	262 (16.2)
Other related	12 (75.0)	1 (11.1)	1 (33.3)	208 (22.5)	8 (1.5)	9 (6.3)	239 (14.8)
8/8 matched URD	0 (0.0)	0 (0.0)	1 (33.3)	176 (19.0)	88 (17.0)	35 (24.3)	300 (18.6)
7/8 mismatched URD	1 (6.3)	0 (0.0)	0 (0.0)	61 (6.6)	30 (5.8)	20 (13.9)	112 (6.9)
<= 6/8 mismatched URD;	0 (0.0)	0 (0.0)	0 (0.0)	9 (1.0)	2 (0.4)	1 (0.7)	12 (0.7)
Multi-donor	0 (0.0)	0 (0.0)	0 (0.0)	17 (1.8)	0 (0.0)	0 (0.0)	17 (1.1)
Unrelated (matching TBD)	0 (0.0)	0 (0.0)	0 (0.0)	13 (1.4)	5 (1.0)	5 (3.5)	23 (1.4)
Cord blood	1 (6.3)	1 (11.1)	1 (33.3)	283 (30.6)	314 (60.7)	48 (33.3)	648 (40.2)
Disease status at time of HCT - no. (%)							
PIF	1 (6.3)	0 (0.0)	0 (0.0)	14 (1.5)	6 (1.2)	3 (2.1)	24 (1.5)
CR1	7 (43.8)	5 (55.6)	2 (66.7)	404 (43.7)	204 (39.5)	69 (47.9)	691 (42.8)
CR2	7 (43.8)	3 (33.3)	0 (0.0)	386 (41.8)	220 (42.6)	53 (36.8)	669 (41.5)
>=CR3	0 (0.0)	1 (11.1)	0 (0.0)	88 (9.5)	74 (14.3)	10 (6.9)	173 (10.7)
Relapse	1 (6.3)	0 (0.0)	1 (33.3)	32 (3.5)	13 (2.5)	9 (6.3)	56 (3.5)

Characteristic	9.0 - 9.9 GY	10.0 - 10.9 GY	11.0 - 11.9 GY	12.0 - 12.9 GY	13.0 -13.2 GY	>13.2 GY	Total
Conditioning regimen - no. (%)							
TBI/Cy	5 (31.3)	5 (55.6)	2 (66.7)	353 (38.2)	140 (27.1)	89 (61.8)	594 (36.8)
TBI/Cy/Flu	0 (0.0)	0 (0.0)	1 (33.3)	76 (8.2)	303 (58.6)	23 (16.0)	403 (25.0)
TBI/Cy/Flu/TT	0 (0.0)	0 (0.0)	0 (0.0)	7 (0.8)	0 (0.0)	0 (0.0)	7 (0.4)
TBI/Cy/TT	0 (0.0)	0 (0.0)	0 (0.0)	157 (17.0)	0 (0.0)	13 (9.0)	170 (10.5)
TBI/Cy/VP	0 (0.0)	1 (11.1)	0 (0.0)	81 (8.8)	8 (1.5)	2 (1.4)	92 (5.7)
TBI/VP	0 (0.0)	2 (22.2)	0 (0.0)	68 (7.4)	51 (9.9)	15 (10.4)	136 (8.4)
TBI/Mel	3 (18.8)	0 (0.0)	0 (0.0)	28 (3.0)	1 (0.2)	1 (0.7)	33 (2.0)
TBI/Flu	8 (50.0)	1 (11.1)	0 (0.0)	138 (14.9)	10 (1.9)	1 (0.7)	158 (9.8)
TBI/other(s)	0 (0.0)	0 (0.0)	0 (0.0)	16 (1.7)	4 (0.8)	0 (0.0)	20 (1.2)
TBI Dose (in GY) - median (min-max)	9.9 (9.0-9.99)	10.0 (10.0-10.50)	11.40 (11.25-11.65)	12.0 (12.0-12.95)	13.2 (13.2-13.2)	13.75 (13.5-30.0)	12.0 (9.0-30.0)
Year of current transplant - no. (%)							
2008	0 (0.0)	1 (11.1)	1 (33.3)	123 (13.3)	49 (9.5)	41 (28.5)	215 (13.3)
2009	0 (0.0)	1 (11.1)	0 (0.0)	77 (8.3)	49 (9.5)	13 (9.0)	140 (8.7)
2010	0 (0.0)	1 (11.1)	0 (0.0)	47 (5.1)	48 (9.3)	7 (4.9)	103 (6.4)
2011	1 (6.3)	0 (0.0)	1 (33.3)	45 (4.9)	37 (7.2)	8 (5.6)	92 (5.7)
2012	1 (6.3)	0 (0.0)	0 (0.0)	48 (5.2)	36 (7.0)	10 (6.9)	95 (5.9)
2013	2 (12.5)	1 (11.1)	0 (0.0)	63 (6.8)	42 (8.1)	6 (4.2)	114 (7.1)
2014	3 (18.8)	3 (33.3)	1 (33.3)	77 (8.3)	51 (9.9)	14 (9.7)	149 (9.2)
2015	0 (0.0)	1 (11.1)	0 (0.0)	76 (8.2)	56 (10.8)	15 (10.4)	148 (9.2)
2016	0 (0.0)	1 (11.1)	0 (0.0)	85 (9.2)	44 (8.5)	16 (11.1)	146 (9.1)
2017	3 (18.8)	0 (0.0)	0 (0.0)	67 (7.3)	37 (7.2)	5 (3.5)	112 (6.9)
2018	3 (18.8)	0 (0.0)	0 (0.0)	67 (7.3)	26 (5.0)	3 (2.1)	99 (6.1)
2019	1 (6.3)	0 (0.0)	0 (0.0)	72 (7.8)	20 (3.9)	5 (3.5)	98 (6.1)

Characteristic	9.0 - 9.9 GY	10.0 - 10.9 GY	11.0 - 11.9 GY	12.0 - 12.9 GY	13.0 -13.2 GY	>13.2 GY	Total
2020	0 (0.0)	0 (0.0)	0 (0.0)	16 (1.7)	10 (1.9)	0 (0.0)	26 (1.6)
2021	1 (6.3)	0 (0.0)	0 (0.0)	10 (1.1)	3 (0.6)	1 (0.7)	15 (0.9)
2022	1 (6.3)	0 (0.0)	0 (0.0)	51 (5.5)	9 (1.7)	0 (0.0)	61 (3.8)
Follow-up of survivors - median (range)	47.7 (3.0-102.9)	168.7 (66.0-191.7)	NE (.-.)	72.3 (3.3-193.5)	83.9 (2.0-194.1)	80.2 (3.5-193.1)	73.8 (2.0-194.1)

Field	Response
Proposal Number	2410-85-FRAINT
Proposal Title	Is There an Optimal CD34+ Cell Dose In Pediatric Allogeneic Hematopoietic Cell Transplantation Performed for Malignant Diseases?
Key Words	CD34+ cell dose; TNC dose; ALL; AML; MDS; Pediatric allogeneic stem cell transplant
Principal Investigator #1: - First and last name, degree(s)	Ellen Fraint MD
Principal Investigator #1: - Email address	fraint@gmail.com
Principal Investigator #1: - Institution name	Nemours Children's Health
Principal Investigator #1: - Academic rank	Assistant Professor
Junior investigator status (defined as ≤5 years from fellowship)	Yes
Do you identify as an underrepresented/minority?	No
Principal Investigator #2 (If applicable): - First and last name, degree(s):	Tristan E. Knight MD, FRCPC
Principal Investigator #2 (If applicable): - Email address:)	knight.tristan@gmail.com
Principal Investigator #2 (If applicable): - Institution name:	Seattle Children's Hospital / University of Washington School of Medicine
Principal Investigator #2 (If applicable): - Academic rank:	Clinical Assistant Professor
Junior investigator status (defined as ≤5 years from fellowship)	Yes
Do you identify as an underrepresented/minority?	No
We encourage a maximum of two Principal Investigators per study. If more than one author is listed, please indicate who will be identified as the corresponding PI below:	Ellen Fraint
If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:	-
Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.	None current; Tristan Knight was previously principle investigator on the recently completed PC20-01 project.
Do any of the PI(s) within this proposal have a CIBMTR WC study in manuscript preparation >6 months?	No
PROPOSED WORKING COMMITTEE:	Pediatric Cancer
Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.	Yes
If you have already spoken with a scientific director or working committee chair regarding this study, then please specify who:	Larisa Broglie (Pediatric Cancer)
RESEARCH QUESTION:	Is there an optimal CD34+ and TNC cell doses for pediatric patients undergoing hematopoietic cell transplant (HCT) for malignant disease indications, and if so, what is it?

Field	Response
RESEARCH HYPOTHESIS:	- The infusion of higher CD34+ cell doses will be associated with superior overall survival (OS), superior event free survival (EFS), reduced relapse rate (RR), and faster time to neutrophil and platelet engraftment in children undergoing allogenic HCT for malignancy. Higher CD34+ cell doses will not correlate with increased rates of aGVHD or NRM. These associations will be observed irrespective of graft source, donor type, conditioning intensity, or graft manipulation (either in-vivo or ex-vivo). - The infusion of higher TNC doses will be associated with superior OS, superior EFS, reduced RR, and faster time to neutrophil and platelet engraftment in children undergoing allogenic HCT for malignancy. These associations will be observed irrespective of graft source, donor type, and conditioning intensity. - Higher T-cell doses (approximated as TNC/CD34 ratio) will be correlated with increased rates of GVHD and lower risk of relapse, but only in T-cell replete grafts. This effect will not be seen in cases with T-cell depletion including post-transplant cyclophosphamide.

Field	Response
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	- We will analyze OS, EFS, RR, NRM, incidence of aGVHD, and time to neutrophil and platelet engraftment in pediatric patients who have undergone allogenic HCT for malignancy based upon the CD34+ cell dose and TNC dose of their grafts, with the analyses for CD34+ and TNC content performed independent of each other, as well as in the form of a TNC/CD34+ ratio for those patients with both data points. EFS will be the primary study endpoint, defined as alive and in continuous remission. Secondary endpoints will include OS, the occurrence of relapse, NRM, aGVHD, cGVHD, and time to neutrophil and platelet engraftment. Optimal cut-points for both CD34+ dose and TNC will be determined using the maximum likelihood method, fit into the model as binary variables (above/below cut-point), using EFS as the primary outcome. CD34+ doses and TNC doses will additionally be stratified by quartiles to identify whether an optimal dose range exists, based on EFS. - Pending a determination of whether an adequate sample size is available, sub-analyses will be conducted to determine the magnitude and direction of any association between CD34+ dose and the above outcomes, and between TNC dose and the above outcomes, based on: Indication for transplant Graft type Donor type (matched sibling donor, matched unrelated donor, or mis-matched unrelated donor), Conditioning regimen (MAC or RIC) T-cell depleted (in-vivo or ex-vivo, including post-transplant cyclophosphamide) versus T-cell replete

SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.	Physicians engaged in the performance of hematopoietic cell transplant (HCT) have a degree of control over the final cellular contents of a graft. A CD34+ collection target is typically specified at the time of peripheral blood stem cell (PBSC) collection or bone marrow (BM) harvest and is often set at 2-5 x10^6 CD34+ cells per kilogram of recipient body weight. Moreover, in instances where a surplus of CD34+ cells have been harvested (e.g. above the standard 2-5 x10^6 CD34/kg threshold), the actual CD34+ cell dose infused is under the discretion of the transplant physician. At present, decisions about product infusions are not informed by evidence about optimal graft composition or cell dose. The goal of this project is to establish an evidence base for these decisions by (a) determining whether an optimal CD34+ dose exists and (b), whether an optimal target TNC dose exists. In pediatric allogeneic HCT, current general practice is to target a CD34+ cell dose of approximately 2-5x10^6/kg. However, emerging data has challenged this standard, with a number of studies among adults suggesting that cell doses above this range may result in superior outcomes (1-9). As such, it is possible that pediatric patients might likewise benefit via the use of higher standard target CD34+ doses. Available data are heterogeneous, with some studies showing no association between increased CD34+ cell dose and improved outcomes, or only showing an effect in certain sub-populations (10-17). More recent and more well powered studies (2, 18), however, show a clear improvement in outcomes by targeting CD34+ doses in the 5-8 x10^6/kg range, and reduced survival below this threshold. Put another way: adults who receive CD34+ doses in the standard pediatric dose range of 2-5x10^6/kg have worse outcomes, and it is possible that children may likewise demonstrate this trend. However, as these studies have been performed in adults, pediatric data is necessary. The optimal TNC dose is also an unsettled question, as some studies have identified positive effects associated with higher TNC doses (13, 14), while others have identified no such association (17, 19). There is also a concern that a higher TNC dose, by virtue of the larger number of potentially alloreactive lymphocytes, may increase the risk of GVHD (14, 20), but this effect is not universally observed (17). As the CD3+ dose is only available in a small proportion of patients within CIBMTR database, TNC will be examined as the best available proxy for understanding T-cell dose in relation to CD34+ cell dose. As alternative donor sources and graft manipulations have become more varied and more common over time, determining the optimal cellular components of a graft has become both more important and more complex. The importance of a threshold TNC and CD34+ cell dose

Field	Response
	for optimal survival is relatively well established in cord blood transplant (21), but this issue remains unanswered for PBSC and BM grafts. Although an approximate minimum cell dose needed to facilitate engraftment is generally agreed upon, the authors of published studies on this matter have reached rather different conclusions about the utility of higher cell doses (17). The increasing usage of post-transplant cyclophosphamide provides an opportunity to further differentiate the effects of CD34+ dose versus alloreactive passenger lymphocytes, which are heavily depleted via this therapy; any outcome difference in this population would, therefore, be attributable to the CD34+ dose alone. This proposal therefore seeks to examine patient outcomes across a range of malignant indications, conditioning regimens, donor/graft sources, and graft manipulation methodologies, with the goal of determining the optimal cellular components for pediatric allogenic grafts. If such outcomes are indeed found to vary as a function of the infused graft contents, collection targets may require re-evaluation. As such an effect size may be small, this proposed analysis would likely be impossible at a single or multi-institutional level and necessitates the use of the CIBMTR database.

