Not for publication or presentation

A G E N D A
CIBMTR WORKING COMMITTEE FOR PEDIATRIC CANCER
San Antonio, TX
Thursday, February 22, 2024, 1:00 – 3:00 PM CST

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Statistician:	**Rasha Atshan, MS; CIBMTR Statistical Center, Milwaukee, WI; E-mail: ratshan@mcw.edu**

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1. **Introduction**

   a. **Minutes from February 2023 Tandem meeting** (Attachment 1)
   b. **Instructions for signing-in and voting**
   c. **Introduction of incoming WC Co-Chairs**
      1. **Parinda Mehta MD:** Cincinnati Children's Hospital, Cincinnati, OH
      2. **Christine L. Phillips:** Cincinnati Children's Hospital, Cincinnati, OH

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

3. **Presentations, Published, or Submitted papers**

   a. **PC20-01** 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. **PC20-01** 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 (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). **Analysis.**

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). **Protocol development.**

d. **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.**

e. **PC23-01** Post-transplant cyclophosphamide vs. TCR αβ/CD19+ deplete approaches for haploidentical transplant in pediatric patients with acute leukemias and myelodysplastic syndrome. (A Li/ H Rangarajan/ P Satwani). **Protocol development.**

f. **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.**

5. Future/proposed studies

a. **PROP 2310-60** Transplantation and Cellular Therapy for Children and Young Adults with Down's Syndrome and Acute Leukemia (L Appell/ S Rotz) (Attachment 4)

b. **PROP 2310-91** Evaluation of Allogeneic Hematopoietic Cell Transplantation Outcomes and Prognostic Factors in Acute Megakaryoblastic Leukemia: A CIBMTR and EBMT Joint Study.
(A Sharma/ N Bhatt) (Attachment 5)

c. **PROP 2310-106** Influence of Pre-Transplant Chemotherapy Cycles on Allogeneic Transplant Outcomes in Pediatric Acute Myeloid Leukemia Patients in Complete Remission.
(E Krieger/ A Hoover) (Attachment 6)

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.
(A Lake/ C Duncan) (Attachment 7)

e. **PROP 2310-233** Transplant outcomes in pediatric, adolescent, and young adult patients with hypoplastic myelodysplastic syndrome.
(R Chakravarthy/ M Ginocchio) (Attachment 8)

Proposed studies; not accepted for consideration at this time

f. **PROP 2309-18** Determining the Optimal CD34+ Cell Dose and TNC Content in Pediatric Allogeneic Hematopoietic Cell Transplantation Performed for Malignant Diseases (E Fraint/ T Knight). *Dropped due to feasibility (few patients with both TNC and CD34 available).*

g. **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)(L Davis/ P Satwani). *Dropped due to feasibility (too few patients and events for analysis at this time).*

h. **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? (H Rangarajan/ P Satwani) *Dropped due to feasibility (all times when radiation given is not collected).*

i. **PROP 2310-81** Validating the Disease Risk Stratification System (DRSS) in Pediatric Patients: A collaborative study between CIBMTR and EBMT(A Lipsitt/ A Sharma). *Dropped due to overlap with a published study.*

j. **PROP 2310-129** Does radiation-based preparation improve transplant outcomes in pediatric AML patients with CNS involvement? (T Takahashi/ A Keating) *Dropped due to overlap with ongoing study.*

k. **PROP 2310-131** Post HCT outcomes for pediatric AML in remission with incomplete hematologic recovery prior to conditioning (T Takahashi/ A Keating). *Dropped due to feasibility (data not collected by CIBMTR).*

l. **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 (E Krieger). *Dropped due to overlap with ongoing study.*

m. **PROP 2310-214** Outcomes of autologous stem cell transplant for relapsed/refractory germ cell tumors in women(E Bezerra/ S Jaglowski). *Dropped due to feasibility (ovarian germ cell tumors are not currently collected as disease indication, forms to be updated).*

6. Other business

MINUTES AND OVERVIEW PLAN
CIBMTR WORKING COMMITTEE FOR PEDIATRIC CANCER
Orlando, Florida
Friday, February 17th, 2023, 12 pm – 2 pm

Co-Chair:	**Gregory Yanik, MD, The University of Michigan**
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1. **Introduction**

   The Pediatric Cancer Working Committee (PCWC) meeting was called at 12:05 pm on Friday, February 17, 2023, by Dr. Larisa Broglie. The chairs, scientific director, and statistical team were present at the meeting. Attendees were asked to have their 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. Broglie welcomed the attendees on behalf of the working committee leadership and introduced the current WC leadership. Dr. Broglie thanked the leaving chair, Dr. Gregory Yanik, for his contribution to the PCWC and she welcomed Dr. Akshay Sharma as incoming chair. Dr. Broglie proceeded to take the attendees through the committee's goals, expectations, and limitations. She described the CIBMTR COI policy. Then she provided an overview of CIBMTR, data availability & retrievals, publicly available datasets, and Early Career Investigators opportunities. Dr. Broglie introduced Dr. Yanik as the next speaker to provide an overview of PCWC and Accruals report summary.

2. **Accrual summary**

   Dr. Yanik introduced himself to the attendees and reminded them about WC participation, membership, and rules of authorship. Then he directed the attendees' attention to the accrual summaries included in the meeting materials. Dr. Yanik provided a concise summary of the numbers of pediatric patients available in the CIBMTR database.

3. **Presentations, Published or Submitted Papers**

   Dr. Broglie announced that PC20-01 was accepted by TCT and she thanked the PCWC members for their contributions. Then, Dr. Broglie gave an overview of fellowship study SC21-08 and she introduced the study investigator Nicole Liberio. Nicole introduced herself and provided an overview of the study and the corresponding findings.

a. **PC20-01:** Autologous graft cell dose and post-transplant granulocyte colony stimulating factor in post-transplant outcomes among pediatric patients undergoing Autologous Hematopoietic Stem Cell Transplantation. (Knight T/ Wall D/ Chiengthong K), **Submitted.**
b. **SC21-08:** Optimizing Haploidentical Donor Selection for Pediatric HCT. (Liberio N/ Broglie L), **Manuscript in preparation.**
Comments from discussion:

i. A question was asked if there was a difference between PBSCS and Marrow in the GVHD evaluation. Nicole replied that graft source was significant for aGVHD outcome in the univariate analysis, but this finding was adjusted in the multivariable analysis.
ii. Another question was asked about the severity and extent of cGVHD outcomes. Nicole replied that the details of such an outcome could be evaluated in future analysis.
iii. Another question about the ability to break down graft manipulation to CD34 selection, Alpha Beta, vs. others. Nicole replied that CIBMTR data forms didn't provide graft manipulation data. Dr. Broglie added that the CIBMTR forms changed over time. She added CIBMTR collected CD34 selection or T-Cell depletion but in recent years the graft manipulation questions were moved to CRF retrieval adding Alpha Beta T-Cell depletion.
iv. A question was asked about data collection forms for siblings and half siblings. Nicole replied that half siblings were included in the study population if they were categorized as Haploidentical donors without knowing if they are full sibling or not. Dr. Broglie added that the study didn't distinguish full sibling Haploidentical from half sibling Haploidentical donors. The attendees clarified if they study distinguish between sibling donors and other donors, and Nicole replied confirmed that the study does.
v. A follow-up comment about the insight of graft manipulation (T-Cell depletion) data into the study findings.
vi. A question about considering compounding variables like multiparity and age with the outcomes. Nicole replied that parity is being considered for future analysis.
vii. Another question about considering Nima and Nepa in the analysis. The attendee added that Nima is the non-inherited maternal antigen while Nepa is the non-inherited paternal antigen. Nicole replied that it isn't part of the study, but it is something to consider evaluating in future analysis.
viii. Another question about considering specific HLA-mismatches and correlation with the outcomes. Dr. Broglie replied that this was discussed previously and was excluded from the study, and she added that this should be considered in future analysis.
ix. Dr. Yanik asked about the age of the youngest donor in the registry for this study and how many donors were younger than ten years old. Nicole replied that wasn't certain at the time of how many donors were younger than ten years old. She added that she is considering categorizing the age groups for father, mother, and sibling donors who are younger than ten years old. She added that the sample size of these donor and age groups needs to be evaluated to check if analysis results will have enough statical power to support the findings.

4. Studies in Progress

Dr. Schultz introduced himself to the attendees and he provided an overview of the WC portfolio of the active studies.

a. **PC19-02:** Does mixed peripheral blood T Cell Chimerism predict relapse? (Prockop S/Boelens J/Peggs K), **Protocol Development/ Data file preparation.**
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), **Protocol Development/ Data file preparation.**

c. **PC20-02:** Germline genetics of pediatric Myelodysplastic Syndromes (MDS). (Poynter J/ Spector L), **Sample Typing/ Data file preparation.**
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), **Protocol Development.**
Comments from discussion:

i. A question about the range of years that will be included in this study. Dr. Broglie replied that the initial protocol is looking for those cases of patients enrolled on the early COG relapse refractory studies and the hope is to expand the study as early as 2000.

f. **SC21-08:** Optimizing Haploidentical Donor Selection for Pediatric HCT. (Liberio N/ Broglie L), **Manuscript in preparation.**

5. Future/Proposed Studies

Dr. Muna Qayed reminded the attendees of the proposals scoring logistics. She also reminded the presenters that each presentation duration is five minutes followed by five minutes for the Questions & Answers session. Dr. Qayed announced the collaborative session where PCWC proposal will be presented, then she added the Collaborative Session date, time, and location. Dr. Qayed introduced each proposal title and the presenters to the audience in the following order.

a. **PROP 2210-104:** 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. (Li A/Rangarajan H/Satwani P).
Dr. Li presented the proposal on behalf of the group. The proposal hypothesizes that outcomes in pediatric patients with Acute Leukemias and Myelodysplastic syndrome undergoing haploidentical. hematopoietic stem cell transplants (haplo HCT) will be comparable between alpha-beta T-cell receptor deplete (TCR αβ/CD19+) and post-transplant cyclophosphamide (PTCY) transplant approaches.
Comments from discussion:

i. A Comment regarding the limited number of centers that use TCR αβ, the attendee added the patients with positive MRD had poor outcomes after HCT, and he added the value of using Disease Risk Index to categorization. He also added that CIBMTR should consider data linkage for this study with COG for example. Dr. Broglie replied that the goal is to collaborate with EBMT to complete this study.
ii. A comment about COG prospective study initially investigates TCR αβ vs PTCY vs CB. Since CB is used less in HCT and the statistical power issues of comparing three cohort, the investigators decided to exclude CB. The attendees suggested using CB in this study since the retrospective data is available. He states that there is a lack of pediatrics data in comparison to adults' data.
iii. Another attendee emphasized the center effect on the analysis, he added that this effect needs to be addressed and explained. He also added the ethics principles in a bias study and that researchers can investigate any scientific questions.
iv. An attendee asked the COG faculty about the statistical power issues in the COG prospective study that investigated TCR αβ vs PTCY vs CB. An Attendee replied that it was difficult to consider the statical power.

v. Dr. Schultz added that the bias in the COG study is a consideration, but waiting for five years to answer the question doesn't seem reasonable when there is rich and retrospective data available. As for the center biased effect, Europe will be biased towards TCR αβ data in compared to PTCY.
vi. A question about the volume of TCR αβ in European database. Dr. Broglie replied that EBMT database has more TCR αβ data than CIBMTR database. Dr. Broglie stated that she wasn't certain of the EBMT data volume at the time.
vii. A question about including GVHD, relapse free survival outcomes. Dr. Li replied that these outcomes are being investigated in the study.
viii. An attendee from Spain emphasized that their center is willing to collaborate by sharing the TCR αβ data with CIBMTR to complete this study.
ix. An attendee added that this is an important question regardless of the fact that this data belongs to a prospective trial. She added that the centers that are using TCR αβ think it is more effective for HCT with haploidentical donors. Then, she added that not every center is able to use TCR αβ, also from statistical standpoint if there is enough sample size to use matched pair analysis, using heterogeneous groups by disease, by DR, by MRD, to compare TCR αβ vs PTCY. She also added that the investigators should consider factors like cost analysis and policies & procedures for initial hospitalization within 100 days.
x. Dr. Li commented that coming from an institution with a limited budget for TCR αβ, this study will contribute to patients' treatment if it shows how TCR αβ is optimal for specific population and not others than these findings.
xi. Dr. Schultz asked the audience about adding CB as a third cohort to this study. The audience were in favor of adding CB cohort.
xii. A question about fertility data collection on CRF forms, Dr. Broglie replied that this data isn't collected at the time.
xiii. Dr. Yanik asked about considering the variation between sites in terms of methodology and infused cell dose when using TCR αβ in stem cell transplant. An attendee confirmed that methodology and infused cell dose are considered.

b. **PROP 2210-120:** Comparison of myeloablative conditioning regimens for acute myeloid leukemia in children and young adults. (Pfeiffer T/Shenoy S).
Dr. Pfeiffer presented the proposal virtually on behalf of the group. The proposal hypothesizes that the optimal conditioning regimen for children with AML undergoing allogeneic hematopoietic cell transplantation (allo-HCT) is subject of ongoing debate. Clinical trials prospectively evaluating different conditioning regimens are lacking. Registry data suggest similar non-relapse mortality (NRM), overall (OS) and relapse-free survival (RFS) for pediatric AML patients receiving busulfan either with cyclophosphamide (Bu/Cy) or fludarabine (Bu/Flu) (1). Total body irradiation (TBI) based regimens were recently shown to result in similar outcomes despite increased toxicity (2). Further improvement of disease control may be achieved through the addition of melphalan and the resultant increase in (leukemic) stem cell toxicity. Indeed, recent European data demonstrate superior outcomes with Bu/Cy/Mel conditioning compared to Bu/Flu and Bu/Cy (3). Additional validation of these data is now needed. We hypothesize that OS and RFS rates may be improved with Bu/Cy/Mel conditioning compared to other Busulfan based myeloablative regimens.
<u>Comments from discussion:</u>

i. A comment about considering the morbidity at 100 days and remembering the effect of Alkylators being high in the analysis. Dr. Pfeiffer thanked the attendee and added that it is a good suggestion to investigate such outcomes, but the data collection forms need to be reviewed to check the availability of this data.

ii. An attendee added that each centers combine the drugs differently and he asked if the data forms collect the time the drug was gives to a patient. Dr. Broglie replied that the data forms collect the drug combination but not the time a drug was given. The attendee added that this is a limitation to the study but not a big limitation.
iii. Dr. Yanik asked if the database contains information like Flu/Bu2 vs Flu/Bu4. Dr. Broglie replied that the database provides information on the intended dose and the target.
iv. Dr. Pfeiffer added that is a limitation to the study as it relates to toxicity, and the effect on the analysis.
v. Dr. Broglie asked about considering toxicity between regimens like VOD. Dr. Pfeiffer replied that toxicity is an important outcome to consider and one of the hesitations in deducting this study was toxicity vs Leukemia control and there is not a particular answer to this question, and he added that VOD and other toxicity is something the study team is curious about analyzing.

