Not for publication or presentation

CIBMTR®
CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH

A G E N D A
CIBMTR WORKING COMMITTEE FOR NON-MALIGNANT DISEASES
Orlando, Florida
Wednesday, February 19, 2020, 12:15pm – 2:15pm

Co-Chair:	**Christopher Dvorak, MD, University of California San Francisco Medical Center, San Francisco, CA;** **E-mail: christopher.dvorak@ucsf.edu**
Co-Chair:	**George Georges, MD, Fred Hutchinson Cancer Research Center, Seattle, WA;** **E-mail: ggeorges@fredhutch.org**
Co-Chair:	**Andrew Gennery, MD, Newcastle General Hospital / The Royal Victoria Infirmary, Newcastle, UK;** **E-mail: a.r.gennery@ncl.ac.uk**
Co-Chair:	**Vikram Mathews, MD, DM, MBBS, Christian Medical College Hospital, Vellore, India;** **E-mail: vikram@cmcvellore.ac.in**
Scientific Director:	**Mary Eapen, MBBS, MS, CIBMTR Statistical Center, Milwaukee, WI;** **E-mail: meapen@mcw.edu**
Statistical Director:	**Soyoung Kim, PhD, CIBMTR Statistical Center, Milwaukee, WI;** **E-mail: skim@mcw.edu**
Statistician:	**Kyle Hebert, MS, CIBMTR Statistical Center, Milwaukee, WI;** **E-mail: khebert@mcw.edu**

---

1. **Introduction**
   a. Minutes and Overview Plan from February 2019 meeting (Attachment 1)

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

3. **Presentations, published or submitted papers**
   a. **NM17-03** Eapen M, Brazauskas R, Walters MC, Bernaudin F, Bo-Subait K, Fitzhugh CD, Hankins JS, Kanter J, Meerpohl JJ, Bolaños-Meade J, Panepinto JA, Rondelli D, Shenoy S, Williamson J, Woolford TL, Gluckman E, Wagner JE, Tisdale JF. Effect of donor type and conditioning regimen intensity on allogeneic transplantation outcomes in patients with sickle cell disease: a retrospective multicentre, cohort study. ***The Lancet Haematology. 2019 Nov;6(11):e585-e596.***
   b. **NM17-02** Li C, Mathews V, Kim S, George B, Hebert K, Jiang H, Li C, Zhu Y, Keesler DA, Boelens JJ, Dvorak CC, Agarwal R, Auletta JJ, Goyal RK, Hanna R, Kasow K, Shenoy S, Smith AR, Walters MC, Eapen M. Related and unrelated donor transplantation for β-thalassemia major: results of an international survey. ***Blood Advances. 2019 Sep 10;3(17):2562-2570.***
   c. **NM16-04** Bejanyan N, Kim S, Hebert KM, Kekre N, Abdel-Azim H, Ahmed I, Aljurf M, Badawy SM, Beitinjaneh A, Boelens JJ, Diaz MA, Dvorak CC, Gadalla S, Gajewski J, Gale RP, Ganguly S, Gennery AR, George B, Gergis U, Gómez-Almaguer D, Vicent MG, Hashem H, Kamble RT, Kasow KA, Lazarus HM, Mathews V, Orchard PJ, Pulsipher M, Ringden O, Schultz K, Teira P, Woolfrey AE, Saldaña BD, Savani B, Winiarski J, Yared J, Weisdorf DJ, Antin JH, Eapen M. Choice of

conditioning regimens for bone marrow transplantation in severe aplastic anemia. ***Blood Advances. 2019 Oct 22;3(20):3123-3131.***

d. **NM14-02** Outcomes of allogeneic hematopoietic cell transplant in patients with Shwachman diamond syndrome (K Myers) **Submitted**

4. Studies in progress (Attachment 3)

a. **AA13-02** Malignancies in patients with fanconi anemia (J Wagner) **Manuscript Preparation**

b. **NM15-01** Outcome of Allogeneic Hematopoietic Cell Transplant in Erythropoietic Porphyria (A Saad/D Moshous) **Manuscript Preparation**

c. **NM16-03** Results of transplants from genetically-identical twin donors in persons with aplastic anemia (RP Gale) **Data File Preparation**

d. **NM17-01** Late effects after hematopoietic stem cell transplantation in patients with HLH (A Horne/KS Baker/K Beutel) **Protocol Development**

e. **NM18-01** Impact of choice of serotherapy in pediatric stem cell transplantation for non-malignant disease (A Prakash/ D Wall/ K Paulson) **Data File Preparation**

f. **NM19-01** Conditional and cause-specific mortality of patients with severe aplastic anemia surviving at least one year after alloHCT or immunosuppressive therapy (R Nakamura/FL Wong/ S Armenian/N Young) **Data File Preparation**

g. **NM19-02** Impact of Conditioning on Allogeneic HCT Outcomes for HLH (R Marsh) **Analysis**

h. **NM19-03** Hematopoietic Stem Cell Transplantation for Congenital Amegakaryocytic Thrombocytopenia (F Boulad/M Cancio/JJ Boelens) **Analysis**

i. **AC18-02** Prospective Cohort study of Recipients of Autologous Hematopoietic cell Transplant for Systemic Sclerosis (G Georges) **Data Collection**

5. Future/proposed studies

a. **Prop 1906-02** CIBMTR Retrospective Study of Allogeneic Stem Cell Transplant Outcomes in Severe Aplastic Anemia (SAA) using Fludarabine, Cyclophosphamide and Alemtuzumab ('FCC') Conditioning (Shafqat Inam; Judith Marsh) (Attachment 4)

b. **Prop 1910-07/Prop 1911-132** Haploidentical Donor Transplantation for Severe Aplastic Anemia: A Combined CIBMTR-EBMT Study (Akshay Sharma; Abhishek A. Mangaonkar and colleagues) (Attachment 5)

c. **Prop 1910-13** Impact of immunosuppressive therapy (IST) duration on hematopoietic cell transplantation (HCT) outcomes in patients with severe aplastic anemia (SAA) (Jessica E. Knight-Perry; Michael R. Verneris) (Attachment 6)

d. **Prop 1911-142/Prop 1909-03/Prop 1911-118** Hematopoietic Stem Cell Transplantation for Fanconi anemia (Farid Boulad; Seth J. Rotz; Hesham Eissa and colleagues) (Attachment 7)

e. **Prop 1911-150** Clinical Outcome and Health Care Utilization of Children with Hemophagocytic Lymphohistiocytosis who received Hematopoietic Stem Cell Transplantation (Ram Kalpatthi; Meghan McCormick; Archana Ramgopal; Matt Hall; Jignesh Dala) (Attachment 8)

6. Dropped proposed studies

a. **Prop 1910-09** Effect of mixed host-donor chimerism on graft failure/rejection after hematopoietic cell transplantation for non-malignant hematological disorders
Dropped due to feasibility

b. **Prop 1911-24** Influence of GVHD prophylaxis in Aplastic Anemia and transplant outcomes in the era of newer conditioning regimens
Dropped due to overlap with recent committee study NM16-04

c. **Prop 1911-35** Composite Graft versus Host Disease and Graft Failure Free Survival (GFFS) in non-malignant hematologic disorders patients undergoing allogeneic stem cell transplantation with post-transplant cyclophosphamide: The novel composite endpoint
Dropped due to heterogeneity of diseases and overlap with other disease-specific studies

d. **Prop 1911-75** Evaluation of Outcomes following Allogeneic Hematopoietic Cell Transplantation in Patients with Diamond-Blackfan Anemia and other red cell aplasias: A CIBMTR Analysis.
Dropped due to overlap with previous publications

e. **Prop 1911-104** Impact of Time to Transplant in Severe Aplastic Anemia Patients Receiving Prior Immunosuppressive Therapy
Dropped due to feasibility

f. **Prop 1911-125** Determining the Effect of Recipient-Donor Race Matching on Outcomes forSickle Cell Patients Transplanted with Matched Unrelated Donors
Dropped due to low sample size

g. **Prop 1911-138** Allogeneic hematopoietic stem cell transplantation (HCT) outcomes with total body irradiation (TBI)-conditioning regimens versus non-TBI regimens among patients with severe aplastic anemia (SAA)
Dropped due to overlap with recent study NM16-04

h. **Prop 1911-153** Impact of non-infectious encephalopathy on outcomes among children undergoing allogeneic hematopoietic stem cell transplant for non-malignant disorders.
Dropped due to feasibility

i. **Prop 1911-156** Trends of Early Mortality Within First Two Years Following Allogeneic Hematopoietic Cell Transplantation in Children and Adolescents with Non-Malignant Disorders
Dropped due to heterogeneity of diseases and overlap with other disease-specific studies

j. **Prop 1911-165** Patterns of use and outcomes of donor lymphocyte infusions for non-malignant diseases
Dropped due to low sample size

k. **Prop 1911-202** Graft versus host disease (GVHD) free and Rejection Free Survival (GRFS) and Chronic GVHD and Rejection Free Survival (CRFS) in patients undergoing allogeneic hematopoietic stem cell transplant for non-malignant disorders.
Dropped due to heterogeneity of diseases and overlap with other disease-specific studies

l. **Prop 1911-211** Comparing incidence of acute and chronic graft versus host disease (GVHD) with different conditioning and GVHD prophylaxis regimens used in alternative donor transplants for non-malignant conditions.
Dropped due to heterogeneity of diseases and overlap with other disease-specific studies

m. **Prop 1911-218** To study the outcomes after autologous hematopoietic stem cell transplantation for multiple sclerosis
Dropped due to feasibility and overlap with other recent publications

MINUTES AND OVERVIEW PLAN
CIBMTR WORKING COMMITTEE FOR PRIMARY IMMUNE DEFICIENCIES, INBORN ERRORS OF METABOLISM AND OTHER NON-MALIGNANT MARROW DISORDERS
Houston, Texas
Friday, February 22, 2019, 12:15pm – 2:15pm

Co-Chair:	**Christopher Dvorak, MD, University of California San Francisco Medical Center, San Francisco, CA;** **Telephone: 415-476-2188; E-mail: christopher.dvorak@ucsf.edu**
Co-Chair:	**Jaap Jan Boelens, MD, PhD, Memorial Sloan Kettering Cancer Center, New York, NY;** **Telephone: 212-639-3641; E-mail: boelensj@mskcc.org**
Co-Chair:	**Vikram Mathews, MD, DM, MBBS, Christian Medical College Hospital, Vellore, India;** **Telephone: +011 91 416 228 2891; E-mail: vikram@cmcvellore.ac.in**
Scientific Director:	**Mary Eapen, MBBS, MS, CIBMTR Statistical Center, Milwaukee, WI;** **Telephone: 414-805-0700; E-mail: meapen@mcw.edu**
Statistical Director:	**Soyoung Kim, PhD, CIBMTR Statistical Center, Milwaukee, WI;** **Telephone: 414-955-8271; E-mail: skim@mcw.edu**
Statistician:	**Kyle Hebert, MS, CIBMTR Statistical Center, Milwaukee, WI;** **Telephone: 414-805-0673; E-mail: khebert@mcw.edu**

1. Introduction

The CIBMTR Working Committee for Primary Immune Deficiencies, Inborn Errors of Metabolism and other Non-Malignant Marrow Disorders met on Friday, February 22nd, 2019 at 12:15pm. Dr. Dvorak welcomed the audience and introduced the working committee leadership, reviewed the committee's goals, expectations, and limitations. Dr. Andrew Gennery and Dr. George Georges were introduced as the newest committee chairs. Dr. Jaap-Jan Boelens was thanked for his contributions to the committee as chair as his term as committee chair has concluded. There was a motion to approve the 2018 working committee meeting minutes, and a second. The motion passed. Dr. Dvorak then reviewed the CIBMTR guidelines for committee membership and rules for authorship of studies. The links to additional working committee related information were also provided. Dr. Dvorak also re-emphasized for the committee members that the CIBMTR data is collected on two tracks: the Transplant Essential Data (TED) and the Comprehensive Report Form (CRF), and that it is important to keep in mind that only CRF-level patients have detailed disease-specific data collected, which is often relevant to this committee that studies rare diseases.