SCIENTIFIC JUSTIFICATION: Provide a background summary of previous related research and their strengths and weaknesses, justification of your research and why your research is still necessary.	Identifying the optimal CD34+ cell dose and TNC dose using pediatric-specific data is important for a variety of reasons. Since children are smaller and have a wider range in body size, data regarding cell dose per unit of body weight should be analyzed separately from data on adults. In addition, there are significant differences between pediatric and adult HCT which may influence the conclusions about optimal cell doses, for example the fact that children often receive haploidentical grafts from parents instead of siblings or offspring, or the markedly more frequent use of reduced intensity conditioning in adults, or the over-representation of PBSC grafts in adult HCT as compared to BM used more commonly in children. Using a large, robust set of pediatric-specific data to determine optimal cell doses for pediatric HCT is also important because of the downstream implications. Pediatric HCT recipients often have sibling donors who are themselves small children, and the considerations surrounding cell dose targets become even more complex when the donors are smaller than their recipient siblings. Reaching a well-supported and precise understanding of the necessary cell doses for successful HCT will enable us to plan collection volumes with improved accuracy, which in turn will aid in donor selection and optimization. Meanwhile, the increasing use of haploidentical transplants means that parents or other adults are being used ever more frequently as donors for children. Regardless of whether marrow or PBSCs are being collected, this means that doses of CD34+ cells well in excess of the traditional 2-5x10^6 per kg of recipient weight are often achievable. Given our limited current understanding of the optimal CD34+ cell dose and T-cell dose however, it is unclear whether the administration of these higher doses would be beneficial or detrimental. In the autologous pediatric HCT setting, findings from the pediatric cancer working committee study PC20-01 have suggested a possible association between CD34+ dose and key outcomes (22, 23). Specifically, among children with CNS tumors, higher CD34+ doses were associated with superior progression-free survival and overall survival. A similar finding was not seen in children with neuroblastomas. Importantly, in both populations, PC20-01 did not identify a higher incidence of post-transplant endothelial injury complications or non-relapse mortality among patients receiving higher CD34+ cell doses. In the autologous setting at least, it has therefore been suggested that higher CD34+ cell doses appear safe and may improve patient outcomes in some contexts. It is unknown whether a similar effect may be observed in the pediatric allogeneic HCT setting. Improving our understanding of optimal cell doses would ease the planning of cell collection and

	provide more flexibility in the administration and storage of cell doses for immediate versus future use. These analyses would also answer important questions about whether larger-than-necessary cell doses actually lead to any harm or not. For instance, some studies have observed an association between larger infused TNC doses and increased rates of GVHD (14, 20), but others have not (17, 19). Mechanistically, it has been proposed that such an effect may be mediated by the larger number of potentially alloreactive lymphocytes contained within a graft with a higher TNC (14). In examining survival- and relapse-related outcomes, it is also therefore important to assess for associations between GVHD risk and TNC/CD34+ cell doses. Multiple recent large studies of adult patients have highlighted populations in which a positive effect is seen via the administration of relatively higher CD34+ cell doses: • In a study of approximately 200 adults undergoing HCT for hematological malignancies using matched sibling donor PBSCs, CD34+ cell doses of 6–7x10^6/kg were associated with superior OS and lower TRM, while doses of <5x10^6/kg led to increased relapse but reduced cGVHD. Higher cell doses were also correlated with reduced rates of aGVHD grade 2-4 (6). • A study of nearly 400 adults undergoing HCT for hematological malignancies with matched sibling donor PBSCs identified superior 5-year OS and more rapid platelet and neutrophil engraftment among patients receiving higher CD34+ cell doses, with indications that this effect may scale with increasing dose. No association was identified with TRM, RR, or grade 2-4 aGVHD, but cGVHD did appear more common with increasing CD34+ dose. The authors identified an ideal target CD34+ cell dose of >7.5x10^6/kg for this population (2). • Data from other studies of adults suggests that similar findings are also observed following reduced intensity conditioning. A 2014 study of more than a thousand adult patients undergoing HCT for AML or MDS using RIC regimens found that grafts containing <4x10^6 CD34+/kg (matched sibling donors) or <6x10^6 CD34+/kg (unrelated donors) were associated with higher OS and NRM, without any effect on RR or GVHD (8). Conversely, a separate but similar analysis of approximately 100 patients, this time including in-vivo T-cell depletion via ATG, found no association between CD34+ dose and any of aGVHD, cGVHD, NRM, RR, and OS (9). • More recently, Pedraza et al conducted a single-center retrospective analysis of 221 consecutive adult patients who underwent allo-HCT using a variety of donor sources and subsequently received post-transplant cyclophosphamide-based GVHD prophylaxis. Patients receiving higher- CD34+-

Field	Response
	dose grafts had significantly shorter median times to neutrophil engraftment and platelet engraftment. Moreover, while CD34+ cell dose did not impact survival outcomes after matched sibling donor, matched unrelated donor, or mismatched unrelated donor HCT, infusions containing <5 × 10^6/kg CD34+ cells was associated with reduced overall survival in haploidentical recipients (18). Given the observed improvements in outcomes associated with higher CD34+ cell doses among adult patients, it is not unreasonable to expect a similar effect in children. However, given the differences between pediatric versus adult HCT patients, specific studies of this population are warranted. It is this knowledge gap which therefore provides the scientific justification to conduct an authoritative study on the question, via the CIBMTR database.
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	- Inclusion criteria: o Recipient of an allogeneic hematopoietic cell transplant o Malignant disease indication for transplant: ▯ ALL ▯ AML ▯ MDS o Transplant performed between 01/01/2000 – 12/31/2023 o Recipients aged 0 to 21 at time of transplant o BM or PBSC grafts (i.e. any graft other than cord) o T-cell replete or T-cell depleted HCT (in vivo or ex vivo, including post-transplant cyclophosphamide) o CD34+ dose OR TNC dose reported; absence of one or the other will not disqualify patients; patients with only CD34+ or TNC dose will be included only in the relevant analyses. - Exclusion criteria: o Data missing regarding any of: ▯ Disease and patient status at 100-days post-transplant (e.g. in remission/not-in-remission, alive/not-alive) ▯ Donor source ▯Graft source ▯ Transplant indication o Available follow up is less than 100 days o The absence of data on the following variables will not be an exclusion criterion, but patients will be excluded from the relevant analyses if data is not present: ▯ CD34 dose ▯ TNC dose ▯ Time to neutrophil engraftment ▯ Time to platelet engraftment ▯ Graft manipulation ▯Presence/absence of GVHD o Second transplant; patients who have undergone a second transplant will be eligible for inclusion, but only on the basis of their first transplant characteristics; second transplants will not be examined.
Does this study include pediatric patients?	Yes
If this study does not include pediatric patients, please provide justification:	-

Field	Response
DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion- variables to be considered in the multivariate analyses. Outline any supplementary data required.	The proposed study will not require the collection of supplemental data, nor will it require combining CIBMTR data with data from another group - The following variables will be considered: o Graft characteristics CD34+ cell dose TNC dose TNC/CD34+ cell dose (for patients with both data points) o Patient-related variables: Indication for HCT: • ALL • AML • MDS Donor type (matched, haploidentical, mismatched, related/unrelated) Graft type (BM, PBSC) T-cell depletion (none, ex vivo, in vivo (e.g. post-transplant cyclophosphamide) Conditioning regimen (MAC, RIC) o Outcome Measures: Overall Survival (duration; continuous) Event-free survival (duration; continuous) Relapse rate (relapsed or not-relapsed) Occurrence of acute GVHD (present or not-present) • Grade 1-2 • Grade 3-4 Occurrence of chronic GVHD (present or not-present) Time to neutrophil engraftment (duration; continuous) Time to platelet engraftment (duration; continuous)
Types of cellular therapy data this proposal includes:	Hematopoietic Cell Transplantation (HCT)
PATIENT REPORTED OUTCOME (PRO) REQUIREMENTS: If the study requires PRO data collected by CIBMTR, the proposal should include: 1) A detailed description of the PRO domains, timepoints, and proposed analysis of PROs; 2) A description of the hypothesis speci	Not applicable
MACHINE LEARNING: Please indicate if the study requires methodology related to machine-learning and clinical predictions.	Not applicable
SAMPLE REQUIREMENTS: If the study requires biologic samples from the CIBMTR Repository, the proposal should also include: 1) A detailed description of the proposed testing methodology and sample requirements; 2) A summary of the investigator's previous e	Not applicable
NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required.	Not applicable

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Infused total nucleated cell dose is a better predictor of transplant outcomes than CD34+ cell number in reduced-intensity mobilized peripheral blood allogeneic hematopoietic cell transplantation. Haematologica 2016;101:499-505. 15. Perez-Simon JA, Diez-Campelo M, Martino R, et al. Impact of CD34+ cell dose on the outcome of patients undergoing reduced-intensity-conditioning allogeneic peripheral blood stem cell transplantation. Blood 2003;102:1108-13. 16. Pichler H, Witt V, Winter E, et al. No impact of total or myeloid Cd34+ cell numbers on neutrophil engraftment and transplantation-related mortality after allogeneic pediatric bone marrow transplantation. Biol Blood Marrow Transplant 2014;20:676-83. 17. Remberger M, Torlen J, Ringden
O, et al. Effect of Total Nucleated and CD34(+) Cell Dose on Outcome after Allogeneic Hematopoietic Stem Cell Transplantation. Biol Blood Marrow Transplant 2015;21:889-93. 18. Pedraza A, Salas MQ, Rodríguez-Lobato LG, Charry P, Suárez-Lledo M, Martínez-Cibrian N, Doménech A, Solano MT, Arcarons J, de Llobet N, Rosiñol L, Gutiérrez-García G, Avilés FF, Urbano-Ispízua Á, Rovira M, Martínez C. Effect of CD34+ Cell Dose on the Outcomes of Allogeneic Stem Cell Transplantation with Post-Transplantation Cyclophosphamide. Transplant Cell Ther. 2023 Mar;29(3):181.e1-181.e10. doi: 10.1016/j.jtct.2022.12.005. Epub 2022 Dec 14. PMID: 36526259. 19. Brown CA, Mineishi S, Jagasia M et al. Predictive value for engraftment and survival of total nucleated cell dose (TNC) as compared to CD34+ cell dose after autologous and allogeneic bone marrow transplant (BMT) for hematologic malignancies. JCO 23, 6706-6706(2005). 20. Gupta A, Punatar S, Gawande J, et al. Risk Factors, Pattern and Clinical Outcome of Acute Graft Versus Host Disease in Acute Leukemia Patients Undergoing Allogeneic Stem Cell Transplant. Indian J Hematol Blood Transfus 2015;31:404-12. 21. Barker JN, Scaradavou A,

Field	Response
	Stevens CE. Combined effect of total nucleated cell dose and HLA match on transplantation outcome in 1061 cord blood recipients with hematologic malignancies. Blood 2010;115:1843-9. 22. Knight TE, Woo Ahn K, Herbert KM, et al. Effect of Autograft CD34+ Dose on Outcome in Pediatric Patients Undergoing Autologous Hematopoietic Stem Cell Transplant for Central Nervous System Tumors. Transplant Cell Ther. 2023 Jun;29(6):380.e1-380.e9 23. Knight TE, Woo Ahn K, Herbert KM et al. No impact of CD34+ cell dose on outcome among children undergoing autologous hematopoietic stem cell transplant for high-risk neuroblastoma. Bone Marrow Transplant. 2023 Dec;58(12):1390-1393
CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning?	No, I do not have any conflicts of interest pertinent to this proposal
If yes, provide detail on the nature of employment, name of organization, role, entity, ownership, type of financial transaction or legal proceeding and whether renumeration is >$5000 annually.	-

The below selection criteria were applied

Selection criteria	# excluded	N
Cases available in CIBMTR HCT Essentials Extract *		441766
First Allo Transplant	246638	195128
HCT years 2008-2022	23172	171956
Disease: AML, ALL, other leukemia and MDS	58239	113717
Age at diagnosis: <22 year	95272	18445
Graft Type: BM or PBSC	3177	15268
GVHD prophylaxis as T-cell depletion or CD34 selection excluded	1286	13982
CRF Track	11712	2270
Patient Consented	128	2142
Follow-up present	82	2060

**Data source: HCT Essentials Oct 2024*

Table 1: Patients that underwent first allogeneic HCT for AML, ALL, other leukemia and MDS between 2008-2022.