c. **PROP 2210-217:** Outcomes of children who receive an allogeneic hematopoietic cell transplantation for Juvenile Myelomonocytic Leukemia. (Sharma A/Bhatt N).
Dr. Sharma presented the proposal virtually on behalf of the group. The proposal hypothesizes that the overall and disease-free survival of patients with JMML who undergo allogeneic HCT, especially with HLA-matched sibling donor and myeloablative conditioning with busulfan, cyclophosphamide, and melphalan has improved over time. However, the burden of short-term toxicities and late effects among HCT recipients remains high due to the conditioning intensity.
<u>Comments from discussion:</u>

i. A comment about the population number for JMML is the biggest population the attendee had seen for this disease. He added that the study is too broad for example TBI isn't used for these patients and he wonder if it will be useful to publish such a study in this era. He added that JMML is a rare disease, and it is several different diseases are classified as JMML based on patients' genetic profile; for example, KRAS mutation is easy to transplant while a disease with multiple mutations has dismal outcomes. The attendee added that he doesn't think this data is collected on CIBMTR forms. He referred to Elliot Stevens publication about JMML patients don't go to HCT with pre-transplant remission by molecular basis but the patients that reach remission have better outcomes. Dr. Sharma agreed with attendee that nobody is using TBI these days; and he added that the population can be divided into two cohort by decade. Dr. Sharma addressed the molecular data question, since 47% of the patients have CRF level data and molecular data might by captured by CIBMTR. Then Dr. Sharma asked Dr. Broglie to clarify the data availability, Dr. Broglie replied that CIBMTR database has disease status not MRD status data.
ii. Dr. Schultz asked if the molecular data is available. Dr. Broglie replied that this data is available but may not be consistent. Dr. Schultz also asked the attendee about TBI era vs not TBI era, is that a 10-year range. The attendee confirmed with yes.
iii. Dr. Qayed asked if patients who received TBI should be excluded or divided the population into TBI vs non-TBI. She also asked what the least bias would be.
iv. A comment about published studies did not monitor therapeutic drugs expect for the Japanese study and population numbers were low.
The attendee also recommended that the investigators look at TBI vs non-TBI and the therapeutical drugs monitoring were available or not since that is an effect in morbidity associate with the treatment. His second comment regarding the pre-transplant chemotherapy treatment; he added that the data isn't collected on CIBMTR data forms. He also added that people in the field agree that this is an important factor in the treatment to decrease the size of the disease before transplant. He recommended including such data in the analysis. Dr. Sharma replied that CIBMTR collects the pre-

transplant chemotherapy data; CRF forms collect BCR ABL, KRAS and NRAS, PTPN 11 mutations, that data is collect for at 47% of population.

v. Another comment about including post-transplant drugs in the analysis. Dr. Sharma replied that the team is interested in acute short-terms and late effects outcomes.

vi. Dr. Yanik asked what is the follow up time for late effects. Dr. Sharma replied that analyzing late effect outcomes at 2 years seems reasonable based on pervious CIBMTR studies.

Future/proposed studies to be presented at the CIBMTR Collaborative Working Committee Study Proposals Session

Dr. Qayed reminded the attendees that proposal "**PROP 2210-276**: 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)." was selected to be presented at the Collaborative Session. She also reminded the attendees of the voting logistics.

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 2209-10:** Feasibility and Outcomes of Third Allogeneic Hematopoietic Cell Transplantation in Individuals with Relapsed or Refractory Acute Leukemia. *Dropped due to overlap with ongoing study.*

b. **PROP 2210-47:** Outcomes of Allogeneic Hematopoietic Cell Transplantation (Allo-HCT) after Blinatumomab Salvage Therapy in Pediatric Patients with Relapsed/Refractory B-cell Lineage Acute Lymphoblastic Leukemia (BL-ALL). *Dropped due to overlap with an ongoing corporate study.*

c. **PROP 2210-102:** Determinants of Outcome for Children with Acute Leukemia or MDS Who Receive a Third or Subsequent Allogeneic Hematopoietic Cell Transplant. *Dropped due to overlap with ongoing study.*

d. **PROP 2210-144:** Determining the Optimal CD34+ Cell Dose and TNC Content in Pediatric Allogeneic Hematopoietic Cell Transplantation Performed for Malignant Diseases. *Dropped due to heterogeneous population.*

e. **PROP 2210-166:** Post-Transplant Clinical Outcomes and Neoplastic Risk in Fanconi Anemia. *Dropped due to overlap with ongoing study.*

f. **PROP 2210-167:** Impact of Epstein Barr virus (EBV) infection on outcomes of allogenic hematopoietic cell transplantation (HCT) for hematologic malignancies. *Dropped due to feasibility, data not collected by CIBMTR.*

g. **PROP 2210-216:** Prognostic Impact of Cytogenetic and Molecular Risk Classification in AML after Hematopoietic Stem Cell Transplant in Pediatrics, Adolescents, and Young Adults. *Dropped due to overlap with a published study.*

h. **PROP 2210-243:** Impact of Sorafenib after Allo-HSCT as prevention of AML relapse in children. *Dropped due to feasibility, data not reliably reported to CIBMTR.*

i. **PROP 2210-281:** Comparison of umbilical cord blood transplants and unmanipulated haploidentical stem cell transplants in children undergoing allogeneic transplant for hematological malignancies. *Dropped due to Overlap with a published study.*

7. Concluding Notes

The meeting was adjourned at 1:35 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 2023-2024		
Study number and title	**Status**	**Chairs priority**
PC19-02: Does mixed peripheral blood T cell chimerism predict relapse?	Protocol development/ Data file preparation	4
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.	Protocol development/ Data file preparation	2
PC20-01: Autologous graft cell dose and post-transplant granulocyte colony stimulating factor in post-transplant outcomes among pediatric patients undergoing autologous hematopoietic stem cell transplantation.	Manuscript preparation	1
PC20-02: Germline genetics of pediatric myelodysplastic syndromes.	Sample Typing/ Data file preparation	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	5
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	8
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	6
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	7

PCWC 2024 accruals: Characteristics of patients aged <= 18 years reported to the CIBMTR between 2010 - 2022

Characteristic	TED, N (%)	CRF, N (%)	Total
Disease - no. (%)			
AML	3134 (18.9)	1032 (39.0)	4166 (21.7)
ALL	4279 (25.8)	1090 (41.1)	5369 (27.9)
Other Leukemia	316 (1.9)	77 (2.9)	393 (2.0)
CML	258 (1.6)	57 (2.2)	315 (1.6)
MDS	954 (5.8)	277 (10.5)	1231 (6.4)
NHL	534 (3.2)	89 (3.4)	623 (3.2)
HD	921 (5.6)	17 (0.6)	938 (4.9)
MM-PCD	5 (0.0)	1 (0.0)	6 (0.0)
Others/Solid tumors	6171 (37.2)	9 (0.3)	6180 (32.2)
Donor type - no. (%)			
Autologous	7306 (44.1)	0 (0.0)	7306 (38.0)
HLA-identical sibling	2764 (16.7)	365 (13.8)	3129 (16.3)
Twin	9 (0.1)	8 (0.3)	17 (0.1)
Other related	1837 (11.1)	466 (17.6)	2303 (12.0)
Well-matched unrelated (8/8)	2216 (13.4)	405 (15.3)	2621 (13.6)
Partially-matched unrelated (7/8)	714 (4.3)	150 (5.7)	864 (4.5)
Mis-matched unrelated (<= 6/8)	26 (0.2)	14 (0.5)	40 (0.2)
Multi-donor	29 (0.2)	3 (0.1)	32 (0.2)
Unrelated (matching TBD)	679 (4.1)	22 (0.8)	701 (3.6)
Cord blood	944 (5.7)	1216 (45.9)	2160 (11.2)
Not reported	48 (0.3)	0 (0.0)	48 (0.2)
Graft type - no. (%)			
Bone marrow	5832 (35.2)	1001 (37.8)	6833 (35.5)
Peripheral blood	9796 (59.1)	432 (16.3)	10228 (53.2)
Umbilical cord blood	944 (5.7)	1216 (45.9)	2160 (11.2)

Data source: January 2022 CRF
January 2022 TED
October 2023 HCT-Essentials
Embargo and consent criteria are not applied

PCWC 2024 accruals: Siblings

Characteristic	TED, N (%)	CRF, N (%)	Total
Disease - no. (%)			
AML	910	155	1065
ALL	1357	153	1510
CML	87	11	98
MDS	224	32	256
NHL	97	21	118
HD	14	2	16
Graft type - no. (%)			
AML			
Bone marrow	695 (76.4)	125 (80.6)	820 (77.0)
Peripheral blood	203 (22.3)	22 (14.2)	225 (21.1)
Umbilical cord blood	12 (1.3)	8 (5.2)	20 (1.9)
ALL			
Bone marrow	1059 (78.0)	128 (83.7)	1187 (78.6)
Peripheral blood	272 (20.0)	17 (11.1)	289 (19.1)
Umbilical cord blood	26 (1.9)	8 (5.2)	34 (2.3)
CML			
Bone marrow	71 (81.6)	10 (90.9)	81 (82.7)
Peripheral blood	15 (17.2)	0 (0.0)	15 (15.3)
Umbilical cord blood	1 (1.1)	1 (9.1)	2 (2.0)
MDS			
Bone marrow	184 (82.1)	27 (84.4)	211 (82.4)
Peripheral blood	39 (17.4)	2 (6.3)	41 (16.0)
Umbilical cord blood	1 (0.4)	3 (9.4)	4 (1.6)
NHL			
Bone marrow	71 (73.2)	16 (76.2)	87 (73.7)
Peripheral blood	25 (25.8)	5 (23.8)	30 (25.4)
Umbilical cord blood	1 (1.0)	0 (0.0)	1 (0.8)
HD			
Bone marrow	7 (50.0)	1 (50.0)	8 (50.0)
Peripheral blood	7 (50.0)	1 (50.0)	8 (50.0)

Data source: January 2022 CRF
January 2022 TED
October 2023 HCT-Essentials
Embargo and consent criteria are applied

PCWC 2024 accruals: Other related donors

Characteristic	TED, N (%)	CRF, N (%)	Total
Disease - no. (%)			
AML	633	166	799
ALL	861	211	1072
CML	39	13	52
MDS	158	44	202
NHL	59	24	83
HD	13	5	18
Graft type - no. (%)			
AML			
Bone marrow	284 (44.9)	94 (56.6)	378 (47.3)
Peripheral blood	345 (54.5)	70 (42.2)	415 (51.9)
Umbilical cord blood	4 (0.6)	2 (1.2)	6 (0.8)
ALL			
Bone marrow	415 (48.2)	118 (55.9)	533 (49.7)
Peripheral blood	442 (51.3)	87 (41.2)	529 (49.3)
Umbilical cord blood	4 (0.5)	6 (2.8)	10 (0.9)
CML			
Bone marrow	23 (59.0)	7 (53.8)	30 (57.7)
Peripheral blood	16 (41.0)	5 (38.5)	21 (40.4)
Umbilical cord blood	0 (0.0)	1 (7.7)	1 (1.9)
MDS			
Bone marrow	76 (48.1)	18 (40.9)	94 (46.5)
Peripheral blood	78 (49.4)	25 (56.8)	103 (51.0)
Umbilical cord blood	4 (2.5)	1 (2.3)	5 (2.5)
NHL			
Bone marrow	30 (50.8)	7 (29.2)	37 (44.6)
Peripheral blood	28 (47.5)	17 (70.8)	45 (54.2)
Umbilical cord blood	1 (1.7)	0 (0.0)	1 (1.2)
HD			
Bone marrow	7 (53.8)	3 (60.0)	10 (55.6)
Peripheral blood	6 (46.2)	2 (40.0)	8 (44.4)

Data source: January 2022 CRF
January 2022 TED
October 2023 HCT-Essentials
Embargo and consent criteria are applied

PCWC 2024 accruals: Matched and mismatched unrelated donor

Characteristic	TED, N (%)	CRF, N (%)	Total
Disease - no. (%)			
AML	1507	710	2217
ALL	2033	723	2756
CML	130	32	162
MDS	568	200	768
NHL	134	42	176
HD	18	10	28
Graft type - no. (%)			
AML			
Bone marrow	795 (52.8)	188 (26.5)	983 (44.3)
Peripheral blood	385 (25.5)	75 (10.6)	460 (20.7)
Umbilical cord blood	327 (21.7)	447 (63.0)	774 (34.9)
ALL			
Bone marrow	1130 (55.6)	136 (18.8)	1266 (45.9)
Peripheral blood	499 (24.5)	62 (8.6)	561 (20.4)
Umbilical cord blood	404 (19.9)	525 (72.6)	929 (33.7)
CML			
Bone marrow	81 (62.3)	18 (56.3)	99 (61.1)
Peripheral blood	36 (27.7)	4 (12.5)	40 (24.7)
Umbilical cord blood	13 (10.0)	10 (31.3)	23 (14.2)
MDS			
Bone marrow	367 (64.6)	51 (25.5)	418 (54.4)
Peripheral blood	116 (20.4)	16 (8.0)	132 (17.2)
Umbilical cord blood	85 (15.0)	133 (66.5)	218 (28.4)
NHL			
Bone marrow	73 (54.5)	11 (26.2)	84 (47.7)
Peripheral blood	38 (28.4)	5 (11.9)	43 (24.4)
Umbilical cord blood	23 (17.2)	26 (61.9)	49 (27.8)
HD			
Bone marrow	12 (66.7)	8 (80.0)	20 (71.4)
Peripheral blood	6 (33.3)	2 (20.0)	8 (28.6)

Data source: January 2022 CRF
January 2022 TED
October 2023 HCT-Essentials
Embargo and consent criteria are applied

PCWC 2024 accruals: Autologous

Characteristic	TED, N (%)	Total
Disease - no. (%)		
NHL	244	244
HD	876	876
Graft type - no. (%)		
NHL		
Bone marrow	13 (5.3)	13 (5.3)
Peripheral blood	231 (94.7)	231 (94.7)
HD		
Bone marrow	13 (1.5)	13 (1.5)
Peripheral blood	863 (98.5)	863 (98.5)
Solid tumors sub-disease - no. (%)		
Sarcoma (osteosarcoma, rhabdomyosarcoma, PNET and other sarcoma)	50	50
Wilm's Tumor	145	145
Testicular	38	38
Other gonadal tumors	22	22
Extragonadal germ cell tumors	167	167
Neuroblastoma	3376	3376
Other solid tumor	2	2
Medulloblastoma	874	874
Retinoblastoma	104	104
Other CNS tumor	753	753

Data source: January 2022 CRF
January 2022 TED
October 2023 HCT-Essentials
Embargo and consent criteria are applied