Dr. Eapen then explained to the audience that the working committee would be absorbing autoimmune diseases and cellular therapies for non-malignant diseases. Additionally, the Primary Immune Deficiencies, Inborn Errors of Metabolism and other Non-Malignant Marrow Disorders Working Committee, with the addition of the autoimmune diseases, will be renamed the Non-Malignant Diseases Working Committee.

2. Accrual summary (Attachment 2)

The accrual tables were referenced for review but not formally presented in the interest of time.

3. Presentations, published or submitted papers

Dr. Dvorak directed the audience to the working committee materials for information regarding the two committee publications from 2018.

The two committee publications from 2018, 1 publication currently under review, and 2 papers ready for submission are listed below:

a. **NM16-01** Rice C, Eikema DJ, Marsh JCW, Knol C, Hebert K, Putter H, Peterson E, Deeg HJ, Halkes S, Pidala J, Anderlini P, Tischer J, Kroger N, McDonald A, Antin JH, Schaap NP, Hallek M, Einsele H, Mathews V, Kapoor N, Boelens JJ, Mufti GJ, Potter V, Pefault de la Tour R, Eapen M, Dufour C. Allogeneic Hematopoietic Cell Transplantation in Patients Aged 50 Years or Older with Severe Aplastic Anemia. ***Biology of Blood and Marrow Transplantation. 2018 Sep; doi: 10.1016/j.bbmt.2018.08.029. [Epub ahead of print]***

b. **NM16-02** Marsh RA, Hebert KM, Keesler D, Boelens JJ, Dvorak CC, Eckrich MJ, Kapoor N, Parikh S, Eapen M. Practice pattern changes and improvements in hematopoietic cell transplantation for primary immunodeficiencies. ***The Journal of Allergy and Clinical Immunology. 2018 Aug; doi: 10.1016/j.jaci.2018.08.010. [Epub ahead of print]***

c. **NM17-03** Impact of Age, Donor Type, and Conditioning Regimen Intensity on Allogeneic Transplant Outcome for Sickle Cell Disease (Eapen M) **Submitted**

d. **NM17-02** Related and Unrelated Donor Transplantation for β Thalassemia major: Results of an International Survey (C Li/ V Mathews) **Ready for submission**

e. **NM16-04** The effect of conditioning regimen on clinical outcomes of allogeneic hematopoietic cell transplantation in severe aplastic anemia (N Bejanyan/N Kekre/D Weisdorf/J Antin) **Ready for submission**

4. Studies in progress (Attachment 3)

Dr. Kasiani Myers presented the results of the ongoing active study entitled *Outcomes of allogeneic hematopoietic cell transplant in patients with Shwachman diamond syndrome*. One audience member asked whether all of the patients who died of AML following HCT for Schwachman-Diamond had AML prior to the transplant. Dr. Myers responded that they did.

Dr. Eapen presented the results of the ongoing active study entitled *Hematopoietic cell transplantation for congenital neutropenia/kostmann agranulocytosis*. One audience member asked whether the non-significant difference in survival between patients transplanted for primary severe combined neutropenia versus those with leukemia may have been a power issue due to low numbers. Dr. Eapen replied that this does not appear to be the case, as the survival estimates actually look quite similar. Another attendee asked whether there might be an interaction between recipient age and donor type. Dr. Eapen responded that interactions were tested for, and there was no such interaction. A concern was raised that it seemed strange to have grouped patients for analysis with the cutoff point of 4 years. The committee leadership clarified that this was merely a typo, and that the cut point used in the analysis had been 4 months. An attendee asked about the prevalence of graft failure in the cohort, and Dr. Eapen responded that in this population, it would have been the inverse of the survival, which would put graft rejection somewhere around 25%, with some patients going to a second transplant and others dying. An attendee asked whether we know if the patients who were transplanted for primary SCN were resistant to G-CSF and whether this was the reason for going to HCT. The response was that we do not have information on the reason the primary SCN patients proceeded to transplant. Another audience member asked whether starting neutrophil counts pre-transplant were available, however this information was not included in the data sent to CIBMTR by the European SCN registry. A committee member asked whether the mismatched unrelated donors in the population included cord bloods, to which Dr. Eapen clarified that they did include cord bloods, however graft type was not tested for survival differences because of heavy confounding with donor type.

Dr. Vikram Mathews presented the results of the upcoming committee paper entitled *Related and Unrelated Donor Transplantation for β Thalassemia major: Results of an International Survey.* One attendee noted that the related mismatched donors appeared to be performing worse even then the mismatched unrelated donors, and wondered whether the leadership believed this to be a genuine effect. Dr. Mathews replied that while this group was quite small in the current analysis and this effect cannot be definitively proven here, this was in fact consistent with his experience at his center and he suspects that there is something there. Dr. Mathews clarified that most of the mismatched related donors in the study population were parents of the recipients. Another attendee asked whether we know about if the parents who served as donors had previously given blood transfusions to the recipients, to which the answer was that we do not have that data. Another audience member asked whether there was a clear winner among the conditioning regimens used to treat these patients in the study, and the leadership responded that it was too difficult to declare a winner in terms of regimen because of heavy confounding with recipient age and donor type.

Meeting attendees were directed to the committee materials for more complete details about all of the rest of the committee's current active studies.

The full list of active committee studies are listed below:

a. **AA13-02** Malignancies in patients with fanconi anemia (J Wagner) **Analysis**

b. **ID13-01** Hematopoietic cell transplantation for congenital neutropenia/kostmann agranulocytosis (C Zeidler/S Keogh/J Connelly) **Manuscript Preparation**

c. **NM14-02** Outcomes of allogeneic hematopoietic cell transplant in patients with Shwachman diamond syndrome (K Myers) **Manuscript Preparation**

d. **NM15-01** Outcome of Allogeneic Hematopoietic Cell Transplant in Erythropoietic Porphyria (A Saad/H Abdel-Azim/J Bloomer) **Analysis**

e. **NM16-03** Results of transplants from genetically-identical twin donors in persons with aplastic anemia (RP Gale) **Data File Preparation**

f. **NM17-01** Late effects after hematopoietic stem cell transplantation in patients with HLH (A Horne/KS Baker/K Beutel) **Protocol Development**

g. **NM18-01** Impact of choice of serotherapy in pediatric stem cell transplantation for non-malignant disease (A Prakash/ D Wall/ K Paulson) **Protocol Development**

5. Future/proposed studies

Dr. Boelens outlined the voting process for the attendees, explaining that voting should be based both on scientific impact and on feasibility using the CIBMTR data.

a. **Prop 1811-110** Impact of Reduced Intensity Conditioning on Allogeneic HCT Outcomes for HLH (R Marsh) (Attachment 4)

Dr. Kasiani Myers presented the proposal on behalf of Dr. Rebecca Marsh. The goal of the study will be to compare patients transplanted for HLH using reduced intensity conditioning to those using myeloablative conditioning for any differences in outcomes.

The CIBMTR identified 431 patients transplanted for HLH with myeloablative conditioning, and 366 patients transplanted for HLH with reduced intensity since the year 2005. One attendee asked whether there is available data on the remission status of these patients. The leadership responded that this data would be available only for the subset of patients with CRF data collected, which includes pre-transplant disease status for this disease. Multiple commenters stressed the importance of carefu;lly defining what is meant by reduced intensity conditioning for this study. Dr. Dvorak pointed out that generally for CIBMTR studies, patients with conditioning regimens containing only a single alkylating agent are classified by the dose of the alkylating agent in mg/kg. A few audience members suggested that using exposure would make for a better analysis, and the leadership agreed that this should be considered. Another audience member suggested changing the primary outcome from overall survival to survival with sustained engraftment. A final question was whether these patients had chimerism data collected, to which Dr. Eapen replied that this would only be available in the CRF subset.

b. **Prop 1810-11** Outcomes of allogeneic hematopoietic stem cell transplant in adult patients with history of hemophagocytic lymphohistiocytosis (M Hegazi) (Attachment 5)

Dr. Hamza Hashmi presented the proposal on behalf of Dr. Hegazi's group. The goal of the study will be to examine the prognostic factors and determine the outcomes of adult patients transplanted for HLH.

The CIBMTR identified 119 adult patients transplanted for HLH since the year 2005, for which only 22 have detailed disease-specific data collected on the CRF track. A few attendees pointed out that this proposal covered the same disease as the previous proposal, and that perhaps this overlap meant that this study could simply be done as part of the previous one. However, others argued that the focus of the two studies were inherently different, with one seeking to explore conditioning regimen choices in the younger population of HLH patients and the other seeking to learn anything possible about older HLH patients. One attendee pointed out that with the proposed restriction to patients younger than age 30 in the regimen proposal, there

really is only an overlap between patients aged 18-30 between the two proposals. Dr. Arjan Lankester, chair of the corresponding working party of the EBMT, provided an update that there was an active EBMT study already at the manuscript phase studying adult patients transplanted for HLH.

c. **Prop 1811-67** Does mixed chimerism after alloHCT in patients with Fanconi Anemia impact on the eventual outcome? (M Ayas) (Attachment 6)

Dr. Mouhab Ayas presented the proposal. Dr. Ayas explained that his group at King Faisal in Saudi Arabia studied approximately 50 patients transplanted for Fanconi Anemia with mixed chimerism post-transplant, and that the study found no significant difference in survival from fully engrafted patients. Dr. Ayas and his colleagues would be interested in confirming these findings on a broader scale.