Characteristic	N (%)
No. of patients	2060
No. of centers	203
Patient age - median (min-max)	13.7 (0.4-22.0)
Age Groups - no. (%)	
<2 year	133 (6.5)
2-10 years	682 (33.1)
11-18 years	822 (39.9)
19-21 years	423 (20.5)
Primary disease - no. (%)	
AML or ANLL	947 (46.0)
ALL	877 (42.6)
Other Leukemia	4 (0.2)
MDS	232 (11.3)
Conditioning Regimen Intensity- no. (%)	
MAC	1761 (85.5)
RIC	187 (9.1)

Characteristic	N (%)
NMA	51 (2.5)
Not Reported	61 (3.0)
Conditioning Regimen - no. (%)	
TBI/Cy	485 (23.5)
TBI/Cy/Flu	68 (3.3)
TBI/Cy/TT	94 (4.6)
TBI/Cy/VP	80 (3.9)
TBI/VP	89 (4.3)
TBI/Mel	22 (1.1)
TBI/Flu	171 (8.3)
TBI/other(s)	12 (0.6)
Bu/Cy/Mel	54 (2.6)
Bu/Cy	507 (24.6)
Bu/Mel	44 (2.1)
Flu/Bu/TT	46 (2.2)
Flu/Bu	283 (13.7)
Flu/Mel/TT	25 (1.2)
Flu/Mel	23 (1.1)
Cy/Flu	3 (0.1)
Cy alone	2 (0.1)
Mel/other(s)	1 (0.0)
Treosulfan	33 (1.6)
Other(s)	16 (0.8)
None	1 (0.0)
Not Reported	1 (0.0)
Donor type - no. (%)	
HLA-identical sibling	573 (27.8)
Other related	490 (23.8)
8/8 matched URD	634 (30.8)
7/8 mismatched URD	258 (12.5)
<= 6/8 mismatched URD;	17 (0.8)
Multi-donor	21 (1.0)

Characteristic	N (%)
Unrelated (matching TBD)	67 (3.3)
CD34+ per Kilogram Count Range (Unit in 10^6 cells) - no. (%)	
0 - 10	1245 (60.4)
>10 - 20	146 (7.1)
>20 - 30	15 (0.7)
>30 - 40	6 (0.3)
>50	14 (0.7)
Not Reported	634 (30.8)
CD34+ Count per Kilogram (Standardized in unit 10^6) - median (min-max)	4.8 (<0.01-6752.3)
TNC per Kilogram Count Range (Unit in10^6 cells) - no. (%)	
0 - 100	81 (3.9)
>100 - 400	492 (23.9)
>400 - 800	491 (23.8)
>800 - 1200	149 (7.2)
>1200 - 1600	54 (2.6)
>1600	45 (2.2)
Not Reported	748 (36.3)
Total Nucleated Cell Count per Kilogram (Standardized in unit 10^6) - median (min-max)	441.3 (<0.01-49333.3)
Year of current transplant - no. (%)	
2008	222 (10.8)
2009	190 (9.2)
2010	148 (7.2)
2011	38 (1.8)
2012	65 (3.2)
2013	153 (7.4)
2014	201 (9.8)
2015	199 (9.7)
2016	208 (10.1)
2017	153 (7.4)
2018	157 (7.6)
2019	146 (7.1)

Characteristic	N (%)
2020	44 (2.1)
2021	47 (2.3)
2022	89 (4.3)
Follow-up of survivors - median (range)	72.1 (1.1-193.9)

Field	Response
Proposal Number	2410-94-ROSSOFF
Proposal Title	Effect of disease burden and pre-transplant therapy in pediatric patients with myelodysplastic syndrome in the current era
Key Words	myelodysplastic syndrome, disease burden, pediatric cancer
Principal Investigator #1: - First and last name, degree(s)	Jenna Rossoff, MD
Principal Investigator #1: - Email address	jrossoff@luriechildrens.org
Principal Investigator #1: - Institution name	Ann & Robert H. Lurie Children's Hospital of Chicago
Principal Investigator #1: - Academic rank	Assistant Professor
Junior investigator status (defined as ≤5 years from fellowship)	Yes
Do you identify as an underrepresented/minority?	No
Principal Investigator #2 (If applicable): - First and last name, degree(s):	Sonali Chaudhury, MD
Principal Investigator #2 (If applicable): - Email address:)	schaudhury@luriechildrens.org
Principal Investigator #2 (If applicable): - Institution name:	Ann & Robert H. Lurie Children's Hospital of Chicago
Principal Investigator #2 (If applicable): - Academic rank:	Professor
Junior investigator status (defined as ≤5 years from fellowship)	No
Do you identify as an underrepresented/minority?	No
We encourage a maximum of two Principal Investigators per study. If more than one author is listed, please indicate who will be identified as the corresponding PI below:	-
If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:	-
Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.	Sonali Chaudhury - Prognostic impact of cytogenetic and molecular risk classification in AML after hematopoietic stem cell transplant in adolescent and young adults (Study #LK23-02)
Do any of the PI(s) within this proposal have a CIBMTR WC study in manuscript preparation >6 months?	No
PROPOSED WORKING COMMITTEE:	Pediatric Cancer
Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.	Yes
If you have already spoken with a scientific director or working committee chair regarding this study, then please specify who:	Larisa Broglie

Field	Response
RESEARCH QUESTION:	Does blast percentage in the bone marrow prior to transplant affect post-transplant disease-free survival (DFS) in pediatric patients with myelodysplastic syndrome (MDS) in the current era?
RESEARCH HYPOTHESIS:	We hypothesize achieving a lower blast percentage in the bone marrow prior to transplant predicts improved DFS for pediatric patients with MDS undergoing allogeneic hematopoietic stem cell transplant (alloHCT) in the current era.
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	- Primary Objective: Determine the effect of pre-transplant bone marrow blast percentage on DFS in pediatric patients with MDS - Secondary Objectives: 1) Determine the difference in DFS between patients receiving pre-transplant chemotherapy versus those proceeding directly to alloHCT; 2) Determine if there is an improvement in DFS in patients who achieved a partial response (PR) or complete response (CR) to pre-transplant chemotherapy versus those who did not achieve a PR or CR prior to transplant
SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.	MDS is rare in pediatric patients compared to older adults, occurring in ~1-4 per million versus ~36 per 100,000, respectively. In pediatric patients, the goal of treatment is curative versus life-prolonging in older adults. AlloHCT provides a potentially curative treatment modality for pediatric patients with MDS, but outcomes remain sub-optimal. By better understanding the impact of both pre-transplant disease burden and pre-transplant therapy, we can develop improved treatment algorithms for these patients thereby optimizing outcomes. We hope to utilize this data to propose a pre-transplant MDS chemotherapy protocol with Venetoclax/Azacytidine to be conducted through the Childrens Oncology Group.

Field	Response
SCIENTIFIC JUSTIFICATION: Provide a background summary of previous related research and their strengths and weaknesses, justification of your research and why your research is still necessary.	Allogeneic hematopoietic stem cell transplant is the treatment of choice for pediatric patients with MDS.1,2 However, outcomes for these patients remain sub-optimal due to both relapse and transplant-related morbidity/mortality.1 Furthermore, there is a lack of consensus on pre-transplant management of pediatric patients with MDS, particularly in the era of venetoclax and azacitidine.3 Previous studies have shown that there is no survival benefit with use of intensive acute myeloid leukemia (AML)-type chemotherapy in patients with MDS, but these studies are often limited by small numbers and heterogeneous populations and also changing definitions of AML/MDS over time.4-6 Additionally, data with use of less intensive chemotherapy (i.e. with hypomethylating agents and/or BCL2 inhibitors) prior to transplant is even further limited to case reports and small case series.7-10 Given the sub-optimal outcomes for these patients, it is imperative that we optimize their pre-transplant management. CIBMTR has data on >1200 pediatric patients who underwent alloHCT for MDS, a significantly higher patient population than has previously been reported. In this study, we hope to further delineate the effect on DFS of pre-transplant disease burden, both with and without the use of pre-transplant chemotherapy, to hopefully set the stage for a prospective clinical trial delving further into the use of less intensive pre-transplant treatment with venetoclax and azacitidine.
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	- Inclusion criteria: Diagnosis of MDS based on 2022 WHO classification11; age <25 years at diagnosis of MDS; underwent first allogeneic stem cell transplant for diagnosis of MDS between 2010-present - Exclusion criteria: receipt of prior allogeneic stem cell transplant for any indication
Does this study include pediatric patients?	Yes
If this study does not include pediatric patients, please provide justification:	-

Field	Response
DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion- variables to be considered in the multivariate analyses. Outline any supplementary data required.	- Age - Sex - Ethnicity - Race with Race Detail - Country of primary residence of recipient - Specify Donor - Specify product type - Specify the related donor type - Specify the biological relationship of the donor to the recipient - Degree of mismatch (related donors only) - Specify unrelated donor type - Donor age, sex - Donor testing if related - Performance score prior to the start of the preparative regimen - <70 versus >70 - Recipient's prescribed preparative regimen- MAC versus RIC - Post-HCT therapy – Y/N - Date of MDS diagnosis- 2010-15, 2015 to 20, >2020 - MDS subtype at diagnosis - MDS therapy-related- Y/N - Predisposing condition? Describe mutations. - Blasts in bone marrow prior to transplant - Impact of Cellularity of bone marrow (hypocellular, normocellular, hypercellular) - Impact of cytogenetics -FISH and karyotyping- Monosomy 7 versus others - Impact of molecular markers - Impact of pre-transplant therapy? Best response to line of therapy. - Impact of progression or transforming to a different MDS subtype or AML between diagnosis and the start of the preparative regimen / cell infusion- Y/N - Impact of post-transplant therapy? Y/N
Types of cellular therapy data this proposal includes:	Hematopoietic Cell Transplantation (HCT)
PATIENT REPORTED OUTCOME (PRO) REQUIREMENTS: If the study requires PRO data collected by CIBMTR, the proposal should include: 1) A detailed description of the PRO domains, timepoints, and proposed analysis of PROs; 2) A description of the hypothesis speci	N/A
MACHINE LEARNING: Please indicate if the study requires methodology related to machine-learning and clinical predictions.	N/A
SAMPLE REQUIREMENTS: If the study requires biologic samples from the CIBMTR Repository, the proposal should also include: 1) A detailed description of the proposed testing methodology and sample requirements; 2) A summary of the investigator's previous e	N/A
NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required.	N/A

REFERENCES:	1. Smith AR, Christiansen EC, Wagner JE, et al. Early hematopoietic stem cell transplant is associated with favorable outcomes in children with MDS. Pediatr Blood Cancer. 2013 Apr;60(4):705-10. doi: 10.1002/pbc.24390. Epub 2012 Nov 14. PMID: 23152304; PMCID: PMC3668778. 2. Hasle H, Kerndrup G, Yssing M, Clausen N, Ostergaard E, Jacobsen N, Jacobsen BB. Intensive chemotherapy in childhood myelodysplastic syndrome. A comparison with results in acute myeloid leukemia. Leukemia. 1996 Aug;10(8):1269-73. PMID: 8709630. 3. Nakano TA, Lau BW, Dickerson KE, et al. Diagnosis and treatment of pediatric myelodysplastic syndromes: A survey of the North American Pediatric Aplastic Anemia Consortium. Pediatr Blood Cancer. 2020 Oct;67(10):e28652. doi: 10.1002/pbc.28652. Epub 2020 Aug 11. PMID: 32779892. 4. Hasle H, Niemeyer CM. Advances in the prognostication and management of advanced MDS in children. Br J Haematol. 2011 Jul;154(2):185-95. doi: 10.1111/j.1365-2141.2011.08724.x. Epub 2011 May 9. PMID: 21554264. 5. Strahm B, Nöllke P, Zecca M, et al. Hematopoietic stem cell transplantation for advanced myelodysplastic syndrome in children: results of the EWOG-MDS 98 study. Leukemia. 2011 Mar;25(3):455-62. doi: 10.1038/leu.2010.297. Epub 2011 Jan 7. PMID: 21212791. 6. Locatelli F, Strahm B. How I treat myelodysplastic syndromes of childhood. Blood. 2018 Mar 29;131(13):1406-1414. doi: 10.1182/blood-2017-09-765214. Epub 2018 Feb 8. PMID: 29438960. 7. Waespe N, Van Den Akker M, Klaassen RJ, et al. Response to treatment with azacitidine in children with advanced myelodysplastic syndrome prior to hematopoietic stem cell transplantation. Haematologica. 2016;101:1508-1515. 8. Marinoff AE, Aaronson K, Agrawal AK, et al. Venetoclax in combination with chemotherapy as treatment for pediatric advanced hematologic malignancies. Pediatr Blood Cancer. 2023 Jun;70(6):e30335. doi: 10.1002/pbc.30335. Epub 2023 Apr 10. PMID: 37036306; PMCID: PMC10133180. 9. Winters AC, Maloney KW, Treece AL, Gore L, Franklin AK. Single-center pediatric experience with venetoclax and azacitidine as treatment for myelodysplastic syndrome and acute myeloid leukemia. Pediatr Blood Cancer. 2020 Oct;67(10):e28398. doi: 10.1002/pbc.28398. Epub 2020 Jul 31. PMID: 32735397. 10. Masetti R, Baccelli F, Leardini D, et al. Venetoclax-based therapies in pediatric advanced MDS and relapsed/refractory AML: a multicenter retrospective analysis. Blood Adv. 2023 Aug 22;7(16):4366-4370. doi: 10.1182/bloodadvances.2023010113. PMID: 37216275;

Field	Response
	PMCID: PMC10432591. 11. Khoury JD, Solary E, Abla O, Akkari Y, Alaggio R, Apperley JF, et al. The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours: Myeloid and Histiocytic/Dendritic Neoplasms. Leukemia. 2022;36:1703–19.
CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning?	Yes, I have conflicts of interest pertinent to this proposal
If yes, provide detail on the nature of employment, name of organization, role, entity, ownership, type of financial transaction or legal proceeding and whether renumeration is >$5000 annually.	Medexus advisory board, Abbvie study committee

The below selection criteria were applied 1

Selection criteria	# excluded	N
Cases available in CIBMTR HCT Essentials Extract*		441766
First Allo Transplant	246638	195128
HCT years 2013-2022	76998	118130
Disease: MDS	100709	17421
Age at diagnosis: <= 25 year	16044	1377
Patient Consented	148	1229
Track: CRF	954	275
Follow up present	8	267
Bone Marrow Blast at Prep: <20	1	266

**Data source: HCT Essentials Oct 2024*

Table 1: Patients that underwent first allogeneic HCT for MDS with specified bone marrow blast categories between 2013-2022.