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	4516	1369	1709
Source of data			
CRF	2695 (60)	696 (51)	1060 (62)
TED	1821 (40)	673 (49)	649 (38)
Number of centers	162	123	200
Disease at transplant			
AML	1361 (30)	469 (34)	523 (31)
ALL	1959 (43)	552 (40)	752 (44)
Other leukemia	30 (1)	4 (<1)	10 (1)
CML	273 (6)	90 (7)	132 (8)
MDS	556 (12)	149 (11)	213 (12)
Other acute leukemia	110 (2)	44 (3)	25 (1)
NHL	168 (4)	42 (3)	35 (2)
Hodgkin Lymphoma	46 (1)	8 (1)	14 (1)
MPN	13 (<1)	11 (1)	5 (<1)
AML Disease status at transplant			
CR1	592 (43)	214 (46)	212 (41)
CR2	440 (32)	141 (30)	133 (25)
CR3+	34 (2)	11 (2)	16 (3)
Advanced or active disease	273 (20)	98 (21)	137 (26)
Missing	22 (2)	5 (1)	25 (5)
ALL Disease status at transplant			
CR1	584 (30)	152 (28)	194 (26)
CR2	838 (43)	258 (47)	301 (40)
CR3+	330 (17)	94 (17)	120 (16)
Advanced or active disease	171 (9)	41 (7)	75 (10)
Missing	36 (2)	7 (1)	62 (8)
MDS Disease status at transplant			
Early	178 (32)	37 (25)	40 (19)
Advanced	174 (31)	64 (43)	59 (28)
Missing	204 (37)	48 (32)	114 (54)
NHL Disease status at transplant			
CR1	31 (18)	8 (19)	10 (29)
CR2	44 (26)	20 (48)	9 (26)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
CR3+	18 (11)	1 (2)	1 (3)
PR	14 (8)	2 (5)	1 (3)
Advanced	57 (34)	11 (26)	7 (20)
Missing	4 (2)	0	7 (20)
Recipient age at transplant			
0-9 years	2171 (48)	650 (47)	825 (48)
10-17 years	2345 (52)	719 (53)	884 (52)
Median (Range)	10 (0-18)	11 (0-18)	10 (0-18)
Recipient race			
White	3562 (85)	1085 (85)	1211 (82)
Black or African American	325 (8)	88 (7)	135 (9)
Asian	149 (4)	47 (4)	77 (5)
Native Hawaiian or other Pacific Islander	12 (<1)	2 (<1)	11 (1)
American Indian or Alaska Native	33 (1)	12 (1)	10 (1)
Other	17 (<1)	10 (1)	8 (1)
More than one race	71 (2)	29 (2)	18 (1)
Unknown	347 (N/A)	96 (N/A)	239 (N/A)
Recipient ethnicity			
Hispanic or Latino	824 (24)	224 (22)	294 (25)
Non Hispanic or non-Latino	2403 (71)	753 (73)	582 (49)
Non-resident of the U.S.	145 (4)	53 (5)	316 (27)
Unknown	1144 (N/A)	339 (N/A)	517 (N/A)
Recipient sex			
Male	2663 (59)	826 (60)	999 (58)
Female	1853 (41)	543 (40)	710 (42)
Karnofsky score			
10-80	690 (15)	244 (18)	293 (17)
90-100	3656 (81)	1073 (78)	1304 (76)
Missing	170 (4)	52 (4)	112 (7)
HLA-A B DRB1 groups - low resolution			
<=3/6	3 (<1)	3 (<1)	1 (<1)
4/6	64 (1)	8 (1)	9 (1)
5/6	988 (22)	253 (21)	359 (23)
6/6	3364 (76)	959 (78)	1209 (77)
Unknown	97 (N/A)	146 (N/A)	131 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	215 (5)	8 (1)	27 (3)
6/8	381 (9)	29 (3)	58 (6)
7/8	1176 (27)	221 (26)	320 (31)
8/8	2608 (60)	583 (69)	615 (60)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Unknown	136 (N/A)	528 (N/A)	689 (N/A)
HLA-DPB1 Match			
Double allele mismatch	1231 (31)	116 (26)	152 (27)
Single allele mismatch	2123 (53)	232 (52)	304 (54)
Full allele matched	632 (16)	97 (22)	105 (19)
Unknown	530 (N/A)	924 (N/A)	1148 (N/A)
High resolution release score			
No	770 (17)	1360 (99)	1507 (88)
Yes	3746 (83)	9 (1)	202 (12)
KIR typing available			
No	3383 (75)	1367 (>99)	1674 (98)
Yes	1133 (25)	2 (<1)	35 (2)
Graft type			
Marrow	3594 (80)	1098 (80)	1307 (76)
PBSC	919 (20)	261 (19)	399 (23)
BM+PBSC	1 (<1)	1 (<1)	1 (<1)
PBSC+UCB	0	5 (<1)	1 (<1)
Others	2 (<1)	4 (<1)	1 (<1)
Conditioning regimen			
Myeloablative	4184 (93)	1284 (94)	1587 (93)
RIC/Nonmyeloablative	307 (7)	80 (6)	98 (6)
TBD	25 (1)	5 (<1)	24 (1)
Donor age at donation			
To Be Determined/NA	58 (1)	54 (4)	29 (2)
0-9 years	2 (<1)	3 (<1)	0
10-17 years	1 (<1)	0	1 (<1)
18-29 years	1975 (44)	627 (46)	670 (39)
30-39 years	1379 (31)	428 (31)	574 (34)
40-49 years	901 (20)	207 (15)	340 (20)
50+ years	200 (4)	50 (4)	95 (6)
Median (Range)	32 (3-61)	30 (1-61)	33 (17-61)
Donor/Recipient CMV serostatus			
+/+	987 (22)	384 (28)	357 (21)
+/-	731 (16)	182 (13)	283 (17)
-/+	1222 (27)	338 (25)	420 (25)
-/-	1412 (31)	380 (28)	517 (30)
CB - recipient +	0	5 (<1)	1 (<1)
CB - recipient -	0	3 (<1)	0
CB - recipient CMV unknown	0	1 (<1)	0
Missing	164 (4)	76 (6)	131 (8)

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	9 (<1)	2 (<1)	3 (<1)
TDEPLETION alone	42 (1)	8 (1)	24 (1)
TDEPLETION +- other	274 (6)	79 (6)	135 (8)
CD34 select alone	29 (1)	12 (1)	9 (1)
CD34 select +- other	56 (1)	21 (2)	29 (2)
Cyclophosphamide alone	8 (<1)	2 (<1)	3 (<1)
Cyclophosphamide +- others	51 (1)	34 (2)	34 (2)
FK506 + MMF +- others	247 (5)	72 (5)	51 (3)
FK506 + MTX +- others(not MMF)	1316 (29)	455 (33)	297 (17)
FK506 +- others(not MMF,MTX)	97 (2)	12 (1)	18 (1)
FK506 alone	56 (1)	15 (1)	12 (1)
CSA + MMF +- others(not FK506)	231 (5)	58 (4)	61 (4)
CSA + MTX +- others(not MMF,FK506)	1612 (36)	450 (33)	781 (46)
CSA +- others(not FK506,MMF,MTX)	199 (4)	60 (4)	97 (6)
CSA alone	147 (3)	48 (4)	89 (5)
Other GVHD Prophylaxis	106 (2)	27 (2)	34 (2)
Missing	36 (1)	14 (1)	32 (2)
Donor/Recipient sex match			
Male-Male	1712 (38)	513 (37)	601 (35)
Male-Female	1031 (23)	291 (21)	368 (22)
Female-Male	930 (21)	300 (22)	388 (23)
Female-Female	813 (18)	240 (18)	330 (19)
CB - recipient M	0	3 (<1)	1 (<1)
CB - recipient F	0	6 (<1)	0
Missing	30 (1)	16 (1)	21 (1)
Year of transplant			
1986-1990	73 (2)	9 (1)	30 (2)
1991-1995	437 (10)	107 (8)	203 (12)
1996-2000	579 (13)	211 (15)	332 (19)
2001-2005	694 (15)	155 (11)	333 (19)
2006-2010	836 (19)	154 (11)	206 (12)
2011-2015	992 (22)	215 (16)	255 (15)
2016-2020	674 (15)	339 (25)	235 (14)
2021-2023	231 (5)	179 (13)	115 (7)
Follow-up among survivors, Months			
N Eval	2345	734	852
Median (Range)	72 (0-353)	45 (0-295)	60 (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	1533	478	599
Source of data			
CRF	1135 (74)	327 (68)	335 (56)
TED	398 (26)	151 (32)	264 (44)
Number of centers	90	75	119
Disease at transplant			
AML	605 (39)	174 (36)	216 (36)
ALL	648 (42)	232 (49)	267 (45)
Other leukemia	10 (1)	1 (<1)	4 (1)
CML	18 (1)	5 (1)	9 (2)
MDS	156 (10)	43 (9)	65 (11)
Other acute leukemia	43 (3)	12 (3)	22 (4)
NHL	46 (3)	11 (2)	11 (2)
Hodgkin Lymphoma	5 (<1)	0	4 (1)
MPN	2 (<1)	0	1 (<1)
AML Disease status at transplant			
CR1	284 (47)	89 (51)	91 (42)
CR2	211 (35)	52 (30)	69 (32)
CR3+	13 (2)	0	5 (2)
Advanced or active disease	96 (16)	33 (19)	47 (22)
Missing	1 (<1)	0	4 (2)
ALL Disease status at transplant			
CR1	223 (34)	76 (33)	99 (37)
CR2	305 (47)	108 (47)	106 (40)
CR3+	97 (15)	34 (15)	45 (17)
Advanced or active disease	22 (3)	13 (6)	17 (6)
Missing	1 (<1)	1 (<1)	0
MDS Disease status at transplant			
Early	61 (39)	14 (33)	35 (54)
Advanced	52 (33)	20 (47)	15 (23)
Missing	43 (28)	9 (21)	15 (23)
NHL Disease status at transplant			
CR1	11 (24)	3 (27)	1 (9)
CR2	18 (39)	6 (55)	7 (64)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
CR3+	5 (11)	1 (9)	0
PR	3 (7)	0	1 (9)
Advanced	9 (20)	1 (9)	2 (18)
Recipient age at transplant			
0-9 years	988 (64)	335 (70)	376 (63)
10-17 years	545 (36)	143 (30)	223 (37)
Median (Range)	7 (0-18)	7 (0-18)	8 (0-18)
Recipient race			
White	1058 (74)	337 (75)	377 (72)
Black or African American	219 (15)	69 (15)	66 (13)
Asian	72 (5)	20 (4)	44 (8)
Native Hawaiian or other Pacific Islander	5 (<1)	2 (<1)	9 (2)
American Indian or Alaska Native	19 (1)	4 (1)	7 (1)
Other	0	0	1 (<1)
More than one race	62 (4)	17 (4)	20 (4)
Unknown	98 (N/A)	29 (N/A)	75 (N/A)
Recipient ethnicity			
Hispanic or Latino	466 (31)	125 (27)	116 (20)
Non Hispanic or non-Latino	1023 (68)	332 (71)	311 (54)
Non-resident of the U.S.	15 (1)	10 (2)	152 (26)
Unknown	29 (N/A)	11 (N/A)	20 (N/A)
Recipient sex			
Male	897 (59)	263 (55)	339 (57)
Female	636 (41)	215 (45)	260 (43)
Karnofsky score			
10-80	246 (16)	79 (17)	100 (17)
90-100	1241 (81)	372 (78)	452 (75)
Missing	46 (3)	27 (6)	47 (8)
HLA-A B DRB1 groups - low resolution			
<=3/6	10 (1)	4 (1)	3 (1)
4/6	423 (29)	113 (30)	143 (25)
5/6	748 (52)	191 (50)	290 (52)
6/6	267 (18)	75 (20)	126 (22)
Unknown	85 (N/A)	95 (N/A)	37 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	590 (43)	123 (39)	198 (42)
6/8	386 (28)	99 (32)	130 (27)
7/8	251 (18)	59 (19)	88 (19)
8/8	145 (11)	31 (10)	59 (12)
Unknown	161 (N/A)	166 (N/A)	124 (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	249 (39)	37 (36)	53 (39)
Single allele mismatch	325 (51)	53 (52)	64 (47)
Full allele matched	65 (10)	12 (12)	20 (15)
Unknown	894 (N/A)	376 (N/A)	462 (N/A)
High resolution release score			
No	995 (65)	447 (94)	588 (98)
Yes	538 (35)	31 (6)	11 (2)
KIR typing available			
No	1092 (71)	473 (99)	591 (99)
Yes	441 (29)	5 (1)	8 (1)
Graft type			
UCB	1513 (99)	469 (98)	589 (98)
PBSC+UCB	8 (1)	5 (1)	7 (1)
Others	12 (1)	4 (1)	3 (1)
Number of cord units			
1	1427 (93)	0	556 (93)
2	106 (7)	0	43 (7)
Unknown	0 (N/A)	478 (N/A)	0 (N/A)
Conditioning regimen			
Myeloablative	1451 (95)	452 (95)	552 (92)
RIC/Nonmyeloablative	81 (5)	26 (5)	45 (8)
TBD	1 (<1)	0	2 (<1)
Donor/Recipient CMV serostatus			
CB - recipient +	922 (60)	301 (63)	359 (60)
CB - recipient -	587 (38)	166 (35)	214 (36)
CB - recipient CMV unknown	24 (2)	11 (2)	26 (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	4 (<1)	0	3 (1)
FK506 + MMF +- others	309 (20)	127 (27)	93 (16)
FK506 + MTX +- others(not MMF)	105 (7)	26 (5)	38 (6)
FK506 +- others(not MMF,MTX)	32 (2)	15 (3)	14 (2)
FK506 alone	9 (1)	6 (1)	5 (1)
CSA + MMF +- others(not FK506)	812 (53)	219 (46)	274 (46)
CSA + MTX +- others(not MMF,FK506)	50 (3)	11 (2)	22 (4)

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
CSA +- others(not FK506,MMF,MTX)	161 (11)	54 (11)	110 (18)
CSA alone	23 (2)	6 (1)	23 (4)
Other GVHD Prophylaxis	8 (1)	4 (1)	5 (1)
Missing	2 (<1)	1 (<1)	3 (1)
Donor/Recipient sex match			
CB - recipient M	897 (59)	263 (55)	338 (56)
CB - recipient F	636 (41)	215 (45)	260 (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	562 (37)	125 (26)	200 (33)
2011-2015	552 (36)	126 (26)	227 (38)
2016-2020	287 (19)	131 (27)	103 (17)
2021-2023	86 (6)	57 (12)	53 (9)
Follow-up among survivors, Months			
N Eval	891	293	324
Median (Range)	68 (0-196)	48 (0-213)	49 (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	1192	184	89
Source of data			
CRF	269 (23)	43 (23)	18 (20)
TED	923 (77)	141 (77)	71 (80)
Number of centers	54	44	37
Disease at transplant			
AML	417 (35)	60 (33)	31 (35)
ALL	536 (45)	88 (48)	47 (53)
Other leukemia	1 (<1)	0	0
CML	37 (3)	1 (1)	2 (2)
MDS	94 (8)	18 (10)	7 (8)
Other acute leukemia	46 (4)	3 (2)	1 (1)
NHL	49 (4)	12 (7)	1 (1)
Hodgkin Lymphoma	9 (1)	2 (1)	0
MPN	3 (<1)	0	0
AML Disease status at transplant			
CR1	257 (62)	41 (68)	18 (58)
CR2	107 (26)	15 (25)	7 (23)
CR3+	6 (1)	1 (2)	1 (3)
Advanced or active disease	45 (11)	1 (2)	5 (16)
Missing	2 (<1)	2 (3)	0
ALL Disease status at transplant			
CR1	198 (37)	32 (36)	19 (40)
CR2	261 (49)	44 (50)	20 (43)
CR3+	66 (12)	11 (13)	6 (13)
Advanced or active disease	11 (2)	1 (1)	2 (4)
MDS Disease status at transplant			
Early	21 (22)	3 (17)	2 (29)
Advanced	59 (63)	9 (50)	2 (29)
Missing	14 (15)	6 (33)	3 (43)
NHL Disease status at transplant			
CR1	15 (31)	3 (25)	1 (100)
CR2	19 (39)	2 (17)	0
CR3+	2 (4)	0	0