The CIBMTR identified 43 patients transplanted for Fanconi Anemia who were confirmed to have mixed chimerism following transplant, since the year 2005. One commenter stated that she had been part of a group that had done a previous study on Fanconi Anemia patients, and that only a very small number of these patients had had mixed chimerism after transplant. As such, there was concern over the small number of mixed chimerism patients that would be available to compare to full donor chimerism patients. A few audience members, as well as the leadership, expressed concern that the chimerism data has a tendency to be inconsistently reported by centers, and that it would also be complicated to ensure that patients with mixed chimerism after transplant ultimately remained as sustained mixed chimerism, rather than failing the graft or recovering.

d. **Prop 1811-94** Conditional and cause-specific mortality of patients with severe aplastic anemia surviving at least one year after alloHCT or immunosuppressive therapy (R Nakamura/ L Wong/ S Armenian) (Attachment 7)

Dr. Nakamura presented the proposal. The goal of the study will be to examine the long-term survival of patients transplanted for severe aplastic anemia who survived at least one year following the transplant, and to compare the conditional survival beyond one year to a separate group of patients with severe aplastic anemia treated with immunosuppressive therapy. The immunosuppressive therapy group would come from the National Heart, Lung, and Blood Institute.

The CIBMTR identified 2,111 patients transplanted for severe aplastic anemia and surviving at least one year since the year 2000. One audience member asked how patients would be addressed who had undergone immunosuppressive therapy first, and then ultimately proceeded to transplant. Dr. Nakamura responded that he thinks that this is indeed the critical question for this study, and that the group would welcome input on this issue. Dr. Nakamura suggested that one possible way to handle this would be to censor patients in the immunosuppressive therapy group at the time of transplant. Others pointed out that a clean approach could be to restrict the study population to only transplant patients with matched sibling donors, as this would still leave a large enough sample size, and it would be reasonable to presume that nearly all of these patients would have gone to transplant as a first-line treatment. Another audience member asked whether time from diagnosis to transplant is captured on the forms, and the leadership confirmed that it is.

e. **Prop 1811-175** Outcomes after Allogeneic Hematopoietic Cell Transplantation in Patients with Griscelli syndrome (P Satwani) (Attachment 8)

Dr. Satwani presented the proposal. The goal of the study will be to examine prognostic factors and describe outcomes for patients undergoing allogeneic transplantation for Griscelli syndrome.

The CIBMTR identified 53 patients transplanted for Griscelli syndrome since the year 2000, of which 24 patients had detailed disease-specific data collected on the CRF track. Of these 53 patients, only 8 were transplanted in the United States. One audience member asked whether this could be a situation where since it is a small number of patients, we could go back and ask centers for CRF-level data if TED data had initially been collected. Dr. Eapen explained that while this could be helpful, it would impose a burden on the transplant centers and that centers are compensated for filling out CRF forms, so collecting this data would require funding. Dr. Lankester was asked whether he knew how many European patients EBMT might be able to contribute to this effort, and Dr. Lankester answered that he could look into that if the study were to proceed.

f. **Prop 1811-180** Hematopoietic Stem Cell Transplantation for Congenital Amegakaryocytic Thrombocytopenia (F Boulad/ M Cancio/ JJ Boelens) (Attachment 9)

Dr. Farid Boulad presented the proposal. The goal of the study will be to explore prognostic factors and describe outcomes in patients undergoing allogeneic transplantation for Congenital Amegakaryocytic Thrombocytopenia (CAMT).

The CIBMTR identified 66 patients transplanted for CAMT in the United States since the year 2000, of which 37 patients have had detailed disease-specific data collected on the CRF track. A few audience members wondered whether it would be possible to combine with EBMT or reach out to the centers to provide a few additional pieces of critical data. Dr. Eapen explained that it would be fairly easy to simply reach out to the centers who contributed patients and ask just a couple of important yes/no questions. One of these questions would be whether or not the diagnosis of CAMT was done via molecular means. The other question would be what was the bone marrow status prior to transplant, for patients who received bone marrow grafts. Another attendee suggested that it would be extremely valuable to include graft failure as an outcome in this study, and also to describe patients who went to a second transplant and their outcomes thereafter. Dr. Eapen confirmed that this was very much possible to add.

6. Dropped proposed studies

The committee received the following additional study proposals, but these proposals were not selected for presentation at the TCT Meeting, for the reasons outlined below.

a. **Prop 1811-14** Post-transplant cyclophosphamide as single agent for GVHD prophylaxis in patients with aplastic anemia undergoing matched-related stem cell transplantation: An observational study
Dropped due to feasibility

b. **Prop 1811-20** Outcomes of allogenic hematopoietic stem cell transplant in pediatric and adult patients with paroxysmal nocturnal hemoglobinuria
Dropped due to existing scientific literature

c. **Prop 1811-29** Outcomes in older patients undergoing HLA-identical sibling allogeneic stem cell transplantation as first line for severe aplastic anemia
Dropped due to overlap with NM16-01

d. **Prop 1811-38** Incidence of mixed chimerism and evaluation of the impact of donor lymphocyte infusion in patients post-transplant for hemoglobinopathies
Dropped due to low sample size

e. **Prop 1811-60** Long term outcome of mixed chimerism in children undergoing allogeneic stem cell transplantation for primary immunodeficiency disorders
Dropped due to overlap with ongoing PIDTC research

f. **Prop 1811-75** Haploidentical alloHCT in pediatric patients with beta thalassemia major; an observational study
Dropped due to overlap with NM17-02

g. **Prop 1811-83** Outcomes post-allogeneic hematopoietic stem cell transplantation in patients with congenital dyserythropoietic anemia
Dropped due to feasibility

h. **Prop 1811-118** Allogeneic hematopoietic stem cell transplantation outcomes for patients with deficiency of adenosine deaminase type 2
Dropped due to feasibility

i. **Prop 1811-127** Retrospective study of the prognostic significance of comorbidities in recipients of allogeneic hematopoietic cell transplantation (alloHCT) for primary immunodeficiency (PID)
Dropped due to overlap with Regimen-related toxicity published study RT07-01b

j. **Prop 1811-131** Impact of non-infectious encephalopathy on outcomes among children undergoing allogeneic hematopoietic stem cell transplant for non-malignant disorders
Dropped due to feasibility

k. **Prop 1811-162** Haplo-identical donor transplants for Thalassemia major
Dropped due to overlap with NM17-02

l. **Prop 1811-166** Long Term Impact of Allogeneic Stem Cell Transplantation on Pulmonary Hypertension and Renal Outcomes in Patients with Sickle Cell Disease
Dropped due to overlap with Late Effects WC active study LE17-01

7 Other Business

a. Meeting adjourned at 1:55pm.

b. Voting on proposals.

After the new proposals were presented, each participant in the meeting had an opportunity to rate each proposal using paper ballots. Based on the voting results, current scientific merit, available number of relevant cases, and the impact of the study on the field, the following three studies were accepted to move forward to be added to the committee's active studies:

Prop 1811-110 Impact of Reduced Intensity Conditioning on Allogeneic HCT Outcomes for HLH (R Marsh)

Prop 1811-94 Conditional and cause-specific mortality of patients with severe aplastic anemia surviving at least one year after alloHCT or immunosuppressive therapy (R Nakamura/ L Wong/ S Armenian/ N Young)

Prop 1811-180 Hematopoietic Stem Cell Transplantation for Congenital Amegakaryocytic Thrombocytopenia (F Boulad/ M Cancio/ JJ Boelens)

c. The following proposals were not accepted as studies, for the reasons specified:

Prop 1810-11 Outcomes of allogeneic hematopoietic stem cell transplant in adult patients with history of hemophagocytic lymphohistiocytosis
Dropped due to feasibility, as there are too few patients with CRF-level data needed to study this disease in this population in-depth. Also, direct overlap with EBMT completed study.

Prop 1811-67 Does mixed chimerism after alloHCT in patients with Fanconi Anemia impact on the eventual outcome?
Dropped due to feasibility, with too few patients available with mixed chimerism, and difficulty of confirming sustained mixed chimerism with the data that is available.

Prop 1811-175 Outcomes after Allogeneic Hematopoietic Cell Transplantation in Patients with Griscelli Syndrome
Dropped due to feasibility, as there are too few patients with CRF-level data needed to study this disease
in this population in-depth.

Working Committee Overview Plan for 2019 - 2020							
Study number and title	**Current status**	**Goal with date**	**Total hours to complete**	**Total hours to goal**	**Hours allocated to 6/30/2019**	**Hours allocated 7/1/2019-6/30/2020**	**Total Hours allocated**
AA13-02 Malignancies in patients with Fanconi Anemia	Manuscript preparation	Submission -June 2019	50	**50**	50	5	**55**
ID13-01 HCT for Congenital Neutropenia/Kostmann Agranulocytosis	Manuscript preparation	Submission -June 2019	10	**10**	10	5	**15**
NM14-02 Allo HCT for Shwachman Diamond Syndrome	Manuscript preparation	Submission -June 2019	20	**20**	20	5	**25**
NM15-01 Outcome of allogeneic Hematopoietic Cell Transplant (HCT) in Erythropoietic Porphyria	Analysis	Submission -June 2019	50	**50**	50	5	**55**
NM16-03 Results of transplants from genetically-identical twin donors in persons with aplastic anaemia	Data File Preparation	Analysis -June 2019	150	**40**	40	110	**150**
NM16-04 The effect of conditioning regimen on clinical outcomes of allogeneic transplantation in severe aplastic anemia	Manuscript Preparation	Submitted -April 2019	10	**10**	10	5	**15**
NM17-01 Late effects after hematopoietic stem cell transplantation in patients with HLH	Data collection/ Protocol Develop-ment	Analysis -June 2019	310	**160**	160	150	**310**
NM17-02 Outcomes of HCT for thalassemia major	Manuscript Preparation	Submitted -March 2019	10	**10**	10	5	**15**

Study number and title	**Current status**	**Goal with date**	**Total hours to complete**	**Total hours to goal**	**Hours allocated to 6/30/2019**	**Hours allocated 7/1/2019-6/30/2020**	**Total Hours allocated**
NM18-01 Impact of choice of serotherapy in pediatric stem cell transplantation for non-malignant disease	Protocol develop-ment	Data File Prepar-Ation -June 2019	310	**60**	60	250	**310**
NM19-01 Conditional and cause-specific mortality of patients with severe aplastic anemia surviving at least one year after alloHCT or immunosuppressive therapy	Protocol pending	Draft protocol received -June 2019	370	**0**	0	140	**140**
NM19-02 Impact of Reduced Intensity Conditioning on Allogeneic HCT Outcomes for HLH	Protocol pending	Draft protocol received -June 2019	330	**0**	0	100	**100**
NM19-03 Hematopoietic Stem Cell Transplantation for Congenital Amegakaryocytic Thrombocytopenia	Protocol pending	Draft protocol received -June 2019	330	**0**	0	100	**100**
AC18-02 Prospective Cohort study of Recipients of Autologous Hematopoietic cell Transplant for Systemic Sclerosis	Protocol pending	Draft protocol received -June 2019	380	**0**	0	150	**150**

Oversight Assignments for Working Committee Leadership (March 2019)