Characteristic	Bone marrow blasts at prep 0-5, N (%)	Bone marrow blasts at prep 6-10, N (%)	Bone marrow blasts at prep 11-19, N (%)	Bone marrow blasts at prep missing/not done, N (%)	Total, N (%)
No. of patients	133	23	18	92	266
No. of centers	74	19	17	58	102
Patient age - median (min-max)	13.8 (0.6-24.6)	13.3 (1.0-23.8)	13.0 (4.6-25.0)	4.6 (0.3-24.3)	12.0 (0.3-25.0)
Age Range - no. (%)					
<2 year	13 (9.8)	1 (4.3)	0 (0.0)	31 (33.7)	45 (16.9)
2 - 10 years	39 (29.3)	7 (30.4)	6 (33.3)	28 (30.4)	80 (30.1)
11 - 18 years	46 (34.6)	10 (43.5)	8 (44.4)	24 (26.1)	88 (33.1)
19 - <=25 years	35 (26.3)	5 (21.7)	4 (22.2)	9 (9.8)	53 (19.9)
Conditioning Regimen Intensity - no. (%)					
MAC	99 (74.4)	15 (65.2)	11 (61.1)	81 (88.0)	206 (77.4)
RIC	21 (15.8)	3 (13.0)	4 (22.2)	4 (4.3)	32 (12.0)
NMA	2 (1.5)	2 (8.7)	2 (11.1)	2 (2.2)	8 (3.0)

Characteristic	Bone marrow blasts at prep 0-5, N (%)	Bone marrow blasts at prep 6-10, N (%)	Bone marrow blasts at prep 11-19, N (%)	Bone marrow blasts at prep missing/not done, N (%)	Total, N (%)
Not Reported	11 (8.3)	3 (13.0)	1 (5.6)	5 (5.4)	20 (7.5)
Conditioning regimen - no. (%)					
TBI/Cy	4 (3.0)	0 (0.0)	0 (0.0)	1 (1.1)	5 (1.9)
TBI/Cy/Flu	11 (8.3)	3 (13.0)	2 (11.1)	2 (2.2)	18 (6.8)
TBI/Cy/Flu/TT	2 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.8)
TBI/Mel	2 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.8)
TBI/Flu	6 (4.5)	2 (8.7)	2 (11.1)	3 (3.3)	13 (4.9)
TBI/other(s)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Bu/Cy/Mel	5 (3.8)	0 (0.0)	4 (22.2)	25 (27.2)	34 (12.8)
Bu/Cy	42 (31.6)	8 (34.8)	4 (22.2)	23 (25.0)	77 (28.9)
Bu/Mel	8 (6.0)	1 (4.3)	1 (5.6)	17 (18.5)	27 (10.2)
Flu/Bu/TT	10 (7.5)	0 (0.0)	0 (0.0)	2 (2.2)	12 (4.5)
Flu/Bu	19 (14.3)	5 (21.7)	2 (11.1)	12 (13.0)	38 (14.3)
Flu/Mel/TT	6 (4.5)	0 (0.0)	0 (0.0)	0 (0.0)	6 (2.3)
Flu/Mel	4 (3.0)	1 (4.3)	2 (11.1)	0 (0.0)	7 (2.6)
Mel/other(s)	1 (0.8)	0 (0.0)	0 (0.0)	1 (1.1)	2 (0.8)
Treosulfan	12 (9.0)	2 (8.7)	1 (5.6)	3 (3.3)	18 (6.8)
Other(s)	0 (0.0)	1 (4.3)	0 (0.0)	2 (2.2)	3 (1.1)
Not Reported	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)
Donor type - no. (%)					
HLA-identical sibling	18 (13.5)	2 (8.7)	3 (16.7)	13 (14.1)	36 (13.5)
Other related	33 (24.8)	9 (39.1)	3 (16.7)	24 (26.1)	69 (25.9)
8/8 matched URD	23 (17.3)	4 (17.4)	6 (33.3)	19 (20.7)	52 (19.5)
7/8 mismatched URD	14 (10.5)	0 (0.0)	3 (16.7)	10 (10.9)	27 (10.2)
<= 6/8 mismatched URD;	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Multi-donor	3 (2.3)	0 (0.0)	0 (0.0)	1 (1.1)	4 (1.5)
Unrelated (matching TBD)	2 (1.5)	0 (0.0)	1 (5.6)	1 (1.1)	4 (1.5)
Cord blood	39 (29.3)	8 (34.8)	2 (11.1)	24 (26.1)	73 (27.4)

Characteristic	Bone marrow blasts at prep 0-5, N (%)	Bone marrow blasts at prep 6-10, N (%)	Bone marrow blasts at prep 11-19, N (%)	Bone marrow blasts at prep missing/not done, N (%)	Total, N (%)
Was disease MDS therapy related? - no. (%)					
No	107 (80.5)	16 (69.6)	14 (77.8)	46 (50.0)	183 (68.8)
Yes	19 (14.3)	6 (26.1)	2 (11.1)	7 (7.6)	34 (12.8)
Not Reported	7 (5.3)	1 (4.3)	2 (11.1)	39 (42.4)	49 (18.4)
Did the recipient have a predisposing condition? - no. (%)					
No	84 (63.2)	14 (60.9)	9 (50.0)	31 (33.7)	138 (51.9)
Yes	41 (30.8)	8 (34.8)	6 (33.3)	14 (15.2)	69 (25.9)
Not reported	8 (6.0)	1 (4.3)	3 (16.7)	47 (51.1)	59 (22.2)
Subdisease classification - no. (%)					
Juvenile CML:	7 (5.3)	1 (4.3)	2 (11.1)	46 (50.0)	56 (21.1)
MDS	43 (32.3)	7 (30.4)	2 (11.1)	18 (19.6)	70 (26.3)
Myelodysplastic syndrome with single lineage dysplasia (MDS-SLD) (RA, RCUD_RA)	15 (11.3)	0 (0.0)	0 (0.0)	0 (0.0)	15 (5.6)
RARS Acquired idiopathic sideroblastic anemia:	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
MDS with excess blasts-1 (MDS-EB-1) (RAEB-1)	14 (10.5)	6 (26.1)	1 (5.6)	3 (3.3)	24 (9.0)
MDS with excess blasts-2 (MDS-EB-2 (RAEB-2)	19 (14.3)	7 (30.4)	11 (61.1)	9 (9.8)	46 (17.3)
Myelodysplastic syndrome with multilineage dysplasia (MDS-MLD) (RCMD)	10 (7.5)	0 (0.0)	2 (11.1)	2 (2.2)	14 (5.3)
5q-syndrome:	3 (2.3)	0 (0.0)	0 (0.0)	1 (1.1)	4 (1.5)

Characteristic	Bone marrow blasts at prep 0-5, N (%)	Bone marrow blasts at prep 6-10, N (%)	Bone marrow blasts at prep 11-19, N (%)	Bone marrow blasts at prep missing/not done, N (%)	Total, N (%)
Childhood myelodysplastic syndrome(Refractory cytopenia of childhood (RCC)):	12 (9.0)	0 (0.0)	0 (0.0)	11 (12.0)	23 (8.6)
Myelodysplastic/myeloproliferative neoplasm,unclassifiable:	9 (6.8)	2 (8.7)	0 (0.0)	1 (1.1)	12 (4.5)
MDS-RS with multilineage dysplasia (MDS-RS-MLD)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)
Year of current transplant - no. (%)					
2013	14 (10.5)	4 (17.4)	1 (5.6)	20 (21.7)	39 (14.7)
2014	18 (13.5)	4 (17.4)	5 (27.8)	13 (14.1)	40 (15.0)
2015	25 (18.8)	4 (17.4)	0 (0.0)	10 (10.9)	39 (14.7)
2016	19 (14.3)	3 (13.0)	2 (11.1)	13 (14.1)	37 (13.9)
2017	13 (9.8)	4 (17.4)	3 (16.7)	8 (8.7)	28 (10.5)
2018	15 (11.3)	1 (4.3)	3 (16.7)	5 (5.4)	24 (9.0)
2019	14 (10.5)	1 (4.3)	2 (11.1)	11 (12.0)	28 (10.5)
2020	5 (3.8)	1 (4.3)	0 (0.0)	2 (2.2)	8 (3.0)
2021	2 (1.5)	1 (4.3)	1 (5.6)	3 (3.3)	7 (2.6)
2022	8 (6.0)	0 (0.0)	1 (5.6)	7 (7.6)	16 (6.0)
Follow-up of survivors - median (range)	59.9 (3.3-123.2)	58.7 (14.1-104.2)	60.7 (24.6-116.8)	59.1 (1.8-124.1)	59.7 (1.8-124.1)

Field	Response
Proposal Number	2410-176-DAVIS
Proposal Title	Comparison of Risk Factors Associated with Early and Late Disease Relapse Among Patients in Complete Remission at One Month after Tisagenlecleucel (Kymriah) therapy in Pediatric, Adolescent and Young Adult (AYA) Patients Treated for Relapsed or Refractory (r/r) B Cell Acute Lymphoblastic Leukemia (B Cell ALL)
Key Words	Pediatric, AYA, Leukemia Kymriah, Tisagenlecleucel, relapsed, refractory
Principal Investigator #1: - First and last name, degree(s)	Laurie Davis MD PhD
Principal Investigator #1: - Email address	laurie.davis@bcm.edu
Principal Investigator #1: - Institution name	Baylor College of Medicine, CHRISTUS Children's Hospital
Principal Investigator #1: - Academic rank	Assistant Professor
Junior investigator status (defined as ≤5 years from fellowship)	Yes
Do you identify as an underrepresented/minority?	No
Principal Investigator #2 (If applicable): - First and last name, degree(s):	Prakash Satwani, MD
Principal Investigator #2 (If applicable): - Email address:)	ps2087@cumc.columbia.edu
Principal Investigator #2 (If applicable): - Institution name:	Columbia University Medical Center
Principal Investigator #2 (If applicable): - Academic rank:	Professor
Junior investigator status (defined as ≤5 years from fellowship)	No
Do you identify as an underrepresented/minority?	No
We encourage a maximum of two Principal Investigators per study. If more than one author is listed, please indicate who will be identified as the corresponding PI below:	Laurie Davis MD PhD
If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:	-
Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.	None
Do any of the PI(s) within this proposal have a CIBMTR WC study in manuscript preparation >6 months?	Yes
PROPOSED WORKING COMMITTEE:	Acute Leukemia
Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.	No
If you have already spoken with a scientific director or working committee chair regarding this study, then please specify who:	-

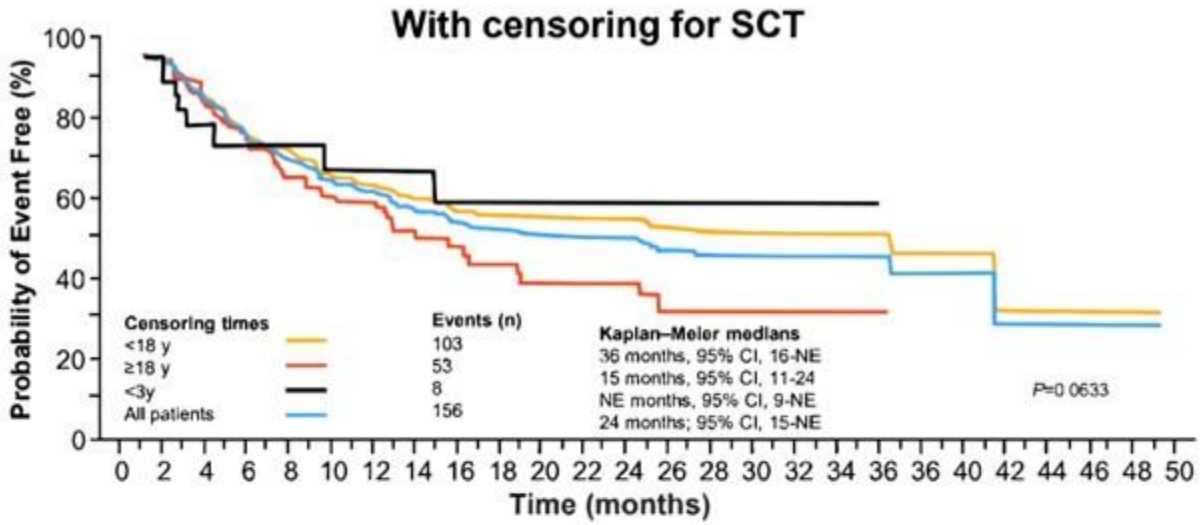
Field	Response
RESEARCH QUESTION:	What are the risk factors associated with early and late disease relapse in patient attaining complete remission at 1 month post Kymriah in pediatric and AYA patients treated for relapsed or refractory B cell ALL?
RESEARCH HYPOTHESIS:	The robust CIBMTR database will be allow for the comparison of risk factors associated with early and late relapse among patients receiving Tisagenlecleucel (Kymriah) therapy in Pediatric, Adolescent and Young Adult (AYA) Patients Treated for Relapsed or Refractory B Cell Acute Lymphoblastic Leukemia (B Cell ALL)
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	Primary Aim: Among patients who have achieved morphological complete remission at 1 month, compare the risk factors affecting early (≤ Day 180) and late relapse (>180 days) of disease following Tisagenlecleucel (Kymriah) therapy in pediatric and AYA patients with relapsed or refractory B Cell ALL.