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Advanced	12 (24)	7 (58)	0
Missing	1 (2)	0	0
Recipient age at transplant			
0-9 years	499 (42)	87 (47)	37 (42)
10-17 years	693 (58)	97 (53)	52 (58)
Median (Range)	12 (0-18)	11 (1-18)	11 (1-18)
Recipient race			
White	795 (75)	125 (77)	65 (81)
Black or African American	142 (13)	21 (13)	3 (4)
Asian	58 (5)	9 (6)	6 (8)
Native Hawaiian or other Pacific Islander	6 (1)	3 (2)	1 (1)
American Indian or Alaska Native	16 (2)	2 (1)	1 (1)
More than one race	47 (4)	2 (1)	4 (5)
Unknown	128 (N/A)	22 (N/A)	9 (N/A)
Recipient ethnicity			
Hispanic or Latino	416 (36)	70 (40)	26 (30)
Non Hispanic or non-Latino	723 (62)	103 (58)	57 (66)
Non-resident of the U.S.	23 (2)	4 (2)	3 (3)
Unknown	30 (N/A)	7 (N/A)	3 (N/A)
Recipient sex			
Male	683 (57)	91 (49)	62 (70)
Female	509 (43)	93 (51)	27 (30)
Karnofsky score			
10-80	211 (18)	40 (22)	16 (18)
90-100	950 (80)	138 (75)	69 (78)
Missing	31 (3)	6 (3)	4 (4)
HLA-A B DRB1 groups - low resolution			
<=3/6	326 (30)	48 (30)	19 (28)
4/6	94 (9)	13 (8)	10 (15)
5/6	32 (3)	8 (5)	5 (7)
6/6	618 (58)	89 (56)	34 (50)
Unknown	122 (N/A)	26 (N/A)	21 (N/A)
High-resolution HLA matches available out of 8			
<=5/8	406 (39)	60 (39)	28 (42)
6/8	18 (2)	5 (3)	0
7/8	21 (2)	2 (1)	5 (7)
8/8	609 (58)	87 (56)	34 (51)
Unknown	138 (N/A)	30 (N/A)	22 (N/A)
HLA-DPB1 Match			
Double allele mismatch	1 (<1)	0	0

Variable	Samples Available for Recipient and Donor N (%)	Samples Available for Recipient Only N (%)	Samples Available for Donor Only N (%)
Single allele mismatch	331 (34)	36 (34)	20 (43)
Full allele matched	635 (66)	69 (66)	26 (57)
Unknown	225 (N/A)	79 (N/A)	43 (N/A)
High resolution release score			
No	624 (52)	177 (96)	82 (92)
Yes	568 (48)	7 (4)	7 (8)
Graft type			
Marrow	871 (73)	106 (58)	62 (70)
PBSC	294 (25)	68 (37)	26 (29)
UCB	1 (<1)	8 (4)	0
BM+PBSC	3 (<1)	0	1 (1)
BM+UCB	3 (<1)	2 (1)	0
Others	20 (2)	0	0
Conditioning regimen			
Myeloablative	1104 (93)	174 (95)	81 (91)
RIC/Nonmyeloablative	85 (7)	8 (4)	6 (7)
TBD	3 (<1)	2 (1)	2 (2)
Donor age at donation			
To Be Determined/NA	3 (<1)	2 (1)	0
0-9 years	317 (27)	50 (27)	23 (26)
10-17 years	313 (26)	48 (26)	24 (27)
18-29 years	240 (20)	35 (19)	20 (22)
30-39 years	180 (15)	34 (18)	17 (19)
40-49 years	113 (9)	10 (5)	3 (3)
50+ years	26 (2)	5 (3)	2 (2)
Median (Range)	17 (0-61)	17 (0-61)	17 (1-53)
Donor/Recipient CMV serostatus			
+/+	457 (38)	76 (41)	32 (36)
+/-	136 (11)	14 (8)	12 (13)
-/+	317 (27)	43 (23)	23 (26)
-/-	266 (22)	38 (21)	19 (21)
CB - recipient +	4 (<1)	6 (3)	0
CB - recipient -	0	4 (2)	0
Missing	12 (1)	3 (2)	3 (3)
GvHD Prophylaxis			
No GvHD Prophylaxis	31 (3)	3 (2)	0
TDEPLETION alone	54 (5)	24 (13)	10 (11)
TDEPLETION +- other	25 (2)	6 (3)	1 (1)
CD34 select alone	12 (1)	0	1 (1)
CD34 select +- other	16 (1)	7 (4)	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	352 (30)	33 (18)	23 (26)
FK506 + MMF +- others	93 (8)	10 (5)	3 (3)
FK506 + MTX +- others(not MMF)	346 (29)	49 (27)	23 (26)
FK506 +- others(not MMF,MTX)	2 (<1)	1 (1)	1 (1)
FK506 alone	9 (1)	2 (1)	1 (1)
CSA + MMF +- others(not FK506)	34 (3)	6 (3)	2 (2)
CSA + MTX +- others(not MMF,FK506)	178 (15)	27 (15)	20 (22)
CSA +- others(not FK506,MMF,MTX)	1 (<1)	2 (1)	0
CSA alone	28 (2)	9 (5)	1 (1)
Other GVHD Prophylaxis	4 (<1)	1 (1)	1 (1)
Missing	4 (<1)	3 (2)	0
Donor/Recipient sex match			
Male-Male	393 (33)	47 (26)	33 (37)
Male-Female	239 (20)	46 (25)	14 (16)
Female-Male	287 (24)	39 (21)	29 (33)
Female-Female	269 (23)	42 (23)	13 (15)
CB - recipient M	3 (<1)	5 (3)	0
CB - recipient F	1 (<1)	5 (3)	0
Year of transplant			
2006-2010	31 (3)	3 (2)	4 (4)
2011-2015	262 (22)	33 (18)	21 (24)
2016-2020	549 (46)	88 (48)	34 (38)
2021-2023	350 (29)	60 (33)	30 (34)
Follow-up among survivors, Months			
N Eval	915	146	58
Median (Range)	24 (0-142)	18 (0-147)	14 (0-122)

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CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH

TO: Pediatric Cancer Working Committee Members

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

RE: Studies in Progress Summary

PC19-02: Does mixed peripheral blood T Cell Chimerism predict relapse? (S Prockop/ J Boelens/ K Peggs). The objectives of this study include determining the incidence of persistence of host T-cells after transplant for non-T cell malignant diseases in pediatric patients. Other study objectives include exploring whether the incidence of relapse is higher in patients with persistence of host T cell populations and determining whether reactivation of CMV in patients who were CMV seropositive prior to transplant influence the incidence of host T cells after transplant.
The study protocol is being developed with particular focus on reviewing chimerism data and categorizing chimerism based on the data and timepoints available. The goal is to have the data file prepared for analysis by August 2024.

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 post-transplant outcomes, including overall survival and disease-free survival. This study is currently in analysis. The study protocol was recently updated, and years expanded to include more recent data and disease characteristics like the pediatric DRI. The goal is to have the analysis completed by April 2024 with a subsequent manuscript prepared by January 2025.

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 CIBMTR data file was sent in October 2023 and genotyping results of samples are in process. Study analysis will be finalized once sample testing is completed.

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 acute Graft Versus Host Disease (aGVHD) and chronic GVHD 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 paediatric DRI classification.

The study protocol is being developed. The goal is to finalize the protocol and begin data analysis by August 2024.

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. To 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.

The study protocol is being developed, an approach to data linkage being evaluated, and data use agreement being developed. Finalization of the protocol is pending the Data Use Agreement between CIBMTR and COG. The goal is to finalize the protocol and begin merging data by August 2024.

PC23-01: Post-transplant cyclophosphamide vs. TCR αβ/CD19+ deplete approaches for haploidentical transplant in pediatric patients with acute leukemias and myelodysplastic syndrome (A Li/ H Rangarajan/ P Satwani). The primary objective of this study is to compare post-transplant cyclophosphamide and alpha-beta T-Cell depletion for Haploidentical donors who receive allo HCT for ALL and AML. This is a collaborative study with EBMT and has been approved by the Pediatric Diseases Working Party, pending final numbers of each treatment group. The protocol has been in development with both CIBMTR and EBMT input. PCWC sent queries to retrieve TCR αβ data from centers. The goal is to finalize the protocol and share CIBMTR data with EBMT by August 2024.

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 objective of this study is to evaluate graft source (BM versus PBSC) in haploidentical transplants using post-transplant cyclophosphamide. The study protocol is being developed and using a previously available dataset. The goal is to finalize the protocol and begin data analysis by March 2024.

SC21-08: Optimizing Haploidentical Donor Selection for Pediatric HCT (N Liberio/ L Broglie). The primary objective of this study is to determine the effect of donor age and donor relationship on the outcomes of related Haploidentical HCT. Outcomes include acute and chronic GVHD, relapse, graft failure, and overall survival. This study is being performed by a pediatric hematology/oncology fellow at the Medical College of Wisconsin as part of a Master's Degree Thesis and is supported by additional funding. This study falls outside traditional working committee practices but is of interest to the pediatric community. The results were presented at last year's PCWC meeting, EBMT, and ASPHO in 2023. The study is in manuscript preparation, the goal is to publish the manuscript by June 2024.

Field	Response
Proposal Number	2310-60-APPELL
Proposal Title	Transplantation and Cellular Therapy for Children and Young Adults with Down's Syndrome and Acute Leukemia
Key Words	Down syndrome, pediatric oncology, AYA, acute leukemia
Principal Investigator #1: - First and last name, degree(s)	Lauren Appell, MD
Principal Investigator #1: - Email address	leappell@uams.edu
Principal Investigator #1: - Institution name	Arkansas 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):	Seth Rotz, MD
Principal Investigator #2 (If applicable): - Email address:)	rotzs@ccf.org
Principal Investigator #2 (If applicable): - Institution name:	Cleveland Clinic Foundation
Principal Investigator #2 (If applicable): - Academic rank:	Assistant professor
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:	Lauren Appell
Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.	Ana Alarcon Tomas, MD, Lauren E. Appell, MD, Evandro Bezerra, MD, Lohith Gowda, MD, Yi Lin MD, PhD, Miguel Perales, MD, Akshay Sharma, MBBS, Abu-Sayeef Mirza, MD, Guru Subramanian Guru Murthy, MD. CD19-CAR-T cell therapy failure: Impact of subsequent therapy in patients with B-cell malignancies. -Lauren Appell role: co-investigator
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:	Akshay Sharma, Larissa Broglie

Field	Response
RESEARCH QUESTION:	In the current era of cellular therapy, what are the implications (overall response rate, overall survival, event free survival, and toxicities) of cellular therapy and the need for bone marrow transplant in children and young adults with Down syndrome and acute leukemia?
RESEARCH HYPOTHESIS:	We hypothesize 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, we hypothesize 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.
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	Primary Objective 1: Determine if outcomes for children and AYA with DS and acute leukemia (ALL and AML) undergoing HCT have improved in more recent eras. Primary Objective 2: Compare outcomes of CAR T-cell therapy for children and AYA with DS and relapsed/refractory ALL to HCT. Secondary Objective 1: Describe the overall response rate, overall survival, and toxicities of CAR T-cell therapy for children and AYA with DS and relapsed/refractory 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.	No consensus guidelines exist for the treatment of children and AYA patients with DS and relapsed/refractory acute leukemia. Previous data has suggested a high burden of both transplant related mortality and relapse for DS patients, and poor outcomes compared to patients without DS.(Hitzler, et al 2013, Hitzler, et al 2014, Rubin, et al 1996) With improved supportive care approaches and additional attention to minimal residual disease in more recent eras, these outcomes may have improved, however they have not been recently studied. Better understanding of the risks and benefits of HCT in this population may help improve clinical decision making and counseling of patients and families. CAR T-cell therapy has significantly altered the treatment landscape for children and AYA with relapsed/ refractory ALL. Although overall response rates are quite favorable, many patients will eventually relapse or require HCT.(Pasquini, et al 2020) Given the poor outcomes of HCT for DS ALL, CAR T-cell therapy is an attractive alternative. More recently, a small number of DS-ALL patients enrolled in CAR T-cell clinical trials were analyzed, and results appeared similar to patients without DS.(Laetsch, et al 2022) However, follow-up was limited in these patients. More clearly understanding the outcomes of patients with DS ALL undergoing CAR T-cell therapies including acute toxicities, risk of relapse, and necessity to proceed to HCT will help inform clinicians about the optimal treatment approach for these patients.

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.	Historical outcomes for patients with DS and ALL undergoing HCT are dismal. The CIBMTR previously reported a 3-year disease free survival of 24% among children and AYA patients with DS ALL undergoing HCT from 2000-2009.(Hitzler, et al 2014) When children with DS ALL receive upfront conventional chemotherapy, much attention is paid to the increased risk of treatment related mortality. However, a previous analysis from the CIBMTR demonstrated relapse post-HCT was a more common cause of treatment failure than transplant toxicity.(Hitzler, et al 2014) A smaller study from Germany and Austria also demonstrated similar findings.(Meissner, et al 2007) The CIBMTR has also previously reported on outcomes of children with DS Acute Myeloid Leukemia (AML).(Hitzler, et al 2013) Unfortunately, like their counterparts with ALL, children with DS AML undergoing HCT also have very poor outcomes with a 3-year overall survival of 19%. In contrast to patients with ALL, the previous CIBMTR report indicated both relapse and transplant toxicity were major drivers of poor outcomes. A study from Japan also demonstrated similar findings with only 2/8 patients with relapsed/refractory DS AML surviving long-term post-HCT.(Taga, et al 2012) However, given improved supportive care and closer attention to MRD status since these publications, it is unknown if outcomes for patients with DS and acute leukemia have improved in more recent years, and if HCT should be routinely considered in this population. Further, it remains unclear if relapse or treatment related mortality is the biggest risk for patients with DS undergoing HCT, and determining if conditioning intensity or use of TBI impacts outcomes is critical. For patients with relapsed refractory DS ALL, cellular therapy is a promising approach to improve outcomes.,, Laetsch, et al 2022) In the phase II multicenter study of tisagenlecleucel, 6 patients with DS ALL were included, but outcomes for this specific group were not specifically analyzed.(Maude, et al 2018) As of January, 2020 the CIBMTR reported on 13 patients with DS ALL who underwent CAR T-Cell therapy, noting a 100% overall response rate and 100% 6-month overall survival.(Pasquini, et al 2020) A more recent evaluation of 16 DS patients enrolled in 3 clinical trials investigating the utility of CAR T-cell therapy for DS-ALL patients showed high remission rates, manageable toxicity profile, but still with high rates of relapse.(Laetsch, et al 2022) However, longer-term follow-up, duration of response, and use of subsequent HCT for these patients was not reported. Given the optimistic early reports, many additional patients with DS ALL may have

Field	Response
	undergone CAR-T therapies since these publications. Recently, next-generation sequencing of minimal residual disease and loss of B-cell aplasia post-CAR T-cell therapy has been shown to predict relapse (Pulsipher, et al. 2022). Many centers are closely monitoring these tests and opting to perform consolidative HCT based on concerning findings, although if this approach is likely to improve outcomes is not yet known and is the subject of ongoing investigation (NCT05621291). Given the historically poor outcomes of HCT for patients with DS, if this approach is feasible for this population is unclear. The opportunity to specifically study outcomes of cellular therapy in DS ALL will allow for a better understanding the longer-term outcomes of these patients, and help clinicians better understand the risk/benefits of using cellular therapy vs. HCT in this patient population.
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	Age: <40 years (at the time of HCT) Underlying Characteristics: Only patients with Down's syndrome Disease: ALL, AML Disease stage/status at transplant: Any Year of Transplant: 2000-present Transplant Type: Allogeneic, Cellular therapy
Does this study include pediatric patients?	Yes

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.	Outcome Variables All patients: • Overall survival (shorter duration will be the focus for CAR-T outcomes, and longer duration for HCT) • Event free survival • Treatment related mortality • Day +100 survival • Relapse (cumulative incidence) Outcome Variables Cellular-Therapy patients: • CRS • Neurotoxicity (ICANS) • Underwent subsequent HCT • Overall response rate Variables to be described Patient and Disease Variables • Patient age – continuous • Patient sex: male vs. female • Performance score (Lansky/ Karnofsky) • Year HCT was performed (prior to 2010, 2010 and later) • Disease: AML v. ALL • Disease status prior to transplant/cell therapy (CR1, CR2, CR3, less than CR) HCT-related • Conditioning intensity: RIC v. MAC • Conditioning regimen: Total body irradiation (TBI) vs no TBI • Stem cell source: Bone marrow vs. Peripheral blood vs. Cord Blood • Donor Type • aGVHD • cGVHD •prior CAR-T therapies Cellular Therapy-Related • prior HCT • prior blinatumomab • MRD status
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 desc	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 o	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.	We have had preliminary discussions with EBMT regarding the feasibility of a combined dataset, although no definitive plans or commitments have been made.