Vikram Mathews	**AA13-02**	Malignancies in patients with fanconi anemia
Andrew Gennery	**ID13-01**	Second and subsequent hematopoietic cell transplants for congenital neutropenia/kostmann agranulocytosis
Christopher Dvorak	**NM14-02**	Outcomes of allogeneic hematopoietic cell transplant in patients with Shwachman diamond syndrome
Andrew Gennery	**NM15-01**	Outcome of Allogeneic Hematopoietic Cell Transplant in Erythropoietic Porphyria
George Georges	**NM16-03**	Results of transplants from genetically-identical twin donors in persons with aplastic anaemia
Andrew Gennery	**NM17-01**	Late effects after hematopoietic stem cell transplantation in patients with HLH
Christopher Dvorak	**NM18-01**	Impact of choice of serotherapy in pediatric stem cell transplantation for non-malignant disease
George Georges	**NM19-01**	Conditional and cause-specific mortality of patients with severe aplastic anemia surviving at least one year after alloHCT or immunosuppressive therapy
Christopher Dvorak	**NM19-02**	Impact of reduced intensity conditioning on allogeneic HCT outcomes for HLH
Vikram Mathews	**NM19-03**	Hematopoietic stem cell transplantation for Congenital Amegakaryocytic Thrombocytopenia
George Georges	**AC18-02**	Prospective Cohort study of Recipients of Autologous Hematopoietic cell Transplant for Systemic Sclerosis

Accrual Summary for the Non-Malignant Diseases Working Committee

Allogeneic Transplants for Immune Deficiencies reported to the CIBMTR from 2000-2019

Characteristic	CRF N	TED N
Number of patients	**2855**	**5834**
Number of centers	186	277
Disease		
Immune Deficiencies (ID), NOS	26 (0.9)	98 (1.7)
SCID ADA deficiency	94 (3.3)	141 (2.4)
SCID absence of T and B cells	176 (6.2)	293 (5)
SCID absence of T, normal B cell SCID	234 (8.2)	338 (5.8)
Omenn syndrome	100 (3.5)	164 (2.8)
Reticular dysgenesis	11 (0.4)	14 (0.2)
Bare lymphocyte syndrome	42 (1.5)	111 (1.9)
SCID, NOS	146 (5.1)	251 (4.3)
SCID other, specify	323 (11.3)	456 (7.8)
Wiskott Aldrich syndrome	292 (10.2)	534 (9.2)
DiGeorge anomaly	8 (0.3)	15 (0.3)
Chronic granulomatous disease	258 (9)	520 (8.9)
Chediak-Higashi syndrome	31 (1.1)	90 (1.5)
Common variable immunodef	36 (1.3)	91 (1.6)
X-linked lymphoproliferative syndrome	68 (2.4)	154 (2.6)
Leukocyte adhesion deficiencies	53 (1.9)	98 (1.7)
Kostmann agranulocytosis	59 (2.1)	177 (3)
Cartilage hair hypoplasia	26 (0.9)	53 (0.9)
TED Immune deficiency plus neutropenia	0	1 (0)
CD40 ligand deficiency	27 (0.9)	93 (1.6)
Griscelli syndrome type 2	11 (0.4)	21 (0.4)
Combined immunodef dis (CID), NOS	7 (0.2)	12 (0.2)
CID other, specify	17 (0.6)	17 (0.3)
Other immunodeficiencies, specify	198 (6.9)	651 (11.2)
Histiocytic disorder, NOS	5 (0.2)	30 (0.5)
FELH Familial erythrohemophagocytic lymphohis	427 (15)	1025 (17.6)
Langerhans Cell Histiocytosis	37 (1.3)	86 (1.5)
Hemophagocytosis	88 (3.1)	189 (3.2)
Malignant histiocytosis	3 (0.1)	15 (0.3)
Other histiocytic disord	52 (1.8)	96 (1.6)

*Only first transplants are included in this accrual.

Abbreviations: ADA = adenosine deaminase; NOS = not specified; SCID = severe combined immunodeficiency

Allogeneic Transplants for Inborn Errors of Metabolism reported to the CIBMTR from 2000-2019

Characteristic	CRF N	TED N
Number of patients	**1015**	**1875**
Number of centers	123	195
Disease		
Inherited disorders of metabolism, NOS	3 (0.3)	24 (1.3)
Osteopetrosis	141 (13.9)	317 (16.9)
Lesch-Nyhan(HGPTR defic)	2 (0.2)	2 (0.1)
Neuronal ceroid lipofuscinosis	5 (0.5)	7 (0.4)
Other inherited metabolism disorders, specify	40 (3.9)	82 (4.4)
Mucopolysaccharidosis, NOS	7 (0.7)	16 (0.9)
IH Hurler syndrome	323 (31.8)	523 (27.9)
IS Scheie syndrome	1 (0.1)	1 (0.1)
II Hunter syndrome	25 (2.5)	40 (2.1)
III Sanfillippo	27 (2.7)	32 (1.7)
VI Maroteaux-Lamy	25 (2.5)	41 (2.2)
VII B-glucuronidase deficiency	1 (0.1)	2 (0.1)
V Mucopolysaccharidosis	1 (0.1)	6 (0.3)
Other mucopolysaccharidosis	3 (0.3)	4 (0.2)
Mucolipidoses, NOS	3 (0.3)	4 (0.2)
Gaucher disease	4 (0.4)	14 (0.7)
Metachromatic leukodystrophy(MLD)	87 (8.6)	163 (8.7)
Adrenoleukodystrophy(ALD)	199 (19.6)	395 (21.1)
Globoid leukodystrophy/Krabbe disease	67 (6.6)	106 (5.7)
Neiman-Pick disease	11 (1.1)	22 (1.2)
I-cell disease	16 (1.6)	24 (1.3)
Wolman disease	6 (0.6)	11 (0.6)
Glucose storage disease	0	1 (0.1)
Other mucolipidoses	1 (0.1)	1 (0.1)
Asparty1 glucosaminuria	0	3 (0.2)
Fucosidosis	5 (0.5)	6 (0.3)
Mannosidosis	12 (1.2)	28 (1.5)

*Only first transplants are included in this accrual.

Allogeneic Transplants for non-malignant disorders reported to the CIBMTR from 2000-2019

Characteristic	CRF N	TED N
Number of patients	**7317**	**16108**
Number of centers	330	447
Disease		
Paroxysmal nocturnal hemoglobinuria	242 (3.3)	473 (2.9)
Severe aplastic anemia	3558	8324
Amegakaryocytosis	11 (0.2)	23 (0.1)
Shwachman-Diamond	37 (0.5)	75 (0.5)
Acquired Pure Red Cell Aplasia	31 (0.4)	86 (0.5)
Dyskeratosis congenita	39 (0.5)	75 (0.5)
Other acquired cytopenic syndrome, specify	135 (1.8)	281 (1.7)
Inherited abnormalities of erythrocyte differentiation, not otherwise specified	10 (0.1)	18 (0.1)
Fanconi anemia	801 (10.9)	1506 (9.3)
Diamond-Blackfan anemia	149 (2)	332 (2.1)
Other constitutional anemia	65 (0.9)	175 (1.1)
Thalassemia	1214	2744
Sickle cell disease	1025	1996

*Only first transplants are included in this accrual.

Autologous Transplants for autoimmune diseases reported to the CIBMTR from 2000-2019

Characteristic	CRF N	TED N
Number of patients	**129**	**781**
Number of centers	44	108
Disease		
Autoimmune disease unclassified	0	24 (3.1)
Myasthenia gravis	2 (1.6)	10 (1.3)
Multiple sclerosis	70 (54.3)	382 (48.9)
Rheumatoid arthritis	3 (2.3)	7 (0.9)
Psoriatic arthritis or psoriasis	1 (0.8)	1 (0.1)
Systemic lupus erythematosis (SLE)	9 (7)	60 (7.7)
Polymyositis-dermatomyositis	0	2 (0.3)
System Scleroderma	31 (24)	193 (24.7)
Antiphospholipid syndrome	0	5 (0.6)
Other arthritis, specify	0	1 (0.1)
Other Connective tissue dis	0	9 (1.2)
Churg-Strauss	0	1 (0.1)
Behcets Syndrome	0	2 (0.3)
JIA systemic	0	2 (0.3)
JIA Other, specify	0	1 (0.1)
Other neuro disorder, specify	7 (5.4)	33 (4.2)
ITP- Idiopathic thrombocytopenic purpura	2 (1.6)	4 (0.5)
Evan syndrome	0	1 (0.1)
Crohns disease	3 (2.3)	41 (5.2)
Other bowel disorder, specify	1 (0.8)	2 (0.3)

*Only first transplants are included in this accrual.

CIBMTR®
CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH

TO: Non-Malignant Diseases Working Committee Members

FROM: Mary Eapen, MBBS, MS; Scientific Director for the Primary Immune Deficiencies, Inborn Errors of Metabolism and Other Non-Malignant Marrow Disorders Working Committee

RE: Studies in Progress Summary

AA13-02: Malignancies in patients with Fanconi anemia (J Wagner) The aim of the study is to determine whether the risk of solid cancer is higher after allogeneic transplantation compared to non-transplanted patients with Fanconi anemia, and describe the types of solid cancer and the outcome. The manuscript is being finalized for submission. The goal is to submit the final manuscript by June 2020.

NM14-02: Outcomes of allogeneic hematopoietic cell transplant in patients with Shwachman diamond syndrome (K Myers) The aim of the study is to describe the population of children or adults with Shwachman diamond syndrome who have undergone HCT, and examine the outcomes post-transplant. Descriptive analysis has been completed. The manuscript has been drafted and is being finalized for submission. The goal is to submit the final manuscript by March 2020.

NM15-01: Outcome of allogeneic Hematopoietic Cell Transplant (HCT) in Erythropoietic Porphyria (A Saad/D Moshous) The aim of the study is to describe the population of children or adults with Erythropoietic Porphyria who have undergone HCT, and examine the outcomes post-transplant. U.S. data has been cleaned and prepared for presentation. European supplemental data has been collected and cleaned. Manuscript preparation is in progress. The goal is to submit the final manuscript by June 2020.

NM16-03: Results of transplants from genetically-identical twin donors in persons with aplastic anemia (R P Gale) The goal of this study is to determine the proportion of patients receiving transplant from genetically-identical twin donor for aplastic anemia that recover normal bone marrow function. In doing so, the objective is to estimate the proportion of aplastic anemia cases that result from absent/defective stem or progenitor cells, as opposed to immune-dysfunction. Data file preparation is in progress. The goal is to submit the final manuscript by June 2020.

NM17-01: Late effects after hematopoietic stem cell transplantation in patients with HLH (A Horne/KS Baker/K Beutel) The purpose of this study is to investigate the long-term outcomes and late effects of patients with hemophagocytic lymphohistiocytosis (HLH) who are survivors after hematopoietic cell transplantation (HCT). The main hypothesis is that HLH survivors will be at risk for significant long term medical and neuropsychological late effects that will be dependent upon pre-transplant disease related factors and the intensity of the BMT conditioning regimen. Study protocol is being developed. The goal is to complete preparation of the data file by June 2020.