Field	Response
SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.	Real world data from the CIBMTR has confirmed the reported outcomes of the landmark ELIANA CAR-T study for the use of Tisagenlecleucel (Kymriah) in the treatment of patients up to 25yo with relapsed or refractory (r/r) B cell ALL. Although early outcomes have been quite encouraging, patients have continued to experience relapse after achieving remission with Kymriah therapy. Based on analysis of 2023 data from the CIBMTR, the probability of Event Free Survival (EFS) at 1 year was approximately 60% and 4-year EFS was 30% (Figure 1) [1]. A recent update on the ELIANA trial showed an EFS of 44%, Overall Survival (OS) of 63% and Relapse Free Survival of 52% (with subsequent therapy) vs 48% (without subsequent therapy) [2]. Most events were seen to occur within the first 2 years post Kymriah infusion [2]. The identification of risk factors associated with relapse post Kymriah infusion would help clinicians to tailor clinical management of high-risk patients. It has been shown that relapse can be affected by risk factors such as Next Generation Sequencing (NGS) detection of Minimal Residual Disease (MRD) as well as B cell recovery as early as the first few months post CAR-T infusion [3]. However, B cell recovery did not always precede relapse in all instances and may not be a reliable sole biomarker for relapse. The analysis of the ELIANA trial data was not able to assess pre-infusion prognostic factors such as disease burden and nonresponse to blinatumomab [2]. This analysis was also unable to determine the effect of allogeneic stem cell transplant (alloSCT) post Kymriah therapy, as most of the ELIANA patients did not undergo alloSCT [2]. Utilization of the CIBMTR database to compare risk factors that may contribute to relapse in patients who underwent Kymriah therapy could allow for risk stratification of patients to better optimize clinical management and surveillance post CAR-T infusion. The identification of pre and post Kymriah therapy risk factors would allow for more nuanced and patient specific monitoring approach after Kymriah infusion.

Field	Response
SCIENTIFIC JUSTIFICATION: Provide a background summary of previous related research and their strengths and weaknesses, justification of your research and why your research is still necessary.	Kymriah therapy has been a paradigm shifting treatment for pediatric and AYA patients with r/r B ALL over the last decade. Recent analysis of the landmark ELIANA study has shown that relapse continues to be a significant issue within the first 3 years of therapy for roughly 50% of the patients studied. Analysis of NGS MRD of these patients has helped shed some insight into how to better monitor for relapse in these patients, however disease markers alone may not be able to predict relapse effectively or efficiently enough to improve outcomes. The CIBMTR database would allow for the analysis of both disease specific and patient specific data to compare the risk factors of patients with early and late relapse who attained morphologic complete remission within the first month of therapy. It is known that the response to therapy is not solely dependent on the patient's disease profile and that patient specific factors, including demographics, can affect their response to SCT as well as other cancer therapies [4, 5]. The development of pre and post Kymriah relapse-associated risk factors, based on both disease specific and patient specific characteristics, could allow for the more nuanced management and clinical decision making. This could improve management of patients by providing more timely interventions and could potentially lead to the development of strategies to decrease the incidence of relapse in high-risk patients.
SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF) - Id	F_OcWyuyowMSNZ1FT
SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF) - Name	Kymriah Data.jpg
SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF) - Size	105412
SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF) - Type	image/jpeg
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	Inclusion Criteria: - First time Kymriah therapy Recipients - Year-2017-2025 - Age 0-25 years at time of Tisagenlecleucel (Kymriah) therapy - Disease: Relapsed or Refractory B cell ALL Exclusion Criteria: - Embargoed centers and centers with 5-year completion index of <85%
Does this study include pediatric patients?	Yes
If this study does not include pediatric patients, please provide justification:	-

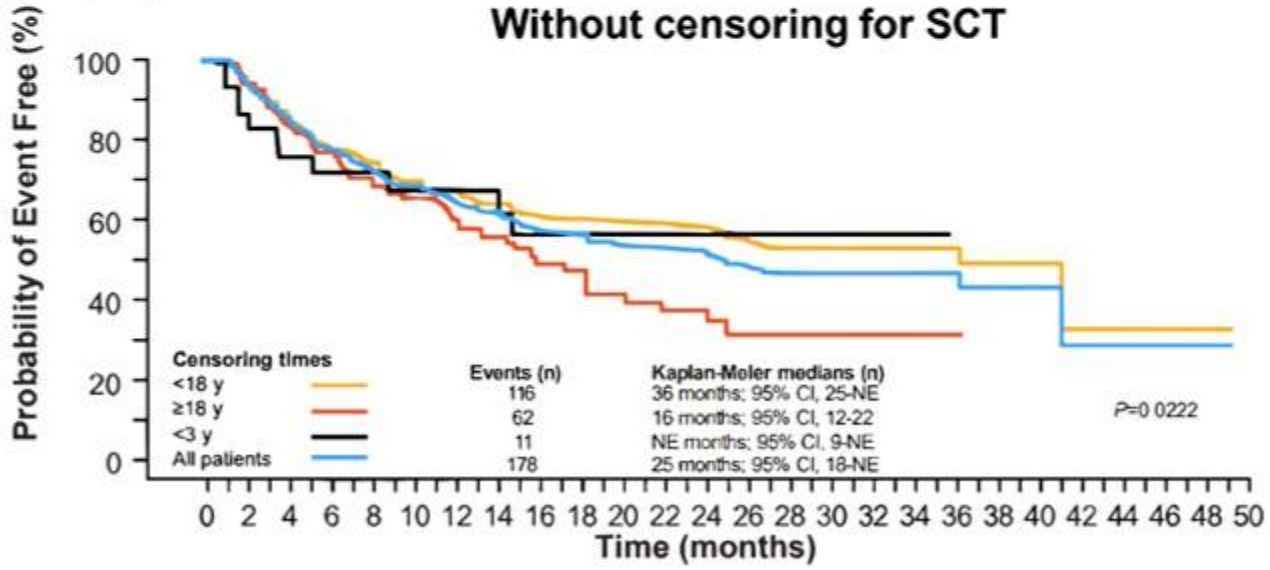
Field	Response
DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion- variables to be considered in the multivariate analyses. Outline any supplementary data required.	Patient and Disease Characteristics - Age - Gender - Performance Score (Lansky/Karnofsky) (<90 vs 90-100) - Ethnicity (Caucasian vs. Hispanic vs. African American vs. Other) - Disease Status: Primary refractory, 1st relapse, ≥3 relapses - Cytogenetics - Ph+ or Ph-like status (yes vs no) - Prior alloHCT (yes vs no) - Prior Blinatumomab treatment (yes vs no) - Prior Inotuzumab treatment (yes vs no) - Time from diagnosis to Kymriah infusion - Prior CNS involvement (yes vs no) - Isolated CNS involvement (yes vs no) - Morphologic CR (yes vs no) at Kymriah infusion - Disease Burden at time of Kymriah Therapy (flow MRD -ve, NGS MRD -ve, <5% or ≥5%) - Flow MRD Status at day 30, 100- and 1-year post Kymriah infusion: MRD+ vs. MRD -ve - B Cell aplasia at day 30, 100- and 1-year post Kymriah infusion (yes vs no) - Next generation sequencing (NGS) - CD19 negative relapse (yes vs. no) CAR-T Characteristics - Lymphodepletion Regimen - CAR-T Cell dose/kg - Time from start of conditioning to infusion (Days) - Incidence and severity of Cytokine Release Syndrome - Steroid use for Cytokine Release Syndrome (CRS) -Tocilizumab use for CRS (number of doses) - Incidence/Severity of ICANS and treatment of ICANS - Steroid use for ICANS Post CAR-T Therapy Status - SCT following Kymriah infusion (yes vs. no) - Other post Kymriah therapies (yes vs. no) Outcomes for patients in morphologic CR at 1 month - Relapse incidence at 6 months, 1- and 2-years post Kymriah infusion - Overall survival at 1, 2, and 3-years post Kymriah infusion - Causes of death - Development of models to predict early and late relapse
Types of cellular therapy data this proposal includes:	Chimeric Antigen Receptor (CAR) T-Cell Therapy (CAR-T)
PATIENT REPORTED OUTCOME (PRO) REQUIREMENTS: If the study requires PRO data collected by CIBMTR, the proposal should include: 1) A detailed description of the PRO domains, timepoints, and proposed analysis of PROs; 2) A description of the hypothesis speci	N/A
MACHINE LEARNING: Please indicate if the study requires methodology related to machine-learning and clinical predictions.	N/A

Field	Response
SAMPLE REQUIREMENTS: If the study requires biologic samples from the CIBMTR Repository, the proposal should also include: 1) A detailed description of the proposed testing methodology and sample requirements; 2) A summary of the investigator's previous e	N/A
NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required.	N/A
REFERENCES:	1. John, S., et al., Improved Relapse-Free Survival (RFS) for Pediatric and Young Adult Patients with Relapsed or Refractory (R/R) B-Cell Acute Lymphoblastic Leukemia (B-ALL) and Low or Intermediate Preinfusion Disease Burden Treated with Tisagenlecleucel: Results from the CIBMTR Registry. Transplantation and Cellular Therapy, Official Publication of the American Society for Transplantation and Cellular Therapy, 2023. 29(2): p. S37-S38. 2. Laetsch, T.W., et al., Three-Year Update of Tisagenlecleucel in Pediatric and Young Adult Patients With Relapsed/Refractory Acute Lymphoblastic Leukemia in the ELIANA Trial. J Clin Oncol, 2023. 41(9): p. 1664-1669. 3. Pulsipher, M.A., et al., Next-Generation Sequencing of Minimal Residual Disease for Predicting Relapse after Tisagenlecleucel in Children and Young Adults with Acute Lymphoblastic Leukemia. Blood Cancer Discov, 2022. 3(1): p. 66-81. 4. Auletta, J.J., et al., Real-World Data Showing Trends and Outcomes by Race and Ethnicity in Allogeneic Hematopoietic Cell Transplantation: A Report from the Center for International Blood and Marrow Transplant Research. Transplant Cell Ther, 2023. 29(6): p. 346 e1-346 e10. 5. Aristizabal, P., et al., Disparities in Pediatric Oncology: The 21st Century Opportunity to Improve Outcomes for Children and Adolescents With Cancer. Am Soc Clin Oncol Educ Book, 2021. 41: p. e315-e326.
CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning?	No, I do not have any conflicts of interest pertinent to this proposal
If yes, provide detail on the nature of employment, name of organization, role, entity, ownership, type of financial transaction or legal proceeding and whether renumeration is >$5000 annually.	-



Patients still at risk, n

<18y (N=348)	348	287	208	161	136	120	92	70	67	64	63	62	46	34	31	31	31	28	10	3	3	2	2	2	1	0
≥18y (N=149)	149	114	87	69	50	46	34	22	18	17	15	15	10	5	5	5	5	4	0							
<3y (N=31)	31	21	13	11	11	10	9	7	7	6	6	6	4	3	2	2	2	2	0							
All patients (N=497)	497	401	295	230	186	166	126	92	85	81	78	77	56	39	36	36	35	32	10	3	3	2	2	2	1	0



Patients still at risk, n

<18 y (N=348)	348	307	253	210	181	158	127	103	91	85	82	81	63	45	37	34	33	31	13	3	3	2	2	2	1	0
≥18 y (N=149)	149	126	103	86	70	66	50	33	27	24	21	19	12	7	6	5	5	4	0							
<3 y (N=31)	31	25	20	18	17	15	14	11	9	8	8	8	6	4	2	2	2	2	0							
All patients (N=497)	497	433	356	296	251	224	177	136	118	109	103	100	75	52	43	39	38	35	13	3	3	2	2	2	1	0

The below selection criteria were applied

Selection criteria	# excluded	N
Cases available in CIBMTR HCT Essentials Extract *		21336
Year of HCT: 2017-2024	119	21217
First CAR-T	709	20508
Disease: ALL	18115	2393
Age: < 26 years	626	1767
Patient Consented	195	1572
CAR-T product: Kymriah	316	1256
Patients who received commercial CAR-T	0	1256
Clinical Trial Participation: No	11	1245
Centers included: Not Embargoed	97	1148
Best response at 100 days: Complete Remission	354	794
Follow-up present	4	790

**Data source: HCT Essentials Oct 2024*

Table 1: Patients with ALL that underwent CAR-T therapy from 2017-2024.

Characteristic	N (%)
No. of patients	790
No. of centers	118
Age at Infusion - median (min-max)	13.3 (0.5-26.0)
Age Categories (Continuous) - no. (%)	
<2 years	36 (4.6)
2-10 years	275 (34.8)
11-22 years	413 (52.3)
>22 years	66 (8.4)
Disease status at Infusion (ALL) - no. (%)	
CR1	99 (12.5)
CR2	159 (20.1)
CR3+	120 (15.2)
Relapse, 1st	180 (22.8)
Relapse, other	166 (21.0)

Characteristic	N (%)
PIF/Untreated	66 (8.4)
Was lymphodepleting therapy given as systemic therapy prior to the infusion? - no. (%)	
Yes	787 (99.6)
Not reported	3 (0.4)
Time to 100 Days best response from Cellular Therapy (Days) - no. (%)	
1-25 days	381 (48.2)
26-50 days	329 (41.6)
51-75 days	26 (3.3)
76-100 days	21 (2.7)
>100 days	15 (1.9)
Not Reported	18 (2.3)
Year of CT - no. (%)	
2017	9 (1.1)
2018	117 (14.8)
2019	150 (19.0)
2020	137 (17.3)
2021	148 (18.7)
2022	133 (16.8)
2023	92 (11.6)
2024	4 (0.5)
Follow-up of survivors - median (range)	35.0 (1.0-76.0)

Field	Response
Proposal Number	2410-182-DAVIS
Proposal Title	Impact of Planned Post-Transplant Granulocyte Colony Stimulating Factor (G-CSF) on Transplant-Related Outcomes in Pediatric Patients with Malignant Disease Undergoing Haploidentical Hematopoietic Cell Transplant (HCT) with Post-Transplant Cyclophosphamide (ptCy) for Graft vs. Host Disease (GVHD) Prophylaxis
Key Words	Granulocyte Colony Stimulating Factor, Pediatric, malignant, haploidentical, stem cell transplant, post transplant cyclophosphamide, graft vs host disease, prophylaxis
Principal Investigator #1: - First and last name, degree(s)	Laurie Davis, MD, PhD
Principal Investigator #1: - Email address	laurie.davis@bcm.edu
Principal Investigator #1: - Institution name	Baylor College of Medicine, CHRISTUS Children's Hospital
Principal Investigator #1: - Academic rank	Assistant Professor
Junior investigator status (defined as ≤5 years from fellowship)	Yes
Do you identify as an underrepresented/minority?	No
Principal Investigator #2 (If applicable): - First and last name, degree(s):	Prakash Satwani, MD
Principal Investigator #2 (If applicable): - Email address:)	ps2087@cumc.columbia.edu
Principal Investigator #2 (If applicable): - Institution name:	Columbia University Medical Center
Principal Investigator #2 (If applicable): - Academic rank:	Professor
Junior investigator status (defined as ≤5 years from fellowship)	No
Do you identify as an underrepresented/minority?	No
We encourage a maximum of two Principal Investigators per study. If more than one author is listed, please indicate who will be identified as the corresponding PI below:	Laurie Davis MD PhD
If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:	-
Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.	N/A
Do any of the PI(s) within this proposal have a CIBMTR WC study in manuscript preparation >6 months?	Yes
PROPOSED WORKING COMMITTEE:	Graft vs Host Disease
Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.	No

Field	Response
If you have already spoken with a scientific director or working committee chair regarding this study, then please specify who:	-
RESEARCH QUESTION:	What is the impact of Planned Post-Transplant Granulocyte Colony Stimulating Factor (G-CSF) on Transplant-Related Outcomes in Pediatric Patients with Malignant Disease Undergoing Haploidentical Hematopoietic Cell Transplant (HCT) with Post-Transplant Cyclophosphamide (ptcy) for Graft vs. Host Disease (GVHD) Prophylaxis
RESEARCH HYPOTHESIS:	Pediatric patients undergoing haploidentical HCT (HaploHCT) with ptCy who receive planned GCSF will have lower overall survival (OS), disease free survival (DFS) and greater relapse and non-relapse mortality (NRM) compared to those patients who did not receive planned G-CSF.
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	Primary Aim: Compare the outcomes of pediatric patients undergoing HaploHCT with ptCy receiving planned post-transplant G-CSF with those patients who do not receive planned post-transplant G-CSF.