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Field	Response
	toxicity and outcome. Bone Marrow Transplant, 18, 533-540. 9. Taga, T., Saito, A.M., Kudo, K., Tomizawa, D., Terui, K., Moritake, H., Kinoshita, A., Iwamoto, S., Nakayama, H., Takahashi, H., Tawa, A., Shimada, A., Taki, T., Kigasawa, H., Koh, K. & Adachi, S. (2012) Clinical characteristics and outcome of refractory/relapsed myeloid leukemia in children with Down syndrome. Blood, 120, 1810-1815.
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

Table 1. Characteristics of Children and Young Adults with Down's Syndrome who underwent HCT or CT for Acute Leukemia between 2000 and 2022

Characteristic	AML	ALL HCT only	ALL CART+/- HCT	Total
No. of patients	57	66	53	176
No. of centers	32	40	30	73
Patient age at HCT- median (min-max)	3.2 (1.4-31.7)	12.1 (4.0-39.3)	12.7 (3.5-26.9)	9.5 (1.4-39.3)
Receipt age, groups - no. (%)				
0-4	44 (77.2)	6 (9.1)	1 (1.9)	51 (29.0)
5-9	6 (10.5)	21 (31.8)	16 (30.2)	43 (24.4)
10-17	2 (3.5)	20 (30.3)	29 (54.7)	51 (29.0)
18-24	1 (1.8)	8 (12.1)	6 (11.3)	15 (8.5)
25-39	4 (7.0)	11 (16.7)	1 (1.9)	16 (9.1)
Sex of recipient - no. (%)				
Male	31 (54.4)	41 (62.1)	27 (50.9)	99 (56.3)
Female	26 (45.6)	25 (37.9)	26 (49.1)	77 (43.8)
Conditioning intensity - no. (%)				
Myeloablative	47 (82.5)	53 (80.3)	15 (28.3)	115 (65.3)
RIC/NMA	7 (12.3)	12 (18.2)	1 (1.9)	20 (11.4)
TBD /Not reported	3 (5.3)	1 (1.5)	0 (0.0)	4 (2.2)
Not applicable-CT	0 (0.0)	0 (0.0)	37 (69.8)	37 (21.1)
Graft type - no. (%)				
Bone marrow	23 (40.4)	29 (43.9)	10 (18.9)	62 (35.2)
Peripheral blood	12 (21.1)	23 (34.8)	6 (11.3)	41 (23.3)
Umbilical cord blood	22 (38.6)	14 (21.2)	0 (0.0)	36 (20.5)
Not applicable-CT	0 (0.0)	0 (0.0)	37 (69.8)	37 (21.0)
Donor type - no. (%)				
HLA-identical sibling	9 (15.8)	23 (34.8)	5 (9.4)	37 (21.0)
Other related	8 (14.0)	12 (18.2)	6 (11.3)	26 (14.8)

Characteristic	AML	ALL HCT only	ALL CART+/- HCT	Total
Well-matched unrelated (8/8)	11 (19.3)	12 (18.2)	4 (7.5)	27 (15.3)
Partially-matched unrelated (7/8)	3 (5.3)	2 (3.0)	1 (1.9)	6 (3.4)
Mis-matched unrelated (<= 6/8)	3 (5.3)	1 (1.5)	0 (0.0)	4 (2.3)
Unrelated (matching TBD)	1 (1.8)	2 (3.0)	0 (0.0)	3 (1.7)
Cord blood	22 (38.6)	14 (21.2)	0 (0.0)	36 (20.5)
Autologous -CT	0 (0.0)	0 (0.0)	37 (69.8)	37 (21.0)
Types of prior HCTs - no. (%)				
No prior HCT	0 (0.0)	0 (0.0)	51 (96.2)	51 (29.0)
Prior allo-HCT	0 (0.0)	0 (0.0)	2 (3.8)	2 (1.1)
Not applicable/HCT	57 (100)	66 (100)	0 (0.0)	123 (69.9)
Transplant year, groups - no. (%)				
2000-2010	29 (50.9)	28 (42.4)	0 (0.0)	57 (32.4)
2011-2022	28 (49.1)	38 (57.6)	53 (100)	119 (67.6)
Transplant year - no. (%)				
2000	1 (1.8)	1 (1.5)	0 (0.0)	2 (1.1)
2001	4 (7.0)	3 (4.5)	0 (0.0)	7 (4.0)
2002	2 (3.5)	1 (1.5)	0 (0.0)	3 (1.7)
2003	3 (5.3)	1 (1.5)	0 (0.0)	4 (2.3)
2004	2 (3.5)	2 (3.0)	0 (0.0)	4 (2.3)
2005	3 (5.3)	1 (1.5)	0 (0.0)	4 (2.3)
2006	1 (1.8)	4 (6.1)	0 (0.0)	5 (2.8)
2007	3 (5.3)	0 (0.0)	0 (0.0)	3 (1.7)
2008	2 (3.5)	6 (9.1)	0 (0.0)	8 (4.5)
2009	5 (8.8)	8 (12.1)	0 (0.0)	13 (7.4)
2010	3 (5.3)	1 (1.5)	0 (0.0)	4 (2.3)
2012	0 (0.0)	2 (3.0)	0 (0.0)	2 (1.1)
2013	4 (7.0)	0 (0.0)	0 (0.0)	4 (2.3)
2014	1 (1.8)	3 (4.5)	0 (0.0)	4 (2.3)

Characteristic	AML	ALL HCT only	ALL CART+/- HCT	Total
2015	2 (3.5)	1 (1.5)	0 (0.0)	3 (1.7)
2016	4 (7.0)	0 (0.0)	0 (0.0)	4 (2.3)
2017	5 (8.8)	6 (9.1)	0 (0.0)	11 (6.3)
2018	1 (1.8)	2 (3.0)	7 (13.2)	10 (5.7)
2019	2 (3.5)	5 (7.6)	12 (22.6)	19 (10.8)
2020	3 (5.3)	5 (7.6)	12 (22.6)	20 (11.4)
2021	0 (0.0)	3 (4.5)	12 (22.6)	15 (8.5)
2022	6 (10.5)	11 (16.7)	10 (18.9)	27 (15.3)
Indicator of HCT cases in CRF retrieval - no. (%)				
No	18 (31.6)	26 (39.4)	12 (22.6)	56 (31.8)
Yes	39 (68.4)	40 (60.6)	4 (7.5)	83 (47.2)
Not applicable-CT	0 (0.0)	0 (0.0)	37 (69.8)	37 (21.0)

Data source: January 2022 CRF
October 2023 CT
January 2022 TED
October 2023 HCT-Essentials
Embargo and consent criteria are applied

Field	Response
Proposal Number	2310-91-SHARMA
Proposal Title	Evaluation of Allogeneic Hematopoietic Cell Transplantation Outcomes and Prognostic Factors in Acute Megakaryoblastic Leukemia: A CIBMTR and EBMT Joint Study
Key Words	Allogeneic Hematopoietic Cell Transplantation, Acute Megakaryoblastic Leukemia
Principal Investigator #1: - First and last name, degree(s)	Akshay Sharma, MBBS, MSc
Principal Investigator #1: - Email address	akshay.sharma@stjude.org
Principal Investigator #1: - Institution name	St. Jude Children's Research Hospital, Memphis, TN
Principal Investigator #1: - Academic rank	Assistant Member
Junior investigator status (defined as ≤5 years from fellowship)	No
Do you identify as an underrepresented/minority?	Yes
Principal Investigator #2 (If applicable): - First and last name, degree(s):	Neel S. Bhatt, MBBS, MPH
Principal Investigator #2 (If applicable): - Email address:)	nbhatt@fredhutch.org
Principal Investigator #2 (If applicable): - Institution name:	Fred Hutchinson Cancer Research Center, Seattle, WA
Principal Investigator #2 (If applicable): - Academic rank:	Assistant Professor
Junior investigator status (defined as ≤5 years from fellowship)	Yes
Do you identify as an underrepresented/minority?	Yes
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:	Akshay Sharma, MBBS (akshay.sharma@stjude.org)
Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.	Akshay is co-chair of the PCWC and has several ongoing and completed projects with the CIBMTR.
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
RESEARCH QUESTION:	We would like to evaluate the outcomes after allogeneic hematopoietic cell transplantation in pediatric patients with acute megakaryoblastic leukemia (AMKL) in a combined cohort of CIBMTR and EBMT.

Field	Response
RESEARCH HYPOTHESIS:	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.
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	To determine the outcomes (OS, DFS, NRM, Relapse) of allo-HCT in AMKL patients and identify prognostic factors associated with improved outcomes. To determine the effect of remission status (first remission, second remission, progressive/refractory disease) on outcomes (OS, DFS, NRM, Relapse) in patients receiving allo-HSCT for AMKL. To determine the outcomes in AMKL utilizing alternative donor sources and compare them to traditional matched-related donor transplants.
SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.	Acute megakaryoblastic leukemia (AMKL) has a bimodal age distribution with peaks in early childhood (younger than 3 years) and in adulthood.(1) AMKL comprises of approximately 1% of all AML cases in adults and about 10% of all AML cases in children.(2, 3) Children with Down syndrome have a much higher incidence of AMKL, but also have a more favorable prognosis compared to children without AMKL.(4) By understanding factors that are associated with improved outcomes after all0-HSCT for this rare leukemia, we can identify patients who are going to benefit the most from allo-HSCT and develop better treatment algorithms.

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.	AMKL is a rare subtype of acute myeloid leukemia with dismal outcomes.(2, 5-7) Even though approximately half the patients with de novo AMKL achieve complete remission (CR) with conventional chemotherapy, 5-year event-free survival in non-Down syndrome children is only 14-49% and has not improved much in the last few decades.(2, 7-10) Median survival in adults with AMKL is even worse at less than 12 months.(11) Allogeneic hematopoietic stem cell transplantation (allo-HCT) has been suggested to improve outcomes in patients with AMKL, but the available literature is scant and inconsistent.(9, 12) A large study from the European Group for Blood and Marrow Transplantation (EBMT) suggested that allo-HCT in CR1 improves survival (3 year OS 82% in children and 43% in adults). (5) A recent single center analysis performed at our institution of 44 pediatric patients who underwent their first allo-HCT for AMKL between 1986 and 2016 revealed that AMKL continues to have poor outcomes after allo-HCT due a high rate of relapse in the first year post-transplant (3 year OS 34.1%). Two factors which were independently associated with improved OS and less cumulative incidence of relapse after allo-HCT for AMKL were being in CR at the time of transplant (Hazard Ratio=0.4, P=0.02) and non-Hispanic Caucasian race (Hazard Ratio=0.3, P=0.005). Since AMKL is a rare disease, there is limited data on transplant outcomes in this population. A large analysis utilizing the CIBMTR database will allow the transplant community to clearly define the outcomes of allo-HCT in patients with AMKL, identify prognostic markers for improved outcomes, and help to elucidate the utility of both alternative (haploidentical and cord blood) donors against the standard matched-donor transplants. Such an assessment of favorable prognostic factors will help identify patients who have better outcomes with HCT and hence will guide clinicians to recommend HCT to that subset of patients earlier leading to improved overall outcomes.
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	All pediatric patients who underwent allo-HSCT for AMKL reported to the CIBMTR and EBMT between years 2010 and 2022. CIBMTR cohort has about 250 patients who meet this inclusion criteria, half of which have CRF level data. EBMT cohort has another 300 patients who meet this inclusion criteria (personal communication to Akshay Sharma from Jacques-Emmanuel Galimard)
Does this study include pediatric patients?	Yes

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.	This proposed study will require no supplemental data to be collected. The current data is included in the CIBMTR collection forms for Pre-HSCT and Post-HSCT Acute Myelogenous Leukemia. EBMT PDWP Chair Krzysztof Kalwak has already agreed to collaborate on this study and has provided the following details about the number of patients and data available. This study is a retrospective registry analysis of all pediatric patients who received HCT for AMKL between January 2010 and December 2022. CIBMTR cohort has about 250 patients who meet this inclusion criteria, half of which have CRF level data. EBMT cohort has another 300 patients who meet this inclusion criteria (personal communication to Akshay Sharma from Jacques-Emmanuel Galimard). Baseline characteristics and known prognostic variables will be collected from CIBMTR database forms. These characteristics will include: age, sex, de novo or Down's syndrome related, Karnofsky/ Lansky performance status, presence of extra-medullary disease at diagnosis (including CNS), WBC at diagnosis, immune-phenotype at diagnosis, number of prior chemotherapy regimens if available, time from diagnosis to transplant, remission status at transplant (first remission, second or higher remission, progressive/refractory disease), conditioning therapy (chemotherapy-based or total body irradiation based, including chemotherapy type and TBI dose), GvHD prophylactic regimen, use of anti-thymocyte globulin, T-cell depletion of the graft, presence of minimal residual disease prior to transplant (molecular data or flow cytometry data) if available, donor source (peripheral blood, cord, bone marrow), transplant type (haploidentical, 1 or 2 HLA-antigen mismatch unrelated donor, MUD, HLA-identical sibling donor, cord blood), and cytogenetics at diagnosis if available. Transplant outcomes (OS, PFS, cumulative incidence (CI) NRM, and CI Relapse) will be evaluated for all patients, patients in CR1, second remission and greater (CR2+), and those with progressive/refractory disease. Additionally, transplant outcomes will be evaluated for patients receiving haploidentical or cord-Blood transplantation versus matched unrelated donor and matched related donor transplantation. Median overall survival, and progression-free survival will be calculated utilizing Kaplan-Meier analysis and compared utilizing the log-rank test. Cumulative incidences of NRM, Relapse, and GVHD (chronic and acute) will be performed utilizing the cumulative incidence procedure to account for competing risks, and comparison will be performed utilizing the Fine-Gray test. Differences between groups will be evaluated utilizing the Chi-squared test or Fisher's exact test for categorical variables, two-sample test for proportions, or the Wilcoxon rank sum test for