NM18-01: Impact of choice of serotherapy in pediatric stem cell transplantation for non-malignant disease (A Prakash/ D Wall/ K Paulson) The purpose of this study is to compare outcomes following allogeneic HCT for pediatric patients with non-malignant disease based on the specific serotherapy used. Post-transplant outcomes, including overall survival, acute and chronic GVHD, graft failure, and graft-

failure free survival will be compared between patients given alemtuzumab and patients given ATG. The focus will be on non-malignant diseases for which transplant is most commonly used as treatment to establish as much homogeneity as possible in the comparison. Work on preparation of the data file is underway, with significant progress made. The goal is to perform the analysis and prepare a manuscript by June 2020.

NM19-01: Conditional and cause-specific mortality of patients with severe aplastic anemia surviving at least one year after alloHCT or immunosuppressive therapy (R Nakamura/ FL Wong/ S Armenian/ N Young) The objective of this study is to explore the conditional probability at various time points of patients surviving at least one year after HCT for severe aplastic anemia. The trend in survival rates, conditional on surviving up to specific time points following transplant, will be assessed and compared to conditional survival rates of severe aplastic anemia patients treated with immunosuppressive therapy. Preparation of the data file for transplant cases is in progress. The IST cases will require merging of data from the National Heart, Lung, and Blood Institute. The goal is to finalize the study protocol by June 2020.

NM19-02: Impact of Reduced Intensity Conditioning on Allogeneic HCT Outcomes for HLH (R Marsh) The objective of this study is to compare post-transplant outcomes for patients undergoing HSCT for HLH between those using myeloablative (Bu/Cy) and reduced intensity (Flu/Mel) conditioning, as well as comparing regimens that don't fall into either category and are less well-understood (Flu/Mel/TT and Flu/Bu). Preparation of the data file is complete, and the analysis phase is underway. The goal is to submit the final manuscript by June 2020.

NM19-03: Hematopoietic Stem Cell Transplantation for Congenital Amegakaryocytic Thrombocytopenia (F Boulad/ M Cancio/ JJ Boelens) The objective of this study is to explore patient characteristics and post-transplant outcomes of patients transplanted for congenital amegakaryocytic thrombocytopenia. Due to the small number of patients transplanted for this relatively rare indication for transplant, this study will feature descriptive analyses only. Preparation of the data file and univariate analyses are complete. The goal is to submit the final manuscript by June 2020.

AC18-02: Prospective Cohort study of Recipients of Autologous Hematopoietic cell Transplant for Systemic Sclerosis (G Georges) The objective of this study is to explore patient characteristics and post-transplant outcomes of patients undergoing autologous transplant for systemic sclerosis. Co-operation of the transplant centers treating these patients will be solicited for the collection of supplemental data of highest relevance for this specific autoimmune disease. The supplemental data collection form has been created, and the collection of the supplemental data is in progress. The goal is to have the supplemental data collected, and the data file prepared for analysis by June 2020.

Proposal: 1906-02

Title:
CIBMTR Retrospective Study of Allogeneic Stem Cell Transplant Outcomes in Severe Aplastic Anemia (SAA) using Fludarabine, Cyclophosphamide and Alemtuzumab ('FCC') Conditioning

Shafqat Inam, shafqat.inam@nhs.net, King's College Hospital
Judith Marsh, MD, judith.marsh@nhs.net, King's College Hospital/King's College London

Hypothesis:
We hypothesize that evaluation of outcomes after HCT for acquired Severe Aplastic Anemia using FCC conditioning regimen is associated with low incidence of acute and chronic GVHD and high GVHD-free, 'relapse (graft failure)'-free survival (GRFS).

Objectives:
Examine outcomes, including overall survival, GFRS, hematopoietic recovery, graft failure, and GVHD, of patients of all ages receiving HCT for SAA using FCC conditioning since 2000.

Scientific justification:
Outcomes after allogeneic HCT for acquired SAA continue to improve over time, but one of the main issues remains GVHD, which impacts on morbidity, mortality and quality of life. The ideal conditioning regimen for SAA HCT is one that results in sustained myeloid engraftment, ideally stable mixed T cell chimerism, absence of GVHD, and low toxicity from the conditioning regimen in the short and long term, including fertility and second malignancies.
HCT from a matched sibling donor (MSD) is recommended as first line treatment in SAA for patients aged <35-60 years (depending on comorbidities). Matched unrelated donor (MUD) HCT for adult SAA is currently considered after failure of one course of immunosuppressive therapy (IST), although there is current debate about the role of upfront MUD HCT as an alternative option to IST if a MUD is readily available [1,2]. This reflects the continued improved outcomes after MUD HCT; in a large EBMT retrospective study of 1448 patients receiving mostly ATG-based conditioning, outcomes of at least second line MUD HCT were similar to first line MSD among patients with intermediate and high risk SAA; for low risk SAA, although OS after MSD HCT was significantly higher at 93%, OS after MUD HCT was still high at 83%. However, there was significantly more acute and chronic GVHD among MUD transplants compared to MSD transplants [3].
Hence a new approach was needed to reduce the incidence of GVHD. An alternative has been the development of alemtuzumab ('Campath', anti CD52) to replace ATG in the conditioning regimen [4]. This approach was developed primarily in the UK, leading to the so-called 'King's FCC' regimen of fludarabine 30mg/m^2, CY 300mg/m^2 x 4 and alemtuzumab (0.2mg/kg day-7 to-3), with ciclosporin (CSA) alone as post graft immunosuppression. For MUD HCT, compared to FCATG + 2Gy TBI, FCC has the key advantages of being an irradiation-free and methotrexate-free regimen, reduicing short and long term toxicity. A retrospective, multicentre study from UK and Toronto of 50 SAA patients transplanted from MSD and UD, reported 83% OS, 13% acute and 4% chronic GVHD [4,5]. Further studies using FCC in mostly adult patients come from UK (n=100) [6] Toronto (n=41, 2014) [7], and EBMT (n=261, of whom 169 received FCC as opposed to other alemtuzumab-based regimens [8]. The latter showed a significantly lower incidence of acute and chronic GVHD using alemtuzumab versus ATG-based conditinoing.
FCC MUD HCT in children also confirms excellent outcomes with low GVHD, such that upfront MUD HCT is now considered an option for children with SAA who lack a MSD and for whom a MUD is readily available

[9-11]. In order to evaluate further the possible role of upfront MUD HCT in adults using FCC, evaluation of a larger cohort of patients will be of great importance [12].
FCC regimen may be especially useful for older patients with SAA. A combined CIBMTR/EBMT study of 499 patients aged ≥50 years, identified an especially low incidence of acute and chronic GVHD among a subgroup of patients receiving alemtuzumab as part of the conditioning [13]. A recent single centre study from King's College London reported similar outcomes for patients aged ≥50 years and <50 years who received FCC conditioning (oral presentation at 2019 Annual Meeting of EBMT; Sheth et al, manuscript under review) [14].
There is currently much interest in considering using FCC regimen for SAA HSCT on account of its low rate of GVHD and excellent GRFS, and the fact that for MUD HSCT TBI is not needed (that is, it is an irradiation-free regimen) and also methotrexate post HSCT is not needed. Since fewer patients have been reported using FCC regimen, compared to ATG-based conditioning regimens, it is therefore of major importance to establish outcomes in a larger cohort of patients from the CIBMTR.

Study population:
Inclusion criteria:
- Patients of all ages requiring allogeneic HSCT for SAA or Very SAA (VSAA) receiving FCC HCT using MSD or MUD during years 2000-2018
- HLA-identical sibling donor or matched unrelated donor (8/8) by high-resolution HLA typing
- Bone marrow or peripheral blood graft

Exclusion criteria:
- Previous HSCT
- Constitutional SAA
- Second HCT for SAA

Outcomes:
Hematopoietic recovery:
The primary measures for hematopoietic recovery will be:
- Time to neutrophils (ANC) > 0.5 x109/L sustained for three consecutive days within 28 days post-transplant.
- Time to achieve a platelet count of (a) >20 x 109/L independent of platelet transfusions for 7 consecutive days within 100 days post-transplant.
- PB unfractionated, CD3 and CD15 chimersim (if available)

Acute GVHD:
Cumulative incidence of grade II-IV acute GVHD reported in the first 180 days post-transplant, with death without acute GVHD as a competing risk.

Chronic GVHD:
Cumulative incidence of chronic GVHD at 1yr and 3yr post-transplant, with death without chronic GVHD as a competing risk.

Overall survival (OS):

Survival of patients at 1yr and 3yr post-transplant. Death from any cause is considered an event. Surviving patients will be censored at last follow-up.

Graft versus host disease-free, graft failure-free survival (GRFS):

Secondary malignancies:
solid tumors and EBV PTLD

Secondary autoimmune disorders:

Variables to be tested:
Patient-related:

- Patient age: <20yr, 20-40yr, 40-50yr, 50-60yr, 60-69yr, 50-59 years vs. 60-69 years vs. ≥70 years
- Male vs. female
- Karnofsky score: <90% vs. ≥90%
- HCT-Comorbidities Index (HCT-CI): <3 vs. ≥3 (since 2007 when data available)
- CMV serostatus: positive vs. negative

Transplant-related:

- Interval from diagnosis to transplant
- Graft source: bone marrow vs. peripheral blood
- Donor: HLA-identical siblings vs. HLA matched unrelated (8/8)
- Prior immune suppressive therapy: yes vs. no
- GVHD prophylaxis: CNI alone vs CNI + MMF vs. CNI + MTX
- Year of transplant: 2000-2009 vs. 2010-2018

Study design:
Statistical analysis will be conducted by the CIBMTR

Bibliography:

1. Killick SB, Bown N, Cavenagh J, Dokal I, Foukaneli T, Hill A, Hillmen P, Ireland R, Kulasekararaj A, Mufti G, Snowden JA, Samarasinghe S, Wood A, Marsh JC; British Society for Standards in Haematology. Guidelines for the diagnosis and management of adult aplastic anaemia. *Br J Haematol*. 2016 Jan;172(2):187-207
2. Bacigalupo A. How I treat acquired aplastic anemia. Blood 2017; 129(11): 1428-1436.
3. Bacigalupo A et al, for the Aplastic Anemia Working Party of the European Group for Blood and Marrow Transplantation (WPSAA-EBMT). Current outcome of HLA identical sibling vs. unrelated donor transplants in severe aplastic anemia: an EBMT analysis. Haematologica 2015; 100: 696-702
4. Marsh JC, Gupta V, Lim Z, Ho AY, Ireland R, Hayden J, Potter V, Koh MB, Islam SMD, Russell NH, Marks DI, Mufti GJ, Pagliuca A. Alemtuzumab with fludarabine and cyclophosphamide reduces chronic graft versus host disease after allogeneic stem cell transplantation for acquired aplastic anemia *Blood* 2011; 118: 2351-2357.
5. Deeg HJ. GVHD-free with Campath? Blood 2011; 118(8): 2033-2034
6. Marsh JC, Pearce RM, Koh MB, Lim Z, Pagliuca A, Mufti GJ, Perry J Snowden JA, Vora AJ, Wynn RT, Russell N, Gibson B, Gilleece M, Milligan D, Veys P, Samarasinghe S, McMullin M, Kirkland K, Cook G1, on behalf of the British Society for Blood and Marrow Transplantation (BSBMT) Clinical Trials Committee (CTCR 09-03). Retrospective study of Alemtuzumab versus ATG based conditioning

without irradiation for unrelated and matched sibling donor transplants in acquired severe aplastic anaemia: a study from the British Society for Blood and Marrow Transplantation (BSBMT). Bone Marrow Transplantation. Bone Marrow Transplant. 2014; 49:42-48.