Field	Response
SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.	The use of G-CSF post allogeneic HCT has been debated for many decades due to the variability in outcomes related to infection, febrile neutropenia prophylaxis, hospitalization time, and effect on transplant related outcomes such as graft vs host disease (GVHD) and overall survival (OS) [1-4]. With the introduction of ptCy for GVHD prophylaxis, more patients are now receiving HaploHCT, and outcomes have been shown to be on par with other donor types, significantly benefiting minority patient populations [5]. However, due to conflicting data, clinical practices regarding the use of post-transplant G-CSF remain inconsistent, particularly in high-risk GVHD groups such as HaploHCT recipients. G-CSF is commonly used to promote stem cell engraftment and reduce the duration of neutropenia and infection risk early post-transplant [1]. However, recent studies raise concerns about the potentially harmful effects of G-CSF on the recovering immune system. For instance, a CIBMTR analysis showed that the combination of G-CSF with thymoglobulin negatively impacted survival in adult patients undergoing allogeneic HCT (Non-Haploidentical and without ptCy prophylaxis) for myeloid malignancies, likely due to its influence on immune reconstitution [2]. In addition to G-CSF, ptCy itself has immunomodulatory effects that may compound delayed immune reconstitution related issues in adult patients [6]. Despite these findings, no data currently exists on how G-CSF affects pediatric HaploHCT patients who receive ptCy for GVHD prophylaxis. Using data from the CIBMTR database, this study could clarify whether G-CSF administration poses additional risks or benefits, potentially informing future clinical practices to optimize patient outcomes.

Field	Response
SCIENTIFIC JUSTIFICATION: Provide a background summary of previous related research and their strengths and weaknesses, justification of your research and why your research is still necessary.	Over the past decade, the use of HaploHCT in pediatric patients with malignant disorders such as Acute Lymphoblastic Leukemia (ALL), Acute Myeloblastic Leukemia (AML), and Myelodysplastic Syndromes (MDS) has steadily increased, with the highest volume occurring between 2012 and 2022 [7]. The growing adoption of ptCy for GVHD prophylaxis has contributed to improved survival outcomes that are comparable to matched unrelated donor transplants [5, 7]. The use of ptCy in combination with G-CSF in pediatric patients undergoing HaploHCT for malignant disease has yet to be investigated with the use of a robust patient database like that available through the CIBMTR. Despite the widespread use of G-CSF to hasten neutrophil engraftment and reduce hospitalization time, concerns have arisen that G-CSF administration in ptCy-treated patients could increase cytokine-mediated inflammation, thereby heightening the risk of GVHD and other complications [3, 8-10]. While ptCy has been shown to delay T-cell reconstitution, alter T-cell subset composition, and modulate immune responses in adult HCT recipients, its effects in pediatric patients have not been extensively studied [7]. Given that pediatric HaploHCT donors are often adult family members, similar immunological consequences may be expected. The addition of planned G-CSF post-HCT may further impair immune recovery, compounding the effects of ptCy and potentially leading to poorer outcomes. Understanding the interplay between G-CSF and ptCy in pediatric HaploHCT patients is crucial to optimizing treatment protocols and improving survival rates.
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	Inclusion Criteria: - Haploidentical Allogeneic HCT - Year-2000-2024 - Age ≤ 18 years at time of HCT - Diagnoses: ALL, AML, MDS - Stem Cell Source: Peripheral blood stem cell or Bone Marrow - ptCy for GVHD prophylaxis Exclusion Criteria: - Non-Malignant Disease - G-CSF use for clinical indications (e.g., prolonged pancytopenia, infection) - Graft manipulation (e.g., CD34+ selection, alpha-beta depletion) - Second alloHCT - Non-malignant disease - No ptCy for GVHD prophylaxis - Embargoed centers and centers with 5-year completion index of <85%
Does this study include pediatric patients?	Yes
If this study does not include pediatric patients, please provide justification:	-

Field	Response
DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion- variables to be considered in the multivariate analyses. Outline any supplementary data required.	Patient and Disease Characteristics - Age - Gender - Performance Score (Lansky/Karnofsky) (<90 vs 90-100) - Indications: ALL, AML, MDS - Ethnicity - Race - Hematopoietic Cell Transplant Co-Morbidity Index - Disease Status (CR1 v CR2 v >CR2) - Cytogenetics - Disease Risk Index (Low, Intermediate, High) Transplant Characteristics - Conditioning Intensity: Myeloablative vs Reduced intensity - Year of transplant: 2000-2024 - Graft Type (Peripheral Blood v Bone Marrow) - Use of Antithymocyte Globulin (ATG) (yes v no) - CD34 cell dose infused - CD3 cell dose infused - GCSF (yes v no) - GCSF timing (pre v post ptCy, in days) - Abatacept (yes v no) Outcomes - Days to neutrophil engraftment - Days to platelet engraftment - Days to graft failure - Day 100 and day 365 overall survival - Relapse, non-relapse mortality, and Transplant related mortality at day 365 - Incidence of acute/chronic GVHD, significant viral/bacterial/fungal infections in first 100 days and day 101-365 - Incidence of VOD, respiratory failure/mechanical ventilation, TA-TMA, dialysis/CRRT in first 100 days and day 101-365
Types of cellular therapy data this proposal includes:	Hematopoietic Cell Transplantation (HCT)
PATIENT REPORTED OUTCOME (PRO) REQUIREMENTS: If the study requires PRO data collected by CIBMTR, the proposal should include: 1) A detailed description of the PRO domains, timepoints, and proposed analysis of PROs; 2) A description of the hypothesis speci	N/A
MACHINE LEARNING: Please indicate if the study requires methodology related to machine-learning and clinical predictions.	N/A
SAMPLE REQUIREMENTS: If the study requires biologic samples from the CIBMTR Repository, the proposal should also include: 1) A detailed description of the proposed testing methodology and sample requirements; 2) A summary of the investigator's previous e	N/A

Field	Response
NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required.	N/A
REFERENCES:	1. Gupta, A.K., et al., Impact of G-CSF administration post-allogeneic hematopoietic stem-cell transplantation on outcomes: a systematic review and meta-analysis. Am J Blood Res, 2021. 11(5): p. 544-563. 2. Orfali, N., et al., Planned Granulocyte Colony-Stimulating Factor Adversely Impacts Survival after Allogeneic Hematopoietic Cell Transplantation Performed with Thymoglobulin for Myeloid Malignancy. Transplant Cell Ther, 2021. 27(12): p. 993 e1-993 e8. 3. Ringden, O., et al., Granulocyte colony-stimulating factor induced acute and chronic graft-versus-host disease. Transplantation, 2010. 90(9): p. 1022-9. 4. Wang, Y., et al., Efficacy and tolerability of granulocyte colony-stimulating factors in cancer patients after chemotherapy: A systematic review and Bayesian network meta-analysis. Sci Rep, 2019. 9(1): p. 15374. 5. Shaw, B.E., et al., National Marrow Donor Program-Sponsored Multicenter, Phase II Trial of HLA-Mismatched Unrelated Donor Bone Marrow Transplantation Using Post-Transplant Cyclophosphamide. J Clin Oncol, 2021. 39(18): p. 1971-1982. 6. Zhao, C., et al., Post-transplant cyclophosphamide alters immune signatures and leads to impaired T cell reconstitution in allogeneic hematopoietic stem cell transplant. J Hematol Oncol, 2022. 15(1): p. 64. 7. CIBMTR. U.S. Transplant and Survival Statistics on Related Sites. 2022; Available from: https://cibmtr.org/CIBMTR/Resources/Summary-Slides-Reports. 8. Agarwal, P., et al., Capillary Leak syndrome within an hour of G-CSF. J Pediatr Pharmacol Ther, 2023. 28(5): p. 457-459. 9. Deeren, D.H., P. Zachee, and M.L. Malbrain, Granulocyte colony-stimulating factor-induced capillary leak syndrome confirmed by extravascular lung water measurements. Ann Hematol, 2005. 84(2): p. 89-94. 10. Lapidari, P., I. Vaz-Luis, and A. Di Meglio, Side effects of using granulocyte-colony stimulating factors as prophylaxis of febrile neutropenia in cancer patients: A systematic review. Crit Rev Oncol Hematol, 2021. 157: p. 103193.
CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning?	No, I do not have any conflicts of interest pertinent to this proposal

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

The below selection criteria were applied

Selection criteria	# excluded	N
Cases available in CIBMTR HCT Essentials Extract *		441766
First Allo Transplant	246638	195128
HCT years 2008-2022	23172	171956
Age at diagnosis: < 21 year	134246	37710
Disease: ALL, AML, MDS and Lymphoma	19238	18472
Haploidentical/Other Relatives	15008	3464
Patient Consented	585	2879
GVHD Prophylaxis: PTCy + Others	1248	1631
Track: CRF	1228	403
Follow-up present	16	387

**Data source: HCT Essentials Oct 2024*

Table 1: Patients (<21 years) that underwent first allogeneic HCT for ALL, AML, MDS and Lymphoma with haploidentical or other related donor between 2008-2022

Characteristic	N (%)
No. of patients	387
No. of centers	90
Patient age - median (min-max)	13.1 (0.6-21.0)
Age Range - no. (%)	
<2 year	19 (4.9)
2 - 10 years	136 (35.1)
11-<21 years	232 (59.9)
Conditioning Regimen Intensity - no. (%)	
MAC	284 (73.4)
RIC	47 (12.1)
NMA	50 (12.9)
Not Reported	6 (1.6)
Conditioning regimen - no. (%)	
TBI/Cy	37 (9.6)
TBI/Cy/Flu	52 (13.4)
TBI/Cy/TT	3 (0.8)

Characteristic	N (%)
TBI/Cy/VP	3 (0.8)
TBI/VP	4 (1.0)
TBI/Mel	15 (3.9)
TBI/Flu	120 (31.0)
TBI/other(s)	1 (0.3)
Bu/Cy	66 (17.1)
Bu/Mel	13 (3.4)
Flu/Bu/TT	24 (6.2)
Flu/Bu	23 (5.9)
Flu/Mel/TT	11 (2.8)
Flu/Mel	7 (1.8)
Cy/Flu	1 (0.3)
BEAM	1 (0.3)
Mel alone	1 (0.3)
Treosulfan	4 (1.0)
Not Reported	1 (0.3)
Primary disease - no. (%)	
AML or ANLL	146 (37.7)
ALL	163 (42.1)
MDS	30 (7.8)
NHL	18 (4.7)
HD	30 (7.8)
Specify hematopoietic, lymphoid growth factor or cytokine received - no. (%)	
No	69 (17.8)
Yes	310 (80.1)
Not Reported	8 (2.1)
G-CSF given - no. (%)	
FILGRASTIM(NEUPOGEN)	296 (76.5)
FILGRASTIM-SNDZ	1 (0.3)
FILGRASTIM-SNDZ (ZARXIO)	3 (0.8)
LENOGRASTIM	2 (0.5)
NEUKINE	2 (0.5)

Characteristic	**N (%)**
PEGFILGRASTIM(NEULASTA)	2 (0.5)
TBO-FILGRASTIM (GRANIX)	1 (0.3)
ZARXIO	3 (0.8)
Not Reported	77 (19.9)
Year of current transplant - no. (%)	
2008	1 (0.3)
2009	5 (1.3)
2012	3 (0.8)
2013	11 (2.8)
2014	22 (5.7)
2015	34 (8.8)
2016	49 (12.7)
2017	74 (19.1)
2018	69 (17.8)
2019	62 (16.0)
2020	22 (5.7)
2021	11 (2.8)
2022	24 (6.2)
Follow-up of survivors - median (range)	56.1 (1.1-162.9)

Field	Response
Proposal Number	2410-200-LALEFAR
Proposal Title	Hematopoietic Stem Cell Transplant Outcomes for Infant B-cell Acute Lymphoblastic Leukemia
Key Words	Infant leukemia, B-cell ALL, late effects
Principal Investigator #1: - First and last name, degree(s)	Nahal Rose Lalefar, MD
Principal Investigator #1: - Email address	nahal.lalefar@ucsf.edu
Principal Investigator #1: - Institution name	UCSF Benioff Children's Hospital Oakland
Principal Investigator #1: - Academic rank	Associate Professor of Pediatrics
Junior investigator status (defined as ≤5 years from fellowship)	No
Do you identify as an underrepresented/minority?	No
Principal Investigator #2 (If applicable): - First and last name, degree(s):	Hemalatha Rangarajan, MD
Principal Investigator #2 (If applicable): - Email address:)	hemalatha.rangarajan@nationwidechildrens.org
Principal Investigator #2 (If applicable): - Institution name:	Nationwide Children's Hospital
Principal Investigator #2 (If applicable): - Academic rank:	Associate Professor of Pediatrics
Junior investigator status (defined as ≤5 years from fellowship)	No
Do you identify as an underrepresented/minority?	No
We encourage a maximum of two Principal Investigators per study. If more than one author is listed, please indicate who will be identified as the corresponding PI below:	-
If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:	-
Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.	none
Do any of the PI(s) within this proposal have a CIBMTR WC study in manuscript preparation >6 months?	No
PROPOSED WORKING COMMITTEE:	Pediatric Cancer
Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.	No
If you have already spoken with a scientific director or working committee chair regarding this study, then please specify who:	-
RESEARCH QUESTION:	What is the leukemia free survival (LFS) and overall survival (OS) for infants with B-lymphoblastic leukemia who undergo stem cell transplantation and has OS improved for this patient population over the last 20 years?