Field	Response
	medians. For cumulative incidence, the Fine-Gray analysis will be utilized to compare variables with competing risks. Outcomes will be compared between patients in CR1, CR2+, and no-remission/refractory disease. TBI-based conditioning will be compared to chemotherapy based conditioning. Haploidentical/cord blood transplant will be compared to matched-donor transplants normalized for preHCT risk factors. Prognostic variables will be evaluated for their impact on OS, DFS, NRM and Relapse utilizing univariate analysis and multivariate analysis by cox proportional hazards analysis.
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 desc	NA
MACHINE LEARNING: Please indicate if the study requires methodology related to machine-learning and clinical predictions.	NA
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.	EBMT PDWP Chair Krzysztof Kalwak has already agreed to collaborate on this study and EBMT statistician Jacques-Emmanuel Galimard has provided the following details about the number of patients and data available. On the period 2010-2020 there are 295 patients receiving a first allo as child. 170 transplanted in CR1, 33 in CR2, 3 in CR3, 5 in CR but the number is missing, 44 in active disease and 16 missing Cytogenetic ELN classification: 7 good risk, 111 intermediate (including 62 normal Kayotype) and 72 poor (80 missing cytogenetics) 1 secondary AML 61 MSD, 2 syngeneic,7 MOR, 46 haplos, 3 mismatched relative not confirmed as haplo, 2 mismatched relative with 1 mismatch, 66 UD10/10, 17 UD9/10, 16 UD missing HLA, 2 CB relative and 45 unrelated CB (finally 3 missing donor type). 7 TBI based HSCT Median age at HSCT 2.2 [Q1=1.5; Q3=3.5] (min=0.3 max=16.2)

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Field	Response
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

Table 1. Characteristics of Children and Young Adults who underwent HCT for AMKL between 2010 and 2022

Characteristic	N (%)
No. of patients	273
No. of centers	95
Patient age - median (min-max)	2.3 (0.5-20.7)
Receipt age, groups - no. (%)	
0-4	235 (86.1)
5-9	16 (5.9)
10-17	16 (5.9)
18-21	6 (2.2)
Sex of recipient - no. (%)	
Male	135 (49.5)
Female	138 (50.5)
Status at Transplantation: (2400 Q181) - no. (%)	
Primary induction failure	24 (8.8)
1st complete remission	190 (69.6)
2nd complete remission	42 (15.4)
1st relapse	16 (5.9)
2nd relapse	1 (0.4)
Conditioning intensity - no. (%)	
Myeloablative	263 (96.3)
RIC/NMA	10 (3.7)
Graft type - no. (%)	
Bone marrow	134 (49.1)
Peripheral blood	55 (20.1)
Umbilical cord blood	84 (30.8)
GVHD prophylaxis - no. (%)	
None	1 (0.4)
Ex-vivo T-cell depletion	14 (5.1)
CD34 selection	6 (2.2)
PtCy + other(s)	27 (9.9)
TAC + MMF +- other(s) (except PtCy)	26 (9.5)
TAC + MTX +- other(s) (except MMF, PtCy)	59 (21.6)
TAC + other(s) (except MMF, MTX, PtCy)	3 (1.1)
TAC alone	4 (1.5)
CSA + MMF +- other(s) (except PtCy,TAC)	52 (19.0)
CSA + MTX +- other(s) (except PtCy,TAC,MMF)	61 (22.3)

Characteristic	N (%)
CSA + other(s) (except PtCy,TAC,MMF,MTX)	7 (2.6)
CSA alone	9 (3.3)
Other(s)	2 (0.7)
Missing	2 (0.7)
Donor type - no. (%)	
HLA-identical sibling	54 (19.8)
Other related	45 (16.5)
Well-matched unrelated (8/8)	57 (20.9)
Partially-matched unrelated (7/8)	16 (5.9)
Mis-matched unrelated (<= 6/8)	2 (0.7)
Unrelated (matching TBD)	13 (4.8)
Cord blood	84 (30.8)
Not reported	2 (0.7)
Transplant year - no. (%)	
2010	15 (5.5)
2011	31 (11.4)
2012	28 (10.3)
2013	25 (9.2)
2014	20 (7.3)
2015	21 (7.7)
2016	27 (9.9)
2017	22 (8.1)
2018	13 (4.8)
2019	16 (5.9)
2020	22 (8.1)
2021	15 (5.5)
2022	18 (6.6)
Indicator of HCT cases in CRF retrieval - no. (%)	
No	192 (70.3)
Yes	81 (29.7)

Data source: January 2022 CRF January 2022 TED
October 2023 HCT-Essentials
Embargo and consent criteria are applied

Field	Response
Proposal Number	2310-106-KRIEGER
Proposal Title	Influence of Pre-Transplant Chemotherapy Cycles on Allogeneic Transplant Outcomes in Pediatric Acute Myeloid Leukemia Patients in Complete Remission
Key Words	AML, Allogeneic Transplant, Pediatric
Principal Investigator #1: - First and last name, degree(s)	Elizabeth Krieger
Principal Investigator #1: - Email address	Elizabeth.krieger@vcuhealth.org
Principal Investigator #1: - Institution name	Virginia Commonwealth 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):	Alex Hoover
Principal Investigator #2 (If applicable): - Email address:)	hoove231@umn.edu
Principal Investigator #2 (If applicable): - Institution name:	University of Minnesota
Principal Investigator #2 (If applicable): - Academic rank:	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:	Elizabeth krieger
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:	Akshay Sharma

Field	Response
RESEARCH QUESTION:	Hematopoietic stem cell transplantation (HSCT) offers a potential curative approach for pediatric patients diagnosed with high-risk Acute Myeloid Leukemia (AML). HCT is often recommended for these patients as a consolidation modality following initial treatment while the patients are in remission. However, the optimal number of pre-transplant chemotherapy cycles that the patients should receive prior to HCT is unknown. On one hand, it is believed that patients in deeper remission prior to undergoing consolidative HCT likely have better chance of durable post-HCT remission, advocating for multiple cycles of chemotherapy. But on the other hand, additional chemotherapy cycles also add to the pre-HCT comorbidities which add to transplant related morbidity and mortality, advocating against them. Thus a pivotal query remains: In pediatric AML patients who attain CR1, does a reduction in the number of chemotherapy cycles prior to HCT enhance post-transplant outcomes?
RESEARCH HYPOTHESIS:	We hypothesize 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.
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	The objective of this study is to evaluate overall survival (OS), leukemia free survival (LFS), relapse incidence (RI) and treatment related mortality (TRM) for pediatric patients with high-risk AML who underwent allo-HCT in CR1 comparing outcomes after differing number of pre-HCT chemotherapy cycles.
SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.	Allogeneic hematopoietic stem cell transplant (HSCT) is a curative therapy for pediatric patients with high-risk AML. However optimal timing of transplant, particularly the number of cycles of induction and intensification therapy prior to HSCT is not delineated. On one hand, it is believed that patients in deeper remission prior to undergoing consolidative HCT likely have better chance of durable post-HCT remission, advocating for multiple cycles of chemotherapy. But on the other hand, additional chemotherapy cycles also add to the pre-HCT comorbidities which add to transplant related morbidity and mortality, advocating against them. In individuals who achieve complete remission, is there an advantage to them receiving additional cycles of chemotherapy? We wish to address that question through this study.

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 (HSCT) has long been recognized as a curative treatment for pediatric patients with high-risk Acute Myeloid Leukemia (AML). Currently, the predominant therapeutic regimen recommended by collaborative pediatric AML clinical trials involves two intensive induction courses followed by one cycle of intensification chemotherapy for high-risk patients prior to transplant regardless of when CR is achieved(NCT04293562). This paradigm has largely been driven by historical outcomes. Yet, with advancements in medical science that now incorporate MRD data and extended cytogenetic risk, there's a growing question to challenge and refine the traditionally accepted approach(Masetti, Muratore et al. 2022). For patients who attain CR1 after first induction, it is unknown if there is a tangible benefit in subjecting patients to additional chemotherapy cycles? Intriguingly, a contemporary adult study conducted by the CIBMTR delved into an analogous question. Their findings indicated that patients who underwent only a single induction cycle to achieve CR, as opposed to multiple cycles, exhibited enhanced overall survival (OS after 1 vs 2 cycles HR 1.32, p < 0.01, ≥3 cycles HR 1.47, p < 0.01). Additionally, for the subset of patients who achieved CR1 after induction 1, consolidation therapy before MAC allo-HCT was positively correlated with better OS (HR 1.57, p < 0.01) compared to those who bypassed consolidation therapy(Boyiadzis, Zhang et al. 2023). It must be noted that the inclination to move to intensification after first induction is more pronounced in adult care setting than in pediatric studies given differences in risk stratification and treatment protocols. Moreover, recent retrospective findings, suggest that in the context of pediatric AML, a shorter time span leading up to HCT doesn't necessarily bolster benefits for patients undergoing transplantation in CR1(Murphy, Miller et al. 2023). Amidst these nuances, there exists a knowledge gap in identifying the ideal chemotherapy regimen before allo-HSCT for pediatric AML patients. Thus, it becomes imperative to design a study that leverages the comprehensive data from the CIBMTR registry, aiming to glean deeper insights into these clinical paradigms. By comprehensively analyzing these parameters, the study would offer a more definitive perspective on optimal preparatory chemotherapy cycles before transplant. This could significantly shape future therapeutic regimens, ensuring pediatric patients receive the most effective, evidence-based care.

Field	Response
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	Inclusion Criteria: - Diseases: AML -First Allo transplant - Donor: HLA-matched sibling, haplo-, unrelated donors, cord blood - Age 0-18 Exclusion Criteria: - Any previous Transplant - Secondary Leukemia
Does this study include pediatric patients?	Yes
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.	Outcome variables: - Overall survival and time to death after HCT - Leukemia free survival after HCT - Time to relapse after HCT - Incidence of grade II-IV GVH following HCT - Non-relapse mortality after HCT - Primary cause of death Variables to be described and/or analyzed Patient-related - Patient age at transplant - Patient gender: male vs. female - Patient race/ethnicity -Karnofsky/Lansky performance score - Year of transplant Disease-related - Number of chemotherapy cycles prior to HCT (ie Induction 1, Induction 2, Consolidation 1 ext.) - Disease: AML - Extramedullary involvement: Yes vs. No - Primary Induction Failure: defined as failure to achieve CR1 after induction 2 - Time to CR1 cont variable - Chemo cycles prior to CR1 - Time between diagnosis and HCT: as a continuous variable - Number of cycles of chemotherapy required to achieve MRD -(may not be available) - MRD at the time of transplant - MRD value at the time of CR1 (may not be available) - Cytogenetics Transplant-related - Conditioning regimen: myeloablative (MAC) versus reduced intensity (RIC) - Donor type/HLA matching - Stem cell source: Bone marrow vs. Peripheral blood vs. Cord blood - Donor Age - Conditioning Regimen
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 desc	None
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 o	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:	Zeller and H. Hasle (2011). "Response-guided induction therapy in pediatric acute myeloid leukemia with excellent remission rate." Journal of Clinical Oncology 29(3): 310-315. Boyiadzis, M., M.-J. Zhang, K. Chen, H. Abdel-Azim, M. B. Abid, M. Aljurf, U. Bacher, T. Badar, S. M. Badawy and M. Battiwalla (2023). "Impact of pre-transplant induction and consolidation cycles on AML allogeneic transplant outcomes: a CIBMTR analysis in 3113 AML patients." Leukemia 37(5): 1006-1017. Masetti, R., E. Muratore, D. Gori, A. Prete and F. Locatelli (2022). "Allogeneic hematopoietic stem cell transplantation for pediatric acute myeloid leukemia in first complete remission: a meta-analysis." Annals of Hematology 101(11): 2497-2506. Murphy, L. A., K. Miller, A. C. Winters, A. R. Franklin, M. R. Verneris and A. K. Keating (2023). "Time to transplantation and pediatric acute myeloid leukemia outcomes." Bone Marrow Transplantation 58(3): 343-345.
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

Table 1. Characteristics of pediatric patients who underwent first Allo HCT for AML in Complete Remission between 2014 and 2021

Characteristic	N (%)
No. of patients	2174
No. of centers	192
Patient age at HCT - median (min-max)	9.8 (0.3-19.0)
Time from diagnosis to HCT, months- median (min-max)	5.2 (0.0-151.1)
Sex of recipient - no. (%)	
Male	1217 (56.0)
Female	957 (44.0)
Conditioning intensity - no. (%)	
Myeloablative	2094 (96.3)
RIC/NMA	80 (3.7)
Conditioning regimen - no. (%)	
TBI/Cy	68 (3.1)
TBI/Cy/Flu	111 (5.1)
TBI/Cy/Flu/TT	9 (0.4)
TBI/Cy/TT	21 (1.0)
TBI/Cy/VP	2 (0.1)
TBI/VP	7 (0.3)
TBI/Mel	12 (0.6)
TBI/Flu	114 (5.2)
TBI/other(s)	6 (0.3)
Bu/Cy/Mel	89 (4.1)
Bu/Cy	811 (37.3)
Bu/Mel	112 (5.2)
Flu/Bu/TT	161 (7.4)
Flu/Bu	472 (21.7)
Flu/Mel/TT	74 (3.4)
Flu/Mel	26 (1.2)
Cy/Flu	1 (0.0)
Cy alone	3 (0.1)
Mel/other(s)	12 (0.6)
Treosulfan	45 (2.1)
Other(s)	18 (0.8)
Donor type - no. (%)	
HLA-identical sibling	517 (23.8)
Other related	503 (23.1)
Well-matched unrelated (8/8)	541 (24.9)
Partially-matched unrelated (7/8)	149 (6.9)

Characteristic	N (%)
Mis-matched unrelated (<= 6/8)	5 (0.2)
Multi-donor	1 (0.0)
Unrelated (matching TBD)	72 (3.3)
Cord blood	368 (16.9)
Not reported	18 (0.8)
Graft type - no. (%)	
Bone marrow	1197 (55.1)
Peripheral blood	609 (28.0)
Umbilical cord blood	368 (16.9)
Number of induction cycles therapy required to achieve 1st complete remission - no. (%)	
1	1040 (47.8)
2	784 (36.1)
≥ 3	294 (13.5)
Not reported	56 (2.6)
Transplant year - no. (%)	
2014	265 (12.2)
2015	241 (11.1)
2016	298 (13.7)
2017	293 (13.5)
2018	250 (11.5)
2019	287 (13.2)
2020	258 (11.9)
2021	282 (13.0)
Indicator of HCT cases in CRF retrieval - no. (%)	
No	1640 (75.4)
Yes	534 (24.6)

Data source: January 2022 CRF
January 2022 TED
October 2023 HCT-Essentials
Embargo and consent criteria are applied

Field	Response
Proposal Number	2310-170-LAKE
Proposal Title	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
Key Words	KMT2Ar Infantile ALL; Conditioning
Principal Investigator #1: - First and last name, degree(s)	Alexander Lake
Principal Investigator #1: - Email address	Alexander_Lake@dfci.harvard.edu
Principal Investigator #1: - Institution name	Boston Children's Hospital/Dana Farber Cancer Institute
Principal Investigator #1: - Academic rank	Pediatric Hematology/Oncology/Stem Cell Transplant Fellow
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):	Christine Duncan
Principal Investigator #2 (If applicable): - Email address:)	Christine_Duncan@dfci.harvard.edu
Principal Investigator #2 (If applicable): - Institution name:	Boston Children's Hospital/Dana Farber Cancer Institute
Principal Investigator #2 (If applicable): - Academic rank:	Associate 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:	Alexander Lake
Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.	Christine Duncan: Co-investigator on a study with the Pediatric GVHD committee
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
RESEARCH QUESTION:	Are outcomes, disease-free survival, transplant related mortality, and late effects in infants who undergo allogeneic stem cell transplant for high-risk KMT2A-rearranged infant ALL significantly different for those who receive TBI vs chemotherapy-based conditioning regimens?