7. Hamad N, Del Bel R, Messner HA, et al. Outcomes of hematopoietic cell transplantation in adult patients with acquired aplastic anemia using intermediate-dose alemtuzumab-based conditioning. Biol Blood Marrow Transplant. 2014;20: 1722-1728
8. Samarasinghe S, Clesham K, Iacobelli S, Sbianchi G, Knol C, Hamladji RM, Socié G, Aljurf M, Koh M, Sengeloev H, Dalle JH, Robinson S, Van Lint MT, Halkes CJM, Beelen D, Mufti GJ, Snowden J, Blaise D, de Latour RP, Marsh J, Dufour C, Risitano AM; Severe Aplastic Anaemia Working Party of the EBMT. Impact of T-cell depletion strategies on outcomes following hematopoietic stem cell transplantation for idiopathic aplastic anemia: A study on behalf of the European blood and marrow transplant severe aplastic anemia working party. Am J Hematol. 2019 Jan;94(1):80-86
9. Samarasinghe S, Veys P, Vora A, Wynn R. Paediatric amendment to adult BSH Guidelines for aplastic anaemia. Br J Haematol. 2018 Jan;180(2):201-205. doi: 10.1111/bjh.15066. Epub 2017 Dec 28.
10. Samarasinghe S, Steward C, Hiwarkar P, Saif MA, Hough R, Webb D, Norton A, Lawson S, Qureshi A, Connor P, Carey P, Skinner R, Vora A, Pelidis M, Gibson B, Stewart G, Keogh S, Goulden N, Bonney D, Stubbs M, Amrolia P, Rao K, Meyer S, Wynn R, Veys P. Excellent outcome of matched unrelated donor transplantation in paediatric aplastic anaemia following failure with immunosuppressive therapy: a United Kingdom multicentre retrospective experience. Br J Haematol. 2012; 157(3):339-46.
11. Dufour C, Veys P, Carraro E, Bhatnagar N, Pillon M, Wynn R, Gibson B, Vora AJ, Steward CG, Ewins AM, Hough RE, de la Fuente J, Velangi M, Amrolia PJ, Skinner R, Bacigalupo A, Risitano AM, Socie G, Peffault de Latour R, Passweg J, Rovo A, Tichelli A, Schrezenmeier H, Hochsmann B, Bader P, van Biezen A, Aljurf MD, Kulasekararaj A, Marsh JC, Samarasinghe S. Similar outcome of upfront-unrelated and matched sibling stem cell transplantation in idiopathic paediatric aplastic anaemia. A study on behalf of the UK Paediatric BMT Working Party, Paediatric Diseases Working Party and Severe Aplastic Anaemia Working Party of EBMT. Br J Haematol. 2015 Nov;171(4):585-94.
12. Marsh JCW, Risitano AM, Mufti GJ. The case for upfront HLA-matched unrelated donor HCT as a curative option for adult acquired severe aplastic anemia. Biol Blood Marrow Transplant. 2019 May 23. pii: S1083-8791(19)30323-4. doi: 10.1016/j.bbmt.2019.05.012. [Epub ahead of print] Review.
13. Rice C, Eikema DJ, Marsh JCW, Knol C, Hebert K, Putter H, Peterson E, Deeg HJ, Halkes CJM, Pidala J, Anderlini P, Tischer J, Kroger N, McDonald A, Antin JH, Schaap NPM, Hallek M, Einsele H, Mathews V, Kapoor N, Boelens JJ, Mufti GJ, Potter V, Pefault de la Tour R, Eapen M, Dufour C. Allogeneic Hematopoietic Cell Transplantation in Patients aged 50 years or older with Severe Aplastic Anemia. Biol Blood Marrow Transplant. 2018 Sep 4. pii: S1083-8791(18)30531-7. doi: 10.1016/j.bbmt.2018.08.029. [Epub ahead of print].
14. Sheth V, Potter V, Gandhi S, Kulasekararaj AG, De Lavallade H, Muus P, Pagliuca A, Rice C, Mehra V, Grimaldi F, Inam S, Barber L, Mufti GM, Marsh JCW. Similar outcomes of alemtuzumab-based hematopoietic cell transplantation for SAA patients older or younger than 50 years. Blood Adv under review 2019.

Number of patients undergoing first allogeneic HCT for severe aplastic anemia from 2010 to 2018 receiving FCC regimen

Characteristic	CRF	TED
No. of patients	**38**	**68**
Age at transplant, years - no. (%)		
Median (min-max)	18.95 (1.49-62.22)	17.72 (1.08-67.53)
<1 to 17	16 (42.1)	35 (51.5)
18 to 29	14 (36.8)	17 (25)
30 to 49	2 (5.3)	8 (11.8)
50 or older	6 (15.8)	8 (11.8)
Donor type - no. (%)		
HLA-identical sibling	6 (15.8)	13 (19.1)
Other relative	0	2 (2.9)
Unrelated donor	32 (84.2)	53 (77.9)
Graft type - no. (%)		
Bone marrow	34 (89.5)	52 (76.5)
Peripheral blood	4 (10.5)	16 (23.5)
Year of transplant - no. (%)		
2010-2012	0	5 (7.4)
2013-2015	17 (44.7)	31 (45.6)
2016-2018	21 (55.3)	32 (47.1)
Follow-up - median (min-max)	34.24 (5.26-61.64)	36.12 (5.26-81.48)

Combined Proposal: 1910-07 /1911-132

Title:
Haploidentical Donor Transplantation for Severe Aplastic Anemia: A Combined CIBMTR-EBMT Study

Akshay Sharma, MBBS, Akshay.Sharma@ STJUDE.ORG, St. Jude Children's Research Hospital
Queralt Salas, MD, queralt.salas87@outlook.es, University of Toronto
Neel S Bhatt, MBBS, MPH, Neel.Bhatt@STJUDE.ORG, St. Jude Children's Research Hospital
Rajat Kumar, MD, FRCPC, rajat.kumar@uhn.ca, University of Toronto
Régis Peffault de Latour, MD, PhD, regis.peffaultdelatour@aphp.fr, Saint-Louis Hospital
Anna Sureda, MD, PhD, asureda@iconcologia.net, ICO Institut Català d'Oncologia-Hospitalet
Pedro de Lima Prata, MD, pedrohenrique.delimaprata@aphp.fr, Saint Louis Hospital
Abhishek A Mangaonkar, MBBS, mangaonkar.abhishek@mayo.edu, Mayo Clinic
Mrinal M Patnaik, MD, Patnaik.mrinal@mayo.edu, Mayo Clinic
Hassan Alkhateeb, MD, alkhateeb.hassan@mayo.edu, Mayo Clinic

Research Hypothesis:
Clinical outcomes after haploidentical hematopoietic cell transplantation for severe aplastic anemia are comparable to matched sibling and matched unrelated donor transplants (historical controls).

Specific aims:
Primary:
To assess the disease free and overall survival at 1 year after haploidentical hematopoietic cell transplantation (HCT) for severe aplastic anemia (SAA) and compare it to matched sibling and matched unrelated donor transplants (historical controls).

Secondary:
- To assess treatment-related mortality (TRM) and incidence of graft failure/rejection after haploidentical HCT for SAA.
- To assess the incidence of acute graft-vs-host disease (GVHD) and chronic GVHD after haploidentical HCT for SAA.
- To assess the 1-year and 3-year GVHD-free disease-free survival after haploidentical HCT for SAA. This will be defined as disease-free survival without Grade III-IV acute GVHD and without extensive chronic GVHD.

Scientific impact:
While an allogeneic matched sibling donor hematopoietic cell transplantation (alloHCT) has emerged as a first line treatment for acquired severe aplastic anemia (SAA) and HLA-matched unrelated donor allogeneic HCT remains the treatment of choice for those who do not respond upfront immunosuppressive therapy. But several patients, especially ethnic minorities and those in low- and middle-income countries, do not have access to matched unrelated donors. Related haploidentical donors are attractive options to expand this treatment modality to those patients who lack a matched donor option. However, there are few studies that have systematically evaluated the outcomes following alternative donor transplantation for SAA. CIBMTR database has data on around 70 patients who have undergone haploidentical HCT for SAA and the EBMT database has an additional 40 patients. Almost all of these transplants have been performed using the post-transplant cyclophosphamide based GVHD prophylaxis approach. A combined analysis utilizing the CIBMTR and EBMT databases will allow

hematologists and transplant physicians to clearly define the outcomes after haploidentical donor HCT in patients with SAA and identify prognostic markers for improved outcomes.

Scientific justification:

Allogeneic HCT from a matched sibling donor (MSD) is the first line treatment strategy for younger patients (less than 40-45 years of age) with SAA.[1-3] Salvage alloHCT with an HLA-matched unrelated donor (MUD) is recommended for patients with refractory SAA, but many patients, especially minorities, are unable to find a MUD in the registry.[4]

Donor availability has remained a major limitation to the expansion and success of BMT in SAA. About 50% to 60% patients of Caucasian descent, 20% Asian and 17% African American patients find a fully HLA-matched and available MUD.[4] MUDs are challenging to find for ethnic minorities as well as those living in low- and middle-income countries where donor registries are not as well developed. At the same time, related haploidentical donors are available for nearly all patients and can be acquired immediately.[5] This is particularly crucial for patients with very severe aplastic anemia (vSAA) who need prompt therapy.[1]

Haploidentical donor transplants have historically been associated with higher risks of graft failure, graft-versus-host disease (GVHD), and transplant-related mortality as compared to MSD transplantation.[4] But with advances in in-vivo regulation of T-cells, optimized conditioning regimens, and improved supportive care, outcomes following haploidentical donor transplants are improving.

Lu and colleagues reported similar 3-year overall survival in young patients with SAA (n=89; HAPLO: 41, MUD: 48) undergoing HCT with HAPLO and MUD donors (80.3% vs 89.6%, p=0.21).[5] While the cumulative incidence of acute GVHD was higher with HAPLO donors, chronic GVHD, disease free survival, and GVHD free failure free survivals were similar in both groups.[5] Recent data from several groups across the worlds suggests that haploidentical donor transplantation with post transplantation cyclophosphamide may have outcomes comparable to matched donor transplants.[6-10] A larger systematic analysis utilizing the combined data from the CIBMTR and EBMT databases will help assess the outcomes following transplant for this rare disorder comprehensively. A recently concluded CIBMTR study (NM16-04, Bejanyan et al. Choice of Conditioning Regimens for Bone Marrow Transplantation in Severe Aplastic Anemia. Submitted.) has evaluated the impact of conditioning regimens on transplant outcomes after MSD and MUD transplants but excludes haploidentical donor transplants. Our proposal is complementary to the currently ongoing analysis and will use the results of that study as a comparator group to compare outcomes after haploidentical donor transplants for SAA.