Field	Response
RESEARCH HYPOTHESIS:	Leukemia free survival (LFS) and overall survival (OS) outcomes for infants with B-ALL who undergo hematopoietic stem cell transplant (HSCT) will show improved outcomes for those who were in complete remission (CR1) at the time of HSCT and those transplanted in the last decade.
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	Primary Objectives 1. Determine the leukemia free survival at 1yr and 3yr for infants with acute B-lymphoblastic leukemia (CR1 vs other) who underwent HSCT between 2003-2022 in 5-year time periods 2. Determine the overall survival at 1yr and 3yr for infants with acute B-lymphoblastic leukemia (CR1 vs other) between 2003-2022 in 5-year time periods Secondary Objectives 1. Determine treatment related morality at 100 days and 1 year for infants with B-ALL 2. Determine incidence of organ toxicities post HCT: veno-occlusive disease, Transplant-associated microangiopathy and Pulmonary toxicity 3. Exploratory objective : Determine incidence of late effects in long term survivors of patients with infant B-ALL who have underwent HCT: Short stature/GH deficiency, Second malignancies, Hypothyroidism, Functional status
SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.	Treatment of infant B-ALL remains very challenging given high risk of relapse. Ninety percent of relapse will occur within 2 years of diagnosis. Traditionally, HSCT has not provided clear survival benefit for infant ALL. The comparisons between HSCT versus chemotherapy alone are based mostly on cooperative studies such as CCG1953, POG9407, Interfant-99 and Interfant-06. The last CIBMTR publication on infant leukemias included patients transplanted up to 2002. Since then, supportive care measures have improved, there is use of less total body irradiation in transplant regimens, and there has been an expansion of donor options. There has also been significant advancement in treatment with the addition of blinatumomab and CAR-T therapies to achieve MRD negativity in high risk patients. If we are able to publish more recent retrospective data showing improvement in HSCT outcomes of infant B-ALL, then it may support the continued use of HSCT in those who are high risk and subgroups of medium risk patients with positive end of induction MRD.

SCIENTIFIC JUSTIFICATION: Provide a background summary of previous related research and their strengths and weaknesses, justification of your research and why your research is still necessary.	This is an updated version of CIBMTR proposal 2110-272 that I previously submitted in 2021. Infant B-ALL prognosis is poor compared to that of older children, particularly those with KMT2A rearrangement. Ninety percent of relapse will occur within 2 years of diagnosis. (van der Sluis, de Lorenzo et al. 2023) Much of the outcome data regarding benefit or lack of benefit from hematopoietic stem cell transplant (HSCT) is based off of data from over 2 decades ago. Older studies did not show benefit of HSCT over chemotherapy for patients with infant leukemia. CCG1953 and POG 9407, which enrolled patients between 1996-2000, showed a 5-year EFS/OS of 48.8%/59.36% (those who received HSCT) versus 48.7%/53.08% (those who received chemotherapy alone) (Dreyer, Dinndorf et al. 2011). However, these outcomes were limited by small patient numbers and differences in overall survival was not statistically significant. In the Interfant-06 cooperative group study, those infants with B-ALL who are considered to be high risk (presence of a KMT2A-rearrangement and age < 6 months at diagnosis, with WBC count 300 x 10e9 /L or more at diagnosis or a poor prednisone response) were eligible to receive HSCT. Patients in the medium risk group (all other KMT2A-r infants) with minimal residual disease (MRD) greater than or equal to 0.0001 at the start of OCTADA(D) were recommended for HSCT because the Interfant-99 update showed a dismal outcome for them. The 6-year EFS of all 164 patients in the Interfant-06 high risk (HR) group was 20.9% , with the intention to perform transplantation in all patients in the HR group who reached CR (n = 143). Only 76 out of 143 received HSCT, because many (n = 54) experienced an early event before HSCT could be performed. Of the 76 patients undergoing transplantation, relapse occurred in 26 (34.2%), 14 (18.4%) died in CR from transplantation-related toxicity, and two developed a second malignancy, with a 4-year DFS after SCT of 44.0% (Pieters, De Lorenzo et al. 2019). Improved outcomes were recently reported in the Japanese Pediatric Leukemia/Lymphoma Study Group (JPLSG) MLL-10 trial. Unlike the historical Interfant-06 trial where only 46% of patient proceeded to transplant, 76% of patients in the MLL-trial proceeded to transplant. In the 43 patients who proceeded to transplant the 3-year EFS/OS was 56.8%/80%. Treatment related was low with only one death reported. 30% of patients relapsed post-transplant. This study demonstrated the benefit of transplant in HR patients. (Tomizawa, Miyamura et al. 2020) There have been two prior CIBMTR studies on HSCT outcomes in patients with infant ALL. The first study compared long-term survival after unrelated and HLA-Matched Sibling Donor HSCT for acute leukemia in children younger than 18 Months. This study included

Field	Response
	both ALL and AML patients who were < 18 months of age who underwent HSCT between 1990-2001. In this cohort of 287 patients, the 3 year LFS was 49%/54% (MSD) and 3yr LFS/OS in CR1 54%/62% (URD)(Eapen, Rubinstein et al. 2006). The second study focused on survival and late effects for patients who underwent HSCT between 1987-2012 for hematologic malignancies under the age of 3 years. It also included patients diagnosed with ALL, AML, JMML and MDS and was not restricted to infants.(Vrooman, Millard et al. 2017) With expanded treatment options such as immunotherapy, wider donor selection (to include haplo-identical donors), broader genetic testing to assess additional prognostic factors (e.g. RAS mutations), and incorporation of next generation minimal residual disease testing, we hypothesize that outcomes for patients with infant ALL have improved over time. Therefore we hope to use CIBMTR outcome data to determine if HSCT may benefit infant B-ALL patients in CR1 beyond what has been described in each of the individual cooperative trials. We will also explore feasible long-term outcomes in a select subset of long-term survivors of infant ALL HCT recipients.
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	Inclusion: Age 0-12 months of age at diagnosis Acute lymphoblastic leukemia (B-cell) Exclusion: T-cell ALL, T-cell/myeloid MPAL, mature B-cell ALL, or Philadelphia chromosome–positive ALL
Does this study include pediatric patients?	Yes
If this study does not include pediatric patients, please provide justification:	-
DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion- variables to be considered in the multivariate analyses. Outline any supplementary data required.	Demographics Age at diagnosis (0-6 months, 7-9 months, 10-12months) Gender Race/Ethnicity Pediatric HCT- CI index Disease status Year of Transplant 2003-2022 Disease status at time of HSCT: morphological CR Y/N MRD pre HCT Primary diagnosis: ALL (MLL/KMT2A germline line vs rearrangement) Prior blina Y/N Prior CAR T Y/N Transplant characteristics and outcomes Donor Type Graft Conditioning Regimen with intensity GVHD prophylaxis Acute GVHD grade I and II versus grade III and IV versus no aGVHD LFS at 1 yr, 3 yr OS at 1, 3 yr Organ toxicity: VOD, pulmonary toxicity, TMA Late effects Short stature/GH deficiency Second malignancies Hypothyroidism Functional status Follow up in months Alive at follow up Y/N Cause of death if applicable.
Types of cellular therapy data this proposal includes:	Hematopoietic Cell Transplantation (HCT)

Field	Response
PATIENT REPORTED OUTCOME (PRO) REQUIREMENTS: If the study requires PRO data collected by CIBMTR, the proposal should include: 1) A detailed description of the PRO domains, timepoints, and proposed analysis of PROs; 2) A description of the hypothesis speci	-
MACHINE LEARNING: Please indicate if the study requires methodology related to machine-learning and clinical predictions.	-
SAMPLE REQUIREMENTS: If the study requires biologic samples from the CIBMTR Repository, the proposal should also include: 1) A detailed description of the proposed testing methodology and sample requirements; 2) A summary of the investigator's previous e	-
NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required.	-
REFERENCES:	-
CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning?	No, I do not have any conflicts of interest pertinent to this proposal

Field	Response
If yes, provide detail on the nature of employment, name of organization, role, entity, ownership, type of financial transaction or legal proceeding and whether renumeration is >$5000 annually.	Dreyer, Z. E., P. A. Dinndorf, B. Camitta, H. Sather, M. K. La, M. Devidas, J. M. Hilden, N. A. Heerema, J. E. Sanders, R. McGlennen, C. L. Willman, A. J. Carroll, F. Behm, F. O. Smith, W. G. Woods, K. Godder and G. H. Reaman (2011). "Analysis of the role of hematopoietic stem-cell transplantation in infants with acute lymphoblastic leukemia in first remission and MLL gene rearrangements: a report from the Children's Oncology Group." J Clin Oncol 29(2): 214-222. Eapen, M., P. Rubinstein, M. J. Zhang, B. M. Camitta, C. Stevens, M. S. Cairo, S. M. Davies, J. J. Doyle, J. Kurtzberg, M. A. Pulsipher, J. J. Ortega, A. Scaradavou, M. M. Horowitz and J. E. Wagner (2006). "Comparable long-term survival after unrelated and HLA-matched sibling donor hematopoietic stem cell transplantations for acute leukemia in children younger than 18 months." J Clin Oncol 24(1): 145-151. Pieters, R., P. De Lorenzo, P. Ancliffe, L. A. Aversa, B. Brethon, A. Biondi, M. Campbell, G. Escherich, A. Ferster, R. A. Gardner, R. S. Kotecha, B. Lausen, C. K. Li, F. Locatelli, A. Attarbaschi, C. Peters, J. E. Rubnitz, L. B. Silverman, J. Stary, T. Szczepanski, A. Vora, M. Schrappe and M. G. Valsecchi (2019). "Outcome of Infants Younger Than 1 Year With Acute Lymphoblastic Leukemia Treated With the Interfant-06 Protocol: Results From an International Phase III Randomized Study." J Clin Oncol 37(25): 2246-2256. Tomizawa, D., T. Miyamura, T. Imamura, T. Watanabe, A. Moriya Saito, A. Ogawa, Y. Takahashi, M. Hirayama, T. Taki, T. Deguchi, T. Hori, M. Sanada, S. Ohmori, M. Haba, A. Iguchi, Y. Arakawa, Y. Koga, A. Manabe, K. Horibe, E. Ishii and K. Koh (2020). "A risk-stratified therapy for infants with acute lymphoblastic leukemia: a report from the JPLSG MLL-10 trial." Blood 136(16): 1813-1823. van der Sluis, I. M., P. de Lorenzo, R. S. Kotecha, A. Attarbaschi, G. Escherich, K. Nysom, J. Stary, A. Ferster, B. Brethon, F. Locatelli, M. Schrappe, P. E. Scholte-van Houtem, M. G. Valsecchi and R. Pieters (2023). "Blinatumomab Added to Chemotherapy in Infant Lymphoblastic Leukemia." N Engl J Med 388(17): 1572-1581. Vrooman, L. M., H. R. Millard, R. Brazauskas, N. S. Majhail, M. Battiwalla, M. E. Flowers, B. N. Savani, G. Akpek, M. Aljurf, R. Bajwa, K. S. Baker, A. Beitinjaneh, M. Bitan, D. Buchbinder, E. Chow, C. Dandoy, A. C. Dietz, L. Diller, R. P. Gale, S. K. Hashmi, R. J. Hayashi, P. Hematti, R. T. Kamble, K. A. Kasow, M. Kletzel, H. M. Lazarus, A. K. Malone, D. I. Marks, T. A. O'Brien, R. F. Olsson, O. Ringden, S. Seo, A. Steinberg, L. C. Yu, A. Warwick, B. Shaw and C. Duncan (2017). "Survival and Late Effects after Allogeneic Hematopoietic Cell Transplantation for Hematologic Malignancy at Less than Three Years of Age." Biol Blood Marrow Transplant 23(8): 1327-1334.