Field	Response
RESEARCH HYPOTHESIS:	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).
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	Specific Aims: 1. To report the overall survival, disease-free survival, and transplant related mortality at 100 days, 3 years, and most recent follow-up in infants diagnosed with HR KMT2Ar infantile ALL who underwent an allogeneic transplantation. 2. To report the differences in overall survival, disease-free survival, transplant related mortality, and late effects of infants with HR KMT2Ar infantile ALL when receiving a total body irradiation vs chemotherapy-based conditioning regimen. 3. To determine the impact of graft source on overall survival, disease-free survival, and transplant related mortality. The primary objectives of this study are to report the overall survival, disease free survival, transplant-related morbidity, late effects, and graft characteristics for both TBI and chemotherapy-based conditioning regimens for infants with high-risk KMT2Ar infantile ALL. We will report survival data on the entire study population in subjects at 100 days, 3 years, and at most recent follow-up. Late effects will only be reported/compared in patients who survived a minimum of 2 years from 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.	Studies of KMT2Ar infantile ALL have primarily focused on improving overall survival and relapsed-free survival in infants with chemotherapy-alone regimens. Through these studies, efforts have been implored to determine which infants, if any, would benefit from a consolidative stem cell transplant. At this time, infants risk stratified as “High Risk” are consolidated with an allogenic transplant. However, there is no standard transplant approach. A large study reporting not only outcomes and late effects, but conditioning and graft characteristics would aid clinicians in transplant planning for this vulnerable population.

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.	Approximately 80% of infants less than 1 year of age diagnosed with acute lymphoblastic leukemia harbor a KMT2A (MLL) gene rearrangement that mediates leukemogenesis. Often these patients present with hyperleukocytosis, organomegaly, central nervous system (CNS) involvement, and higher risk of early treatment-related mortality (Balduzzi et al, 2022). Additionally, these patients have demonstrated a high rate of relapse, particularly in infants stratified as high risk. Infant protocols have defined “High Risk” as <6 months old, KMT2A rearrangement, high leukocyte count (>300 10^9/L), and/or poor prednisone response. Previous clinical studies have reported improvements in the outcomes in infants with KMT2A rearranged ALL using intensified treatments and allogeneic stem cell transplant (Silverman et al, 1997; Kosaka et al, 2004; Jacobsohn et al, 2005; Sanders et al, 2005; Tomizawa et al, 2007; Balduzzi et al, 2022). However, HSCT carries significant toxicity in the infant population and remains a considerable challenge (Sison et al, 2013; Parikh et al, 2019; Balduzzi et al, 2022). Recent studies have demonstrated that low-risk infants can be treated without HSCT whereas high-risk infants may still benefit from an allogeneic HSCT as a consolidation therapy (Tomizawa et al, 2020). TBI based regimens remain the standard in pediatric ALL, but is associated with higher incidence of late complications, especially in infants (Dvorak et al, 2011). As a result, Busulfan (Bu) based conditioning regimens have been tried as an alternative in infants. Outcomes using Bu based conditioning regimens in KMT2Ar infantile ALL reported by the Japan Society for Hematopoietic Cell Transplantation appear comparable to TBI based regimens in their retrospective analysis, however, their study was underpowered (Kato et al, 2014); moreover, Bu conditioning regimens were noted to lead to severe veno-occlusive disease and pulmonary complications (Takachi et al, 2021), which may impact transplant-related mortality and outcomes. In all, optimal allogenic strategies in this population have yet to be determined. This study will report not only the overall survival and disease-free survival of TBI vs chemotherapy-based conditioning regimens in high-risk KMT2Ar infantile ALL but investigate the impact of graft source as well. Furthermore, this study will hope to highlight the various late effects seen post-HSCT in infants who receive these two types of conditioning regimens. As young infants are particularly vulnerable to post-HSCT late effects, it will be crucial to compare in order to weigh clinical decisions with families.

Field	Response
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	Patient Eligibility Population: 1. Diagnosed with high risk infantile KMT2A-r infantile ALL and underwent an allogeneic hematopoietic stem cell transplant. 2. Received either a myeloablative TBI based conditioning regimen or Busulfan based conditioning regimen. 3. Transplantation between 2005-2020. There are no exclusions based on stem cell source or donor.
Does this study include pediatric patients?	Yes
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. Patient-related: • Age at the time of transplant • Sex: Male, female • Race: White, non-white • Lansky performance status at time of transplant: ≤90%, >90% • Time from diagnosis to transplant 2. Underlying disease related • Disease • Disease status at time of transplant CR, CRi, or no CR • MRD negative at time of transplant: yes/no 3. Transplant related: • Donor type: HLA-identical sibling, other matched related, mismatched related, matched unrelated, mismatched unrelated • Stem cell source: Bone marrow vs. Peripheral blood vs. Umbilical cord • Year of transplant • Graft-versus-host disease prophylaxis 4. Post-transplant: • Acute GVHD grades 2-4 post-transplant: yes or no • Chronic GVHD at any time post-transplant: yes or no • Organ impairment/late effect (as listed in CIBMTR form 2100 R8): Veno-occlusive disease, interstitial pulmonary fibrosis (other non-infectious pulmonary abnormality), pericarditis, hypothyroidism requiring replacement therapy, growth hormone deficiency/short stature, gonadal dysfunction requiring hormone replacement, secondary malignancy, and/or cataracts. Late effects will only be reported/compared in patients who survived a minimum of 2 years from transplant • Performance Status (Lansky/Karnofsky) at 2 years and most recent follow- up • Relapse: yes or no • Death: yes or no • Date and cause of death • Date of last follow up
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 desc	No PRO data required.

Field	Response
MACHINE LEARNING: Please indicate if the study requires methodology related to machine-learning and clinical predictions.	No machine-learning required.
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 o	This proposal does not use patient samples or require supplementary data collection.

REFERENCES:	1. Balduzzi A, Buechner J, Ifversen M, Dalle JH, Colita AM, Bierings M. Acute Lymphoblastic Leukaemia in the Youngest: Haematopoietic Stem Cell Transplantation and Beyond. Front Pediatr. 2022 Feb 24;10:807992. doi: 10.3389/fped.2022.807992. PMID: 35281233; PMCID: PMC8911028. 2. Dreyer ZE, Dinndorf PA, Camitta B, Sather H, La MK, Devidas M, et al.. 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. (2011) 29:214–22. 10.1200/JCO.2009.26.8938 3. Dvorak, C.C., Gracia, C.R., Sanders, J.E., Cheng, E.Y., Baker, K.S., Pulsipher, M.A. & Petryk, A. (2011) NCI, NHLBI/PBMTC first international conference on late effects after pediatric hematopoietic cell transplantation: endocrine challenges-thyroid dysfunction, growth impairment, bone health, & reproductive risks. Biology of Blood and Marrow Transplantation, 17, 1725–1738. 4. Jacobsohn, D.A., Hewlett, B., Morgan, E., Tse, W., Duerst, R.E. & Kletzel, M. (2005) Favorable outcome for infant acute lymphoblastic leukemia after hematopoietic stem cell transplantation. Biology of Blood and Marrow Transplantation, 11, 999–1005. 5. Kato, M., Hasegawa, D., Koh, K., Kato, K., Takita, J., Inagaki, J., Yabe, H., Goto, H., Adachi, S., Hayakawa, A., Takeshita, Y., Sawada, A., Atsuta, Y. and Kato, K. (2015), Allogeneic haematopoietic stem cell transplantation for infant acute lymphoblastic leukaemia with KMT2A (MLL) rearrangements: a retrospective study from the paediatric acute lymphoblastic leukaemia working group of the Japan Society for Haematopoietic Cell Transplantation. Br J Haematol, 168: 564-570 6. Kosaka, Y., Koh, K., Kinukawa, N., Wakazono, Y., Isoyama, K., Oda, T., Hayashi, Y., Ohta, S., Moritake, H., Oda, M., Nagatoshi, Y., Kigasawa, H., Ishida, Y., Ohara, A., Hanada, R., Sako, M., Sato, T., Mizutani, S., Horibe, K. & Ishii, E. (2004) Infant acute lymphoblastic leukemia with MLL gene rearrangements: outcome following intensive chemotherapy and hematopoietic stem cell transplantation. Blood, 104, 3527–3534. 7. Parikh SH, Satwani P, Ahn KW, Sahr NA, Fretham C, Abraham AA, et al.. Survival trends in infants undergoing allogeneic hematopoietic cell transplant. JAMA Pediatr. (2019) 173:e190081. 10.1001/jamapediatrics.2019.0081 8. Sanders, J.E., Im, H.J., Hoffmeister, P.A., Gooley, T.A., Woolfrey, A.E., Carpenter, P.A., Andrews, R.G., Bryant, E.M. & Appelbaum, F.R. (2005) Allogeneic hematopoietic cell transplantation for infants with acute

Field	Response
	lymphoblastic leukemia. Blood, 105, 3749–3756. 9. Silverman, L.B., McLean, T.W., Gelber, R.D., Donnelly, M.J., Gilliland, D.G., Tarbell, N.J. & Sallan, S.E. (1997) Intensified therapy for infants with acute lymphoblastic leukemia: results from the Dana-Farber Cancer Institute Consortium. Cancer, 80, 2285–2295. 10. Sison EA, Brown P. Does hematopoietic stem cell transplantation benefit infants with acute leukemia? Hematol Am Soc Hematol Educ Progr. (2013) 2013:601–4. 10.1182/asheducation-2013.1.601 11. Takayuki Takachi, Tomoyuki Watanabe, Takako Miyamura, Akiko Moriya Saito, Takao Deguchi, Toshinori Hori, Tomomi Yamada, Shigeru Ohmori, Masami Haba, Yuki Aoki, Sae Ishimaru, Shinya Sasaki, Junjiro Ohshima, Akihiro Iguchi, Yoshiyuki Takahashi, Nobuyuki Hyakuna, Atsushi Manabe, Keizo Horibe, Eiichi Ishii, Katsuyoshi Koh, Daisuke Tomizawa; Hematopoietic stem cell transplantation for infants with high-risk KMT2A gene–rearranged acute lymphoblastic leukemia. Blood Adv 2021; 5 (19): 3891–3899. 12.Tomizawa, D., Koh, K., Sato, T., Kinukawa, N., Morimoto, A., Isoyama, K., Kosaka, Y., Oda, T., Oda, M., Hayashi, Y., Eguchi, M., Horibe, K., Nakahata, T., Mizutani, S. & Ishii, E. (2007) Outcome of risk-based therapy for infant acute lymphoblastic leukemia with or without an MLL gene rearrangement, with emphasis on late effects: a final report of two consecutive studies, MLL96 and MLL98, of the Japan Infant Leukemia Study Group. Leukemia, 21, 2258–2263. 13. Tomizawa D, Miyamura T, Imamura T, Watanabe T, Moriya Saito A, Ogawa A, et al.. A risk-stratified therapy for infants with acute lymphoblastic leukemia: a report from the JPLSG MLL-10 trial. Blood. (2020) 136:1813–23. 10.1182/blood.2019004741
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

Table 1. Characteristics of infant patients who underwent Allo HCT for KMT2A-r between 2008 and 2021

Characteristic	TBI based	Bu based	Total
No. of patients	67	98	165
No. of centers	43	55	75
Patient age, at diagnosis, years - median (min-max)	0.4 (0.0-1.0)	0.4 (-0.0-1.0)	0.4 (-0.0-1.0)
Patient age at HCT- median (min-max)	1.3 (0.5-5.1)	1.1 (0.3-3.9)	1.2 (0.3-5.1)
Sex of recipient - no. (%)			
Male	28 (41.8)	54 (55.1)	82 (49.7)
Female	39 (58.2)	44 (44.9)	83 (50.3)
Race - no. (%)			
White	51 (76.1)	44 (44.9)	95 (57.6)
Non-White	10 (14.9)	28 (28.6)	38 (23.0)
Missing	6 (9.0)	26 (26.5)	32 (19.4)
Status at Transplantation - no. (%)			
Primary induction failure	0 (0.0)	5 (5.1)	5 (3.0)
1st complete remission	22 (32.8)	46 (46.9)	68 (41.2)
2nd complete remission	39 (58.2)	39 (39.8)	78 (47.3)
1st relapse	1 (1.5)	2 (2.0)	3 (1.8)
>= 3rd complete remission	4 (6.0)	4 (4.1)	8 (4.8)
2nd relapse	1 (1.5)	1 (1.0)	2 (1.2)
Not reported	0 (0.0)	1 (1.0)	1 (0.6)
Conditioning intensity - no. (%)			
Myeloablative	67 (100)	98 (100)	165 (100)
Graft type - no. (%)			
Bone marrow	38 (56.7)	45 (45.9)	83 (50.3)
Peripheral blood	5 (7.5)	10 (10.2)	15 (9.1)
Umbilical cord blood	24 (35.8)	43 (43.9)	67 (40.6)
GVHD prophylaxis - no. (%)			
None	1 (1.5)	0 (0.0)	1 (0.6)
Ex-vivo T-cell depletion	1 (1.5)	1 (1.0)	2 (1.2)
CD34 selection	0 (0.0)	1 (1.0)	1 (0.6)
PtCy + other(s)	9 (13.4)	10 (10.2)	19 (11.5)
PtCy alone	1 (1.5)	0 (0.0)	1 (0.6)
TAC + MMF +- other(s) (except PtCy)	6 (9.0)	10 (10.2)	16 (9.7)
TAC + MTX +- other(s) (except MMF, PtCy)	15 (22.4)	12 (12.2)	27 (16.4)
TAC alone	0 (0.0)	1 (1.0)	1 (0.6)
CSA + MMF +- other(s) (except PtCy, TAC)	17 (25.4)	24 (24.5)	41 (24.8)
CSA + MTX +- other(s) (except PtCy, TAC, MMF)	13 (19.4)	22 (22.4)	35 (21.2)
CSA + other(s) (except PtCy, TAC, MMF, MTX)	3 (4.5)	8 (8.2)	11 (6.7)