Patient eligibility population:

Inclusion criteria:

Patients with SAA who underwent haploidentical HCT at participating CIBMTR and EBMT centers between 2010 and 2019

Exclusion criteria:

SAA patients who had disease progression to MDS or AML prior to alloHCT

Data Requirements:

This proposed study will require no supplemental data to be collected. Data needed for this study is already collected by CIBMTR and EBMT and includes:

- Age at transplant
- Sex
- Performance score
- Donor and recipient CMV status

- Interval between diagnosis to transplant
- Previous immunosuppressive treatment, if any
- Donor age, sex and degree of match
- Graft source (PBSC or BM)
- Conditioning regimen and intensity
- Date of transplant
- Time to neutrophil and platelet recovery
- Graft failure, if any
- GVHD prophylaxis
- T cell depletion (in vivo or ex vivo), if any
- Date of development of acute GVHD, site and severity
- Date of development of chronic GVHD, site and severity
- Date of death or last follow up
- Cause of death

Relevant CIBMTR forms include: 2000, 2028, 2100, 2128

Sample requirements:
No biological samples are required for this study.

Study design:
This study is an observational retrospective registry analysis of all patients reported to the CIBMTR and EBMT who received a haploidentical HCT for SAA between 2010 and 2019.
Definitions:

- Overall Survival (OS): time to death at 1, 3 and 5 years. Death from any cause will be considered an event. Surviving patients will be censored at time of last follow-up.
- Treatment Related Mortality (TRM): Cumulative incidence of TRM at day +100 and 1, 3 and 5 year. TRM is defined as death without preceding graft failure.
- GFRS:
- Acute GVHD: Cumulative incidence of grade II-IV acute GVHD per consensus criteria at day +100, with death as competing event.
- Chronic GVHD: Cumulative incidence of limited and extensive chronic GVHD at 1 year. With death as competing event
- Graft failure: Primary graft failure (GF) will be defined as peripheral blood ANC < 0.5×10^9/L by day +28 in the absence of relapse, and secondary GF as a loss of donor chimerism (<5% donor cells) after initial engraftment and recurrent ANC < 0.5×10^9/L.
- Hematopoietic recovery:
    - Time to neutrophils (ANC) > 0.5 x109/L sustained for three consecutive days. This endpoint will be evaluated at 28-day and 100-day after HCT.
    - Time to achieve a platelet count of >20 x 109/L independent of platelet transfusions for 7 consecutive days within 28- and 100-days post-transplant.
    - This endpoint will be evaluated at 28-day and 100-day after HCT.

Baseline characteristics will be reported using descriptive statistics (counts and percentages). Comparisons between categorical variables would be done using chi-square test. The main variable of interest will be overall survival (OS) and it will be calculated from the date of transplant to the date of death or last date of follow-up. OS estimates will be calculated utilizing Kaplan-Meier analysis. Survival rates would be assessed at 1, 3 and 5 years. Non-relapse mortality would be estimated using the cumulative incidence method to account for death and graft failure as competing risks. Cumulative

incidences of neutrophil and platelet engraftment, graft failure 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.
Prognostic variables (such as age at transplant, previous immunosuppressive therapy, conditioning intensity and regimen etc.) will be evaluated for their impact on OS, graft failure and other secondary endpoints utilizing univariate analysis and multivariate analysis by cox proportional hazards analysis. Variables found to be significant in the univariate analysis would be included in the multivariate analysis. Results will be expressed as hazard ratio (HR). All P-values will be 2-sided and for the statistical analyses, $P < 0.05$ will be considered to indicate a statistically significant result.

Non-CIBMTR data source:
This is a combined study being jointly proposed to the EBMT and the CIBMTR. CIBMTR database has data on around 70 patients who have undergone haploidentical HCT for SAA (from 2013-2018) and the EBMT database has an additional 40 patients. We will combine the data from the two registries to conduct a comprehensive study with ~110 patients. This will be the largest such data set of patients undergoing haploidentical donor transplant for severe aplastic anemia.
No data linkage will be needed between CIBMTR and EBMT records.

Conflicts of interest:
Akshay Sharma: No
Queralt Salas: No
Neel Bhatt: No
Rajat Kumar: No
Régis Peffault de Latour : No
Anna Sureda: No
Pedro de Lima Prata: No

References:
1. Bacigalupo A. How I treat acquired aplastic anemia. Blood 2017;129:1428-36.
2. Bacigalupo A, Brand R, Oneto R, et al. Treatment of acquired severe aplastic anemia: bone marrow transplantation compared with immunosuppressive therapy--The European Group for Blood and Marrow Transplantation experience. Semin Hematol 2000;37:69-80.
3. Yoshida N, Kobayashi R, Yabe H, et al. First-line treatment for severe aplastic anemia in children: bone marrow transplantation from a matched family donor versus immunosuppressive therapy. Haematologica 2014;99:1784-91.
4. Eapen M, Horowitz MM. Alternative donor transplantation for aplastic anemia. Hematology Am Soc Hematol Educ Program 2010;2010:43-6.
5. Lu Y, Sun RJ, Zhao YL, et al. Unmanipulated Haploidentical Hematopoietic Stem Cell Transplantation Achieved Outcomes Comparable With Matched Unrelated Donor Transplantation in Young Acquired Severe Aplastic Anemia. Biol Blood Marrow Transplant 2018;24:1881-7.
6. Elmariah H, Kasamon YL, Zahurak M, et al. Haploidentical Bone Marrow Transplantation with Post-Transplant Cyclophosphamide Using Non-First-Degree Related Donors. Biol Blood Marrow Transplant 2018;24:1099-102.
7. Prata PH, Afanasyev B, Eikema D-J, et al. Haploidentical Transplantation Using High Dose Post-Transplant Cyclophosphamide for Patients with Aplastic Anemia : The European Group for Blood and Marrow Transplantation Experience. Blood 2018;132:486.

8. Clay J, Kulasekararaj AG, Potter V, et al. Nonmyeloablative peripheral blood haploidentical stem cell transplantation for refractory severe aplastic anemia. Biol Blood Marrow Transplant 2014;20:1711-6.
9. Dezern AE, Luznik L, Fuchs EJ, Jones RJ, Brodsky RA. Post-transplantation cyclophosphamide for GVHD prophylaxis in severe aplastic anemia. Bone Marrow Transplant 2011;46:1012-3.
10. Esteves I, Bonfim C, Pasquini R, et al. Haploidentical BMT and post-transplant Cy for severe aplastic anemia: a multicenter retrospective study. Bone Marrow Transplant 2015;50:685-9.

Characteristics of patients undergoing first allogeneic HCT for severe aplastic anemia with a haploidentical donor in the United States, 2014-2018

Characteristic	
No. of patients	**146**
Age at transplant, years - no. (%)	
Median (min-max)	22.68 (0.72-73.25)
<1 to 17	52 (35.6)
18 to 29	48 (32.9)
30 to 49	28 (19.2)
50 or older	18 (12.3)
Graft type - no. (%)	
Bone marrow	118 (80.8)
Peripheral blood	28 (19.2)
Conditioning regimen - no. (%)	
TBI/Cy/Flu	132 (90.4)
TBI/Cy/Flu/TT	2 (1.4)
TBI/Flu	2 (1.4)
Bu/Cy	1 (0.7)
Flu/Bu	2 (1.4)
Flu/Mel/TT	5 (3.4)
Cy/Flu	2 (1.4)
Post tranpslant Cy - no. (%)	
Post-transplant Cy	124 (84.9)
No post-transplant Cy	22 (15.1)
Follow-up - median (min-max)	24.11 (1.88-57.89)

Proposal: 1910-13

Title:
Impact of immunosuppressive therapy (IST) duration on hematopoietic cell transplantation (HCT) outcomes in patients with severe aplastic anemia (SAA)

Jessica E. Knight-Perry**,** MD, MS**,** jessica.knight-perry@cuanschutz.edu**,** University of Colorado School of Medicine
Michael R. Verneris, MD**,** michael.verneris@cuanschutz.edu**,** University of Colorado School of Medicine

Research Hyphothesis:
We hypothesize that SAA patients undergoing allogeneic HCT whose post-HCT IST duration is <6 months will have higher 1 year EFS when compared to patients whose IST duration is ≥6 months. Patients who receive the shorter course of IST will have improved engraftment at 1 year, less secondary graft failure, fewer infections, and less chronic kidney disease (CKD) with no difference in the incidence of GVHD.

Specific aims:
Aim 1:
Determine the difference in EFS between IST duration <6 months vs ≥6 months.

Aim 2*:*
Determine the hazard ratios for secondary graft failure, mixed chimerism, acute graft-versus-host disease (GVHD), chronic GVHD, infection, and CKD with IST duration <6 months as compared to IST duration ≥6 months.

Scientific impact:
We are unaware of any published study that has evaluated impact of IST duration on post-HCT outcomes in any non-malignant patient population.

Scientific justification:
Allogeneic stem cell transplantation is curative for patients with severe aplastic anemia, and overall survival in the modern era is excellent. However, graft failure and GVHD continue to negatively impact quality of life and event-free survival in this population. GVHD prophylaxis has largely consisted of combination IST that includes a calcineurin inhibitor and either methotrexate or mycophenolate mofetil. While these regimens are critical for GVHD prevention, they come with their own risks, including impaired engraftment, delayed immune reconstitution and nephrotoxicity. Because there is no need for graft-versus-leukemia in non-malignant disease, transplant protocols have tended to error on the side of caution. Non-malignant IST regimens frequently extend 6 months or longer, as compared to the early initiation of IST tapers (60-100 days) for patients with malignant disease. While it is reasonable to assume a longer IST duration would reduce the incidence of acute and chronic GVHD, there has been no study of the competing risks and the overall impact on EFS and OS.

Patient eligibility population:
All patients who underwent either matched sibling or unrelated donor hematopoietic stem cell transplantation using bone marrow or peripheral blood stem cells for the treatment of acquired severe aplastic anemia from January 2001 to December 2011.

Data requirements:

Patient Characteristics:

- Gender
- Race/Ethnicity
- Age at transplant
- comorbidities

Transplant Data:

- Pre-transplant therapy: any ATG, any CSA, other, none
- Donor: matched sibling donor (MSD), unrelated donor (URD)
- Graft type: bone marrow, PBSCs
- HLA match
- Time from SAA diagnosis to HCT
- Regimen: Fludarabine based, busulfan based, TBI based, other
- Serotherapy: campath, ATG, none
- TBI dose: ≤800 cGy, >800 cGy, none
- Total nucleated cell dose
- GVHD prophylaxis: tacrolimus-based, CSA-based

Outcome data:

- Date of neutrophil engraftment
- Date of platelet engraftment
- Donor chimerism: whole blood and/or lymphoid and myeloid at day 100, 6 months, 1 year, 2 years
- Acute GVHD
- Chronic GVHD
- CKD (yes/no, defined as persistent decrease in GFR <60ml/min/1.73m2)
- Infection: viral, bacterial, fungal
- Survival
- Cause of death
- Secondary graft failure

Sample requirements:

There are no sample requirements for the proposed study.