The below selection criteria were applied

Selection criteria	# excluded	N
Cases available in CIBMTR HCT Essentials Extract *		441766
HCT years: 2008-2020	111723	330043
First Allo transplants	182296	147747
Disease: ALL	124969	22778
All subdiseases except: Early T-cell precursor lymphoblastic leukemia, Early T-cell precursor lymphoblastic leukemia, t(9;22)(q34;q11); BCR/ABL+, ALL T-lineage/precursor T-cell ALL	9198	13580
Age at diagnosis: < 1 year	13195	385
Patient Consented	48	337
Inconsistent Diagnosis Date/Age	4	333
Follow-up present	16	317

**Data source: HCT Essentials Oct 2024*

Table 1: Patients that underwent first allogeneic HCT for ALL in 2008-2020

Characteristic	N (%)
No. of patients	317
No. of centers	99
Patient age - median (min-max)	1.4 (0.3-56.6)
Age Range - no. (%)	
<1 years	104 (32.8)
1 - <2 years	119 (37.5)
2-5 years	82 (25.9)
6-10 years	3 (0.9)
>10	9 (2.8)
CRF vs Non-CRF - no. (%)	
CRF	114 (36.0)
Not CRF	202 (63.7)
Not Reported	1 (0.3)
Disease Status at the time of HCT - no. (%)	
PIF	8 (2.5)

Characteristic	N (%)
CR1	133 (42.0)
CR2	150 (47.3)
>=CR3	15 (4.7)
Relapse	10 (3.2)
Not reported	1 (0.3)
Donor type - no. (%)	
HLA-identical sibling	55 (17.4)
Other related	51 (16.1)
8/8 matched URD	58 (18.3)
7/8 mismatched URD	11 (3.5)
Unrelated (matching TBD)	20 (6.3)
Cord blood	122 (38.5)
Conditioning Regimen Intensity - no. (%)	
MAC	271 (85.5)
RIC	1 (0.3)
NMA	2 (0.6)
Not Reported	43 (13.6)
TBI vs Non-TBI - no. (%)	
TBI	136 (42.9)
Non-TBI	181 (57.1)
Year of current transplant - no. (%)	
2008	33 (10.4)
2009	19 (6.0)
2010	15 (4.7)
2011	28 (8.8)
2012	29 (9.1)
2013	19 (6.0)
2014	18 (5.7)
2015	17 (5.4)
2016	26 (8.2)
2017	27 (8.5)
2018	30 (9.5)

Characteristic	**N (%)**
2019	27 (8.5)
2020	29 (9.1)
Follow-up of survivors - median (range)	71.4 (3.1-193.5)

Field	Response
Proposal Number	2410-204-BIDGOLI
Proposal Title	Transplantation Outcomes for Children with Hypodiploid Acute Lymphoblastic Leukemia in the Modern Era.
Key Words	Hypodiploid Acute Lymphoblastic Leukemia, allogeneic hematopoietic stem cell transplantation, minimal residual disease, chromosomal abnormalities
Principal Investigator #1: - First and last name, degree(s)	Alan Bidgoli
Principal Investigator #1: - Email address	alan.bidgoli@emory.edu
Principal Investigator #1: - Institution name	Children's Healthcare of Atlanta/Emory University
Principal Investigator #1: - Academic rank	Assistant Professor
Junior investigator status (defined as ≤5 years from fellowship)	Yes
Do you identify as an underrepresented/minority?	No
Principal Investigator #2 (If applicable): - First and last name, degree(s):	Urvi Kapoor
Principal Investigator #2 (If applicable): - Email address:)	kye9004@nyp.org
Principal Investigator #2 (If applicable): - Institution name:	Columbia University
Principal Investigator #2 (If applicable): - Academic rank:	Fellow, Pediatric Hematology, Oncology, Stem Cell transplant.
Junior investigator status (defined as ≤5 years from fellowship)	Yes
Do you identify as an underrepresented/minority?	No
We encourage a maximum of two Principal Investigators per study. If more than one author is listed, please indicate who will be identified as the corresponding PI below:	alan.bidgoli@emory.edu
If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:	-
Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.	None
Do any of the PI(s) within this proposal have a CIBMTR WC study in manuscript preparation >6 months?	No
PROPOSED WORKING COMMITTEE:	Acute Leukemia
Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.	No
If you have already spoken with a scientific director or working committee chair regarding this study, then please specify who:	-
RESEARCH QUESTION:	Have transplantation outcomes for pediatric patients with hypodiploid acute lymphoblastic leukemia improved in the modern era?

Field	Response
RESEARCH HYPOTHESIS:	Hematopoietic stem cell transplant for hypodiploid ALL, when performed in the setting of disease control, offers similar outcomes to other ALL transplants.
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	Primary Outcomes: 1. Leukemia-free survival (LFS): LFS is defined as survival without relapse or progression. Disease relapse/progression and death are treated as events. Surviving patients will be censored at the last follow-up. Secondary Outcomes: 1. Relapse: This is defined as recurrence of the hypodiploid ALL. Patients will be censored at the last follow-up. 2. Non-relapse Mortality (NRM): This event is defined as death in the absence of recurrence of the primary malignancy. Patients will be censored at the last follow-up. 3. Overall Survival (OS): This is defined as the length of time from HCT that patients are still alive.
SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.	This study will have several significant impacts on the field of pediatric hypodiploid ALL treatment: 1. Provide an update on transplant outcomes in more recent years 2011-2012. This will help further stratify patient groups that could benefit from hematopoietic stem cell transplants. 2. It will help identify additional prognostic factors and build on previously studied prognostic factors including the association of conditioning regimens, graft source, chromosome numbers, remission status, and minimal residual disease (MRD) on patient outcomes. 3. Provide an update on the impact of novel immunotherapies on transplant outcomes which has not been previously explored. 4. Provide a framework for the development of future clinical trials for risk-adapted treatment approaches for hypodiploid ALL.

Field	Response
SCIENTIFIC JUSTIFICATION: Provide a background summary of previous related research and their strengths and weaknesses, justification of your research and why your research is still necessary.	Pediatric hypodiploid ALL is a rare subtype of ALL with an incidence of <5% and is associated with poor outcomes with a 5-year event-free survival rate of 50-55%. Due to its rarity, a multi-center database is needed to gather sufficient data for meaningful analysis to further refine and study the changes in outcomes over the last decade. The previous study from CIBMTR on this subtype of leukemia included 78 patients from 1990-2010 who were transplanted in complete remission (CR) 1-3. The study found no improvement in survival outcomes compared to prior reports with a 5-year leukemia-free survival (LFS) of 51%. However, there were significant differences in outcomes when patients were stratified based on chromosome numbers; patients with ≤ 43 chromosomes had a 5-year LFS of 37% vs 64% for those with 44-45 chromosomes. Multivariate analysis showed a higher hazard ratio for patients transplanted in CR2 and above, having chromosome numbers ≤ 43 and transplanted in 1990-1999 compared to 2000-2010. MRD status at the time of HCT was not studied in this patient population. A prior COG study which included 131 patients transplanted between 2003 and 2011 showed that in the 61 patients transplanted in CR1, there was no survival benefit compared to 52 patients who received chemotherapy alone. Interestingly, HCT did not impact survival, regardless of EOI MRD or number of chromosomes. In that time era, the impact of MRD-level disease was not assessed. Another published study by Pui CH, et al analyzed 272 patients with hypodiploid ALL between 1997 and 2013 and showed that negative MRD at the end of induction, high hypodiploidy, and treatment in MRD-stratified protocols were favorable factors with better outcomes for patients. However, allogeneic transplantation did not significantly improve outcomes compared to chemotherapy alone especially for patients with MRD-negative status after induction. In a recent CIBMTR analysis, the pediatric disease risk index was derived and validated as predictive for LFS post-HCT for ALL and AML. For ALL, only age, CR status, and MRD status were significant and included in the final model. The Impact of hypodiploidy as an adverse prognostic factor was not assessed. This proposed study will elaborate on associations between hypodiploidy and HCT outcomes and address the gaps in our current knowledge taking into account transplantation in the last decade with improved tools of MRD assessment, supportive care, and the role of immunotherapy. This will provide valuable insight to guide if any subset of pediatric hypodiploid ALL patients would benefit from HCT.

Field	Response
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	a. Inclusion Criteria: a. Pediatric patients aged 0-21 years who received first allogeneic stem cell transplant for hypodiploid ALL from 2011 to 2021 b. Exclusions Criteria: a. Patients with missing data on cytogenetics
Does this study include pediatric patients?	Yes
If this study does not include pediatric patients, please provide justification:	-
DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion- variables to be considered in the multivariate analyses. Outline any supplementary data required.	Standard CIBMTR forms only, no additional data requested from sites
Types of cellular therapy data this proposal includes:	Hematopoietic Cell Transplantation (HCT)
PATIENT REPORTED OUTCOME (PRO) REQUIREMENTS: If the study requires PRO data collected by CIBMTR, the proposal should include: 1) A detailed description of the PRO domains, timepoints, and proposed analysis of PROs; 2) A description of the hypothesis speci	No PRO requirements.
MACHINE LEARNING: Please indicate if the study requires methodology related to machine-learning and clinical predictions.	No methodology related to machine-learning and clinical procedures.
SAMPLE REQUIREMENTS: If the study requires biologic samples from the CIBMTR Repository, the proposal should also include: 1) A detailed description of the proposed testing methodology and sample requirements; 2) A summary of the investigator's previous e	No biologic samples from the CIBMTR Repository.
NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required.	No external data source is required.

Field	Response
REFERENCES:	Nachman JB, Heerema NA, Sather H, et al. Outcome of treatment in children with hypodiploid acute lymphoblastic leukemia. Blood. 2007 Aug 15;110(4):1112-5. doi: 10.1182/blood-2006-07-038299 Mehta PA, Zhang MJ, Eapen M, et al. Transplantation Outcomes for Children with Hypodiploid Acute Lymphoblastic Leukemia. Biol Blood Marrow Transplant. 2015 Jul;21(7):1273-7. doi: 10.1016/j.bbmt.2015.04.008. Pui CH, Rebora P, Schrappe M,et al; Ponte di Legno Childhood ALL Working Group. Outcome of Children With Hypodiploid Acute Lymphoblastic Leukemia: A Retrospective Multinational Study. J Clin Oncol. 2019 Apr 1;37(10):770-779. doi: 10.1200/JCO.18.00822 McNeer JL, Devidas M, Dai Y, et al. Hematopoietic Stem-Cell Transplantation Does Not Improve the Poor Outcome of Children With Hypodiploid Acute Lymphoblastic Leukemia: A Report From Children's Oncology Group. J Clin Oncol. 2019 Apr 1;37(10):780-789. doi: 10.1200/JCO.18.00884 Qayed M, Ahn KW, Kitko CL, Johnson MH, Shah NN, Dvorak C, Mellgren K, Friend BD, Verneris MR, Leung W, Toporski J, Levine J, Chewning J, Wayne A, Kapoor U, Triplett B, Schultz KR, Yanik GA, Eapen M. A validated pediatric disease risk index for allogeneic hematopoietic cell transplantation. Blood. 2021 Feb 18;137(7):983-993. doi: 10.1182/blood.2020009342. PMID: 33206937; PMCID: PMC7918183.
CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning?	No, I do not have any conflicts of interest pertinent to this proposal
If yes, provide detail on the nature of employment, name of organization, role, entity, ownership, type of financial transaction or legal proceeding and whether renumeration is >$5000 annually.	-

The below selection criteria were applied

Selection criteria	# excluded	N
Cases available in CIBMTR HCT Essentials Extract *		441766
HCT years 2013-2022	164084	277682
Age at diagnosis: <21 year	237033	40649
First Allo Transplant	15126	25523
Disease: AML, ALL, other leukemia and MDS	19798	5725
Subdisease Selected: Hypodiploid ALL (subdis=83)	5562	163
Patient Consented	16	147
Follow-up present	6	141

**Data source: HCT Essentials Oct 2024*

Table 1: Patients that underwent first allogeneic HCT for Hypodiploid ALL between 2013-2022.

Characteristic	N (%)
No. of patients	141
No. of centers	73
Patient age - median (min-max)	11.6 (1.7-20.0)
Age Range - no. (%)	
<2 year	1 (0.7)
2-10 years	65 (46.1)
11-22 years	75 (53.2)
Conditioning Regimen Intensity - no. (%)	
MAC	128 (90.8)
RIC	6 (4.3)
NMA	2 (1.4)
Not Reported	5 (3.5)
Conditioning regimen - no. (%)	
TBI/Cy	54 (38.3)
TBI/Cy/Flu	18 (12.8)
TBI/Cy/TT	30 (21.3)
TBI/Cy/VP	2 (1.4)
TBI/VP	8 (5.7)

Characteristic	N (%)
TBI/Mel	1 (0.7)
TBI/Flu	6 (4.3)
TBI/other(s)	1 (0.7)
Bu/Cy/Mel	1 (0.7)
Bu/Cy	3 (2.1)
Bu/Mel	1 (0.7)
Flu/Bu/TT	1 (0.7)
Flu/Bu	2 (1.4)
Flu/Mel/TT	7 (5.0)
Flu/Mel	2 (1.4)
Treosulfan	3 (2.1)
Not Reported	1 (0.7)
Donor type - no. (%)	
HLA-identical sibling	38 (27.0)
Other related	30 (21.3)
8/8 matched URD	41 (29.1)
7/8 mismatched URD	4 (2.8)
<= 6/8 mismatched URD;	1 (0.7)
Multi-donor	1 (0.7)
Unrelated (matching TBD)	2 (1.4)
Cord blood	24 (17.0)
Disease Status at the time of HCT - no. (%)	
PIF	1 (0.7)
CR1	102 (72.3)
CR2	33 (23.4)
>=CR3	5 (3.5)
CRF vs Non-CRF - no. (%)	
No	98 (69.5)
Yes	41 (29.1)
Not Reported	2 (1.4)
Year of current transplant - no. (%)	
2013	8 (5.7)

Characteristic	N (%)
2014	28 (19.9)
2015	12 (8.5)
2016	15 (10.6)
2017	19 (13.5)
2018	16 (11.3)
2019	8 (5.7)
2020	10 (7.1)
2021	8 (5.7)
2022	17 (12.1)
Follow-up of survivors - median (range)	60.8 (3.2-120.4)