Characteristic	TBI based	Bu based	Total
CSA alone	1 (1.5)	6 (6.1)	7 (4.2)
Other(s)	0 (0.0)	3 (3.1)	3 (1.8)
Conditioning regimen - no. (%)			
TBI/Cy	27 (40.3)	0 (0.0)	27 (16.4)
TBI/Cy/Flu	10 (14.9)	0 (0.0)	10 (6.1)
TBI/Cy/Flu/TT	1 (1.5)	0 (0.0)	1 (0.6)
TBI/Cy/TT	12 (17.9)	0 (0.0)	12 (7.3)
TBI/Cy/VP	7 (10.4)	0 (0.0)	7 (4.2)
TBI/VP	1 (1.5)	0 (0.0)	1 (0.6)
TBI/Mel	2 (3.0)	0 (0.0)	2 (1.2)
TBI/Flu	6 (9.0)	0 (0.0)	6 (3.6)
TBI/other(s)	1 (1.5)	0 (0.0)	1 (0.6)
Bu/Cy/Mel	0 (0.0)	8 (8.2)	8 (4.8)
Bu/Cy	0 (0.0)	35 (35.7)	35 (21.2)
Bu/Mel	0 (0.0)	13 (13.3)	13 (7.9)
Flu/Bu/TT	0 (0.0)	33 (33.7)	33 (20.0)
Flu/Bu	0 (0.0)	9 (9.2)	9 (5.5)
Donor type - no. (%)			
HLA-identical sibling	13 (19.4)	16 (16.3)	29 (17.6)
Other related	11 (16.4)	14 (14.3)	25 (15.2)
Well-matched unrelated (8/8)	15 (22.4)	17 (17.3)	32 (19.4)
Partially-matched unrelated (7/8)	2 (3.0)	2 (2.0)	4 (2.4)
Unrelated (matching TBD)	2 (3.0)	6 (6.1)	8 (4.8)
Cord blood	24 (35.8)	43 (43.9)	67 (40.6)
Transplant year - no. (%)			
2008	7 (10.4)	6 (6.1)	13 (7.9)
2009	3 (4.5)	5 (5.1)	8 (4.8)
2010	2 (3.0)	1 (1.0)	3 (1.8)
2011	6 (9.0)	5 (5.1)	11 (6.7)
2012	4 (6.0)	10 (10.2)	14 (8.5)
2013	4 (6.0)	7 (7.1)	11 (6.7)
2014	5 (7.5)	4 (4.1)	9 (5.5)
2015	4 (6.0)	7 (7.1)	11 (6.7)
2016	7 (10.4)	2 (2.0)	9 (5.5)
2017	4 (6.0)	8 (8.2)	12 (7.3)
2018	4 (6.0)	10 (10.2)	14 (8.5)
2019	5 (7.5)	12 (12.2)	17 (10.3)
2020	3 (4.5)	8 (8.2)	11 (6.7)
2021	9 (13.4)	13 (13.3)	22 (13.3)
Indicator of HCT cases in CRF retrieval - no. (%)			

Characteristic	TBI based	Bu based	Total
No	47 (70.1)	68 (69.4)	115 (69.7)
Yes	20 (29.9)	30 (30.6)	50 (30.3)

Data source: January 2022 CRF
January 2022 TED
October 2023 HCT-Essentials
Embargo and consent criteria are applied

Field	Response
Proposal Number	2310-233-CHAKRAVARTHY
Proposal Title	Transplant outcomes in pediatric, adolescent, and young adult patients with hypoplastic myelodysplastic syndrome
Key Words	Myelodysplastic syndrome, refractory cytopenias of childhood, myeloablative, reduced intensity, hematopoietic cell transplant
Principal Investigator #1: - First and last name, degree(s)	Rohini Chakravarthy, MD, MPH
Principal Investigator #1: - Email address	rohini.chakravarthy@cuanschutz.edu
Principal Investigator #1: - Institution name	University of Colorado/Children's Hospital Colorado
Principal Investigator #1: - Academic rank	Bone Marrow Transplant/Cellular Therapies Fellow
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):	Maria A. Pereda Ginocchio, MD
Principal Investigator #2 (If applicable): - Email address:)	maria.peredaginocchio@cuanschutz.edu
Principal Investigator #2 (If applicable): - Institution name:	University of Colorado/Children's Hospital Colorado
Principal Investigator #2 (If applicable): - Academic rank:	Assistant Professor - Bone Marrow Transplant and Cellular Therapy
Junior investigator status (defined as ≤5 years from fellowship)	Yes
Do you identify as an underrepresented/minority?	Yes
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:	Rohini Chakravarthy, MD, MPH
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

Field	Response
RESEARCH QUESTION:	- Disease free survival (DFS) in patients with hypoplastic myelodysplastic syndrome (MDS) or refractory cytopenias of childhood (RCC) transplanted with a myeloablative conditioning (MAC) versus reduced intensity conditioning (RIC) regimens. Overall survival (OS) and event free survival (EFS) in patients with hypoplastic MDS or RCC transplanted with MAC vs RIC regimens. - Cumulative incidence (CI) of relapse for patients with hypoplastic MDS or RCC treated with MAC vs RIC - Cumulative incidence of transplant related mortality (TRM) for patients with hypoplastic MDS or RCC treated with MAC vs RIC - CI and severity of acute and chronic graft versus host disease (GVHD) in MAC vs RIC - CI and severity of veno occlusive disease (VOD) in MAC vs RIC - CI of graft failure and incidence of second HCT or donor lymphocyte infusion (DLI) in MAC vs RIC - Conditioning regimens and GVHD prophylaxis used for patients with hypoplastic myelodysplastic syndrome and RCC - Cytogenetic characteristics of patients who received MAC vs RIC regimen
RESEARCH HYPOTHESIS:	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.
SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.):	Primary objectives: - 2-year disease free survival after a MAC for hypoplastic MDS - 2-year disease free survival after RIC for hypoplastic MDS Secondary objectives: - Overall survival (OS) and event free survival (EFS) in patients with hypoplastic MDS or RCC transplanted with MA versus RIC regimens. - Description of specific conditioning regimen drugs used in MAC and RIC regimens - Cumulative incidence (CI) of relapse for patients with hypoplastic MDS or RCC treated with MAC versus RIC regimen - Cumulative incidence of grade II-IV acute GVHD and severe acute GVHD (III-IV) - Cumulative incidence of limited and extensive chronic GVHD - Engraftment: neutrophil engraftment time (median), platelet engraftment (median), incidence of graft failure

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.	Given its rarity in pediatrics, few studies have described the outcomes of hematopoietic cell transplant in patients with MDS. There is a further paucity of data regarding the outcomes following a MAC versus RIC regimen in patients with the hypoplastic subtype of MDS. Identifying the outcomes following a RIC regimen and determining the best conditioning regimen for patients with hypoplastic MDS will allow clinicians to safely recommend a RIC for patients and will hopefully lead less transplant related mortality and fewer long-term toxicities that are more commonly associated with a myeloablative conditioning regimen. The data produced from this study will allow us to compare various RIC regimens and compare outcomes to various MAC regimens. The results of this study will also provide data that can be used to design and execute further prospective studies in patients with MDS that will continue to find treatment options with high success rates while minimizing long term adverse 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.	Myelodysplastic syndromes (MDS) are a group of clonal hematopoietic disorders that are characterized by ineffective hematopoiesis and peripheral cytopenias. If left untreated, they have the ability to transform into aggressive leukemias. MDS is generally considered a disease of the elderly. Pediatric MDS is an extremely rare diagnosis with an incidence of 1- 4 per million (1,2) Unlike in adults, pediatric MDS is more commonly a result of an underlying inherited bone marrow failure syndromes or genetic predisposition syndromes. Hematopoietic cell transplant (HCT) generally considered the appropriate standard of care for cure of pediatric MDS assuming a patient as an appropriate donor and can tolerate potential toxicities. A myeloablative conditioning (MAC) regimen is most commonly used prior to transplant; However, in certain cases of MDS, in which patients present with a hypocellular marrow, such as in refractory cytopenia of childhood (RCC), a reduced intensity conditioning regimen may be used. A pilot study conducted in Europe evaluated the use of a reduced intensity conditioning (RIC) regimen with fludarabine, thiotepa, and anti-thymocyte globulin to treat 19 pediatric patients ages 1-17 years with hypocellular refractory cytopenia myelodysplastic syndrome. They found that 3-year overall and event free survival in these patients was comparable with those who received a myeloablative conditioning (3). Similarly, a slightly larger single center Japanese study of 24 pediatric patients ages 3-21 years with RCC, evaluated the outcomes following HCT with a MAC vs RIC regimen. They also reported favorable outcomes in the group receiving a RIC (4). While both studies above suggest that a RIC regimen may be successfully utilized in a certain group of patients with MDS, they are difficult to generalize to a larger population. Both are significantly limited by their small sample sizes and shorter term follow up with an inability to speak to potential long-term reduction in toxicities with a RIC regimen. Furthermore, both of these studies used different RIC regimens; therefore, making it difficult to compare and determine the optimal regimen. It is therefore imperative to examine a larger, more diverse population with longer follow-up times.
PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.	Inclusion criteria: - Patients ages 0-30 years with bone marrow biopsy proven hypoplastic MDS who have received first HCT between the years of 2000 and 2020 Exclusion criteria: - Patients who received an HCT outside of that time period, outside of that age group, and those who received >1 HCT.

Field	Response
Does this study include pediatric patients?	Yes
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.	- Myelodysplastic Syndrome Pre-InfusionRevision: 4.0 - Myelodysplastic Syndrome Post-InfusionRevision: 4.0 - Fungal Infection Supplemental Data Pre-InfusionRevision: 5.0 - Fungal Infection Supplemental Data Post-InfusionRevision: 4.0 - Viral Infection Diagnostic and Treatment Post-InfusionRevision: 1.0 - Donor Lymphocyte InfusionRevision: 1 - Pre-Transplant Essential Data (Pre-TED)Revision: 10.0 - Post-HSCT DataRevision: 8.0 - Recipient Baseline DataRevision: 6.0 - Veno-occlusive Disease/Sinusoidal Obstruction SyndromeRevision: 1.0
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 desc	None
MACHINE LEARNING: Please indicate if the study requires methodology related to machine-learning and clinical predictions.	None
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 o	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. Locatelli F, Strahm B. How I treat myelodysplastic syndromes of childhood. Blood. Mar 29 2018;131(13):1406-1414. doi:10.1182/blood-2017-09-765214 2. Patel SS. Pediatric Myelodysplastic Syndromes. Clin Lab Med. Sep 2021;41(3):517-528. doi:10.1016/j.cll.2021.03.015 3. Strahm B, Locatelli F, Bader P, et al. Reduced intensity conditioning in unrelated donor transplantation for refractory cytopenia in childhood. Bone Marrow Transplant. Aug 2007;40(4):329-33. doi:10.1038/sj.bmt.1705730 4. Inagaki J, Fukano R, Kurauchi K, Noguchi M, Tanioka S, Okamura J. Hematopoietic stem cell transplantation in children with refractory cytopenia of childhood: single-center experience using high-dose cytarabine containing myeloablative and aplastic anemia oriented reduced-intensity conditioning regimens. Biol Blood Marrow Transplant. Mar 2015;21(3):565-9. doi:10.1016/j.bbmt.2014.12.003

Field	Response
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.	N/A

Table 1. Characteristics of pediatric patients who underwent first HCT for MDS-RCC between 2013 and 2021

Characteristic	Myeloablative	RIC/NMA	Total
No. of patients	90	11	101
No. of centers	50	9	55
Patient age at HCT- median (min-max)	8.8 (0.8-21.4)	9.5 (6.7-17.6)	9.2 (0.8-21.4)
Sex of recipient - no. (%)			
Male	52 (57.8)	8 (72.7)	60 (59.4)
Female	38 (42.2)	3 (27.3)	41 (40.6)
Graft type - no. (%)			
Bone marrow	62 (68.9)	8 (72.7)	70 (69.3)
Peripheral blood	16 (17.8)	2 (18.2)	18 (17.8)
Umbilical cord blood	12 (13.3)	1 (9.1)	13 (12.9)
GVHD prophylaxis - no. (%)			
None	3 (3.3)	0 (0.0)	3 (3.0)
Ex-vivo T-cell depletion	1 (1.1)	0 (0.0)	1 (1.0)
CD34 selection	5 (5.6)	0 (0.0)	5 (5.0)
PtCy + other(s)	9 (10.0)	0 (0.0)	9 (8.9)
PtCy alone	1 (1.1)	0 (0.0)	1 (1.0)
TAC + MMF +- other(s) (except PtCy)	8 (8.9)	1 (9.1)	9 (8.9)
TAC + MTX +- other(s) (except MMF, PtCy)	16 (17.8)	0 (0.0)	16 (15.8)
TAC alone	1 (1.1)	2 (18.2)	3 (3.0)
CSA + MMF +- other(s) (except PtCy, TAC)	9 (10.0)	4 (36.4)	13 (12.9)
CSA + MTX +- other(s) (except PtCy, TAC, MMF)	32 (35.6)	3 (27.3)	35 (34.7)
CSA + other(s) (except PtCy, TAC, MMF, MTX)	2 (2.2)	0 (0.0)	2 (2.0)
CSA alone	3 (3.3)	1 (9.1)	4 (4.0)
Conditioning regimen - no. (%)			
TBI/Cy	1 (1.1)	0 (0.0)	1 (1.0)
TBI/Cy/Flu	1 (1.1)	2 (18.2)	3 (3.0)
TBI/Mel	1 (1.1)	0 (0.0)	1 (1.0)
Bu/Cy/Mel	12 (13.3)	0 (0.0)	12 (11.9)
Bu/Cy	37 (41.1)	0 (0.0)	37 (36.6)
Bu/Mel	2 (2.2)	0 (0.0)	2 (2.0)
Flu/Bu/TT	4 (4.4)	0 (0.0)	4 (4.0)
Flu/Bu	16 (17.8)	0 (0.0)	16 (15.8)
Flu/Mel	0 (0.0)	3 (27.3)	3 (3.0)
Cy/Flu	1 (1.1)	3 (27.3)	4 (4.0)
Cy alone	1 (1.1)	0 (0.0)	1 (1.0)
Treosulfan	11 (12.2)	2 (18.2)	13 (12.9)
Other(s)	3 (3.3)	1 (9.1)	4 (4.0)

Characteristic	Myeloablative	RIC/NMA	Total
Transplant type - no. (%)			
Allogeneic	90 (100)	11 (100)	101 (100)
Donor type - no. (%)			
HLA-identical sibling	19 (21.1)	4 (36.4)	23 (22.8)
Other related	14 (15.6)	0 (0.0)	14 (13.9)
Well-matched unrelated (8/8)	30 (33.3)	4 (36.4)	34 (33.7)
Partially-matched unrelated (7/8)	9 (10.0)	0 (0.0)	9 (8.9)
Unrelated (matching TBD)	6 (6.7)	2 (18.2)	8 (7.9)
Cord blood	12 (13.3)	1 (9.1)	13 (12.9)
Transplant year - no. (%)			
2013	1 (1.1)	1 (9.1)	2 (2.0)
2014	16 (17.8)	4 (36.4)	20 (19.8)
2015	15 (16.7)	1 (9.1)	16 (15.8)
2016	6 (6.7)	1 (9.1)	7 (6.9)
2017	10 (11.1)	0 (0.0)	10 (9.9)
2018	14 (15.6)	0 (0.0)	14 (13.9)
2019	10 (11.1)	1 (9.1)	11 (10.9)
2020	11 (12.2)	1 (9.1)	12 (11.9)
2021	7 (7.8)	2 (18.2)	9 (8.9)
Indicator of HCT cases in CRF retrieval - no. (%)			
No	73 (81.1)	10 (90.9)	83 (82.2)
Yes	17 (18.9)	1 (9.1)	18 (17.8)

Data source: January 2022 CRF
January 2022 TED
October 2023 HCT-Essentials
Embargo and consent criteria are applied