Study design:

The above variables will be obtained from the CIBMTR database and will be summarized for all eligible patients. Median and rage will be provided for all continuous variables and frequency with percentage will be provided for all categorical variables. Collected variables will be used to analyze the following primary and secondary outcomes:

Primary outcome:

- Event free survival (EFS) with events being death from any cause, secondary graft failure, and GVHD

Secondary outcomes:

- Overall survival (OS)
- Time to neutrophil and platelet recovery
- Incidence of grade II-IV acute GVHD

- Incidence of any chronic GVHD
- Incidence of CKD
- Incidence of infection
- Incidence of mixed chimerism (10-94% donor cells) at day 100, 6 months, 1 year, 2 years
- Incidence of secondary graft failure

Statistical Analysis:
The probability of EFS and OS will be calculated using the Kaplan-Meier estimator. Multivariate cox regression models will be constructed to evaluate hazard ratios for outcomes with IST duration <6 months as compared to IST duration ≥6 months. Models will be adjusted for graft type (BM vs PBSCs) and donor source (MSD vs URD) and other significant variables detected on univariate analysis.

Data source:
We plan to analyze only data from the CIBMTR Research database for the proposed study.

Conflicts of interest:
The principal investigators have no conflicts of interest to disclose.

Post-transplant immunosuppression duration for patients undergoing first allogeneic HCT for severe aplastic anemia in the United States, CRF track

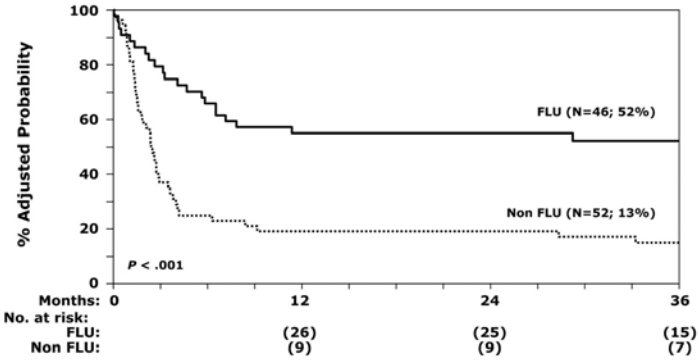
Characteristic	Less than or equal to 6 months	Greater than 6 months
No. of patients	**99**	**255**
Donor - no. (%)		
HLA-identical sibling	47 (47.5)	106 (41.6)
Unrelated donor	52 (52.5)	149 (58.4)
Graft type - no. (%)		
Bone marrow	85 (85.9)	235 (92.2)
Peripheral blood	14 (14.1)	20 (7.8)
Graft versus host disease - no. (%)		
Both Acute and Chronic GVHD	1 (1)	50 (19.6)
Acute GVHD	17 (17.2)	49 (19.2)
Chronic GVHD	2 (2)	42 (16.5)
No GVHD	79 (79.8)	114 (44.7)
Duration of post-transplant immunosuppression – median (min-max)	3.62 (0.03-5.95)	10.66 (6.02-65.89)
Follow-up - median (min-max)	50.69 (5.99-134.97)	59.01 (11.22-128.03)

Combined Proposal: 1911-142/1909-03/1911-118

Title:
Hematopoietic Stem Cell Transplantation for Fanconi anemia: Outcome and Prognostic Factors Including Donors and Grafts

Farid Boulad, MD, bouladf@mskcc.org, Memorial Sloan Kettering Cancer Center
Maria Cancio, MD, canciom@mskcc.org, Memorial Sloan Kettering Cancer Center
Jaap Jan Boelens, boelensj@mskcc.org, Memorial Sloan Kettering Cancer Center
Seth J Rotz, rotzs@ccf.org, Cleveland Clinic Foundation
Rabi Hanna, hanna2@ccf.org, Cleveland Clinic Foundation
Hesham Eissa, Hesham.eissa@cuanschutz.edu, University of Colorado Anschutz Medical Campus / Children's Hospital Colorado
Michael R Verneris, michael.verneris@cuanschutz.edu, University of Colorado Anschutz Medical Campus / Children's Hospital Colorado
Orlando Esparza, Orlando.esparza@cuanschutz.edu, University of Colorado Anschutz Medical Campus / Children's Hospital Colorado

Research hypothesis:
Fanconi anemia (FA) is an inherited bone marrow (BM) failure syndrome. It is characterized by constitutional abnormalities, endocrinopathies, aplastic anemia and increased risks for myeloid hematologic malignancies including myelodysplastic syndrome (MDS) and acute myelogenous leukemia (AML) and solid tumors (1).
FA is the "least rare" of the inherited marrow failure syndromes (IBMFS). It is estimated that approximately 3,000 - 5,000 patients have been described in the literature.
Allogeneic stem cell transplantation for patients with FA started in the 80's, as reported by Gluckman et al. (2). In a follow-up study, Gluckman et al. went on to report on the radiosensitivity in patients with FA. (3). Since these reports, standard of care transplantation for this disease was with low dose TBI, low dose cyclophosphamide (CY), and unmodified grafts.
Over the last 35 years, significant progress has been made in the HSCT of patients with FA in a stepwise fashion. Some of the progress included: the standardization in the dosing of TBI and of cyclophosphamide, improvement in supportive care, the use of fludarabine (FLU), advances of T-cell depletion including CD34 selection and alpha-beta T-cell depletion, and more recently the use of busulfan. More recent publications on HSCT for Fanconi anemia have shown that the results have significantly improved for both patients receiving grafts from HLA matched siblings and those form alternative donors. (4-10)
A review of Unrelated Donor transplantation via CIBMTR was performed by Wagner et al. in 2007 that showed that use of a fludarabine-containing conditioning regimen in the context of T-cell–depleted marrow allografts, and earlier referral for transplantation prior to excessive transfusions in patients with marrow failure (5).



We, at our center, and other, published on T-cell depleted transplantation of Fanconi anemia with cytoreduction including low dose TBI, low dose CY, standard dose FLU and T-cell depleted grafts, and more recently with cytoreduction including low dose busulfan (BU), low dose CY, standard dose FLU and T-cell depleted grafts, with disease-free survival (DFS) results now in the 80+% for transplants from alternative donors with <10% GVHD (4-10) .

A recent non-published review of CIBMTR data for HSCT for Fanconi anemia (1990-2014) is shown below. The CIBMTR shared these numbers with us, as a group of us investigators was writing guidelines about late effects in patients with FA (11, 12). These numbers show that approximately 1,300 patients would have received transplants in the last 18 years, with approximately 700 patients for the first 9 years and 700 patients for the following 9 years. Moreover, the transplants are approximately divided equally between matched related and unrelated donors (Personal communication).

Variable	Fanconi Anemia
Number of patients	1705
Age (years)	
<5	167 (10)
5-9	756 (44)
10-17	597 (35)
18+	185 (11)
Donor type	
HLA-identical sibling	726 (43)
Other relative	187 (11)
URD	792 (46)
Year of transplant	
1990-1994	234 (14)
1995-1999	341 (20)
2000-2004	436 (26)
2005-2009	354 (21)
2010-2014	340 (20)
Overall survival rate	
1-year	68 (66-70)%
3-year	63 (61-65)%
Median follow-up of survivors	61 (3-266)

Now that results of HSCT for FA have significantly improved, including for patients receiving grafts from unrelated, more questions have arisen to better understand our overall treatment and possibly continue to improve these results.
We propose to look at the event-free survival (EFS), and chronic GVHD-free EFS, with comparative questions that include the following:

- Results of HSCT in small Vs large centers
- Results of HSCT comparing 2001-2009 and 2010 - 2018
- Comparison of HSCT based on donors: HLA matched siblings, Unrelated donors and Haploidentical donors
- DFS and GvHD in patients who received unmodified Vs T-cell depleted transplants
- HSCT practice re: cytoreductive regimens: TBI Vs non-TBI regimens
- Age at transplantation i.e. 0-10, 11-18, Vs > 18 years
- Grafts: bone marrow, peripheral blood or cord blood
- Disease AA Vs MDS AML
- If available, incidence of solid tumors with risks in patients who have received TBI, and/or in patients with GvHD

Specific aims:

- Describe the outcome of HSCT in all patients with Fanconi anemia as reported to CIBMTR, including 1 and or 3 year OS, TRM, EFS, grade 2-4 acute GVHD, chronic GVHD, and cGVHD-free EFS.
- Study the impact of the following prognostic factors
    - Age
    - Hematologic status
    - Donor:
        - Matched Related Vs Mismatched Related (haploidentical) Vs Unrelated Donors
    - Graft:
        - Umbilical Cord Blood grafts Vs BM grafts Vs PBSC grafts
    - Type of cytoreduction
    - GvHD prophylaxis:
        - T-cell depletion, Vs Unmodified with calcineurin inhibitor Vs Unmodified with post transplant Cyclophosphamide
    - Transplant center size
- Obtain information on late effects and long term follow up in patients with FA, and in particular, the rate of solid tumors and study of the association of radiation and GVHD with these.

Scientific impact:
Study the outcome of HSCT for Fanconi anemia and influence of several factors on the outcome. These results could guide us on the optimal approach of HSCT for this disease as well as guide us on our future HSCT studies.

Scientific justification:
We are fortunate to have been part of a major improvement of the approach and results of HSCT for Fanconi anemia. Because it is a rare disease, it is important that we take a step back, look at the large numbers of transplants reported to the CIBMTR, and ask the important questions of how to continue to make these results better.

Patient eligibility population:
All patients registered to CIBMTR (and possibly EBMT) database who received a hematopoietic stem cell transplant for Fanconi anemi, without any restrictions.

Data requirements:
Optimally, we would prefer CRF data, that would include the different points included above:

- SCT year: 2001-2009 and 2010 - 2018
- Age 0-10 / 11-18 / > 18 years
- Disease: AA – MDS – AML
- Performance score: > 90% Vs < 90%
- Donors: Matched Related – Unrelated – Mismatched Related
  If mismatched, degree of mismatch and antigen mismatching
- Cytoreduction: TBI-based – Bu-based – Other
- Grafts BM – PBSC - UCB
- GvHD prophylaxis: T-cell depletion – Unmodified + calcineurin inhibitors Unmodified + post transplant CY
- BMT Centers: < 20 transplants per year Vs > 20 transplants per year
- Solid Tumors: If available, data re: solid tumor post transplant

Outcomes

- 1 and 3 year survival
- TRM
- Graft failure
- Grade 2-4 acute GvHD
- Chronic GvHD
- If available: Chimerism studies / DLI
- If available: Late effect outcomes by organ + secondary malignancies

Study design:

- Obtain data on all patients with FA who received an HSCT and have been reported to CIBMTR from 2001 to 2018.
- Analyze data and study prognostic factors on outcome including age, Hematologic status, donor and grafts, type of cytoreduction, GVHD prophylaxis, transplant center size, as well as the presence of post HSCT solid tumors if that data is available

Conflicts of interest:
None

References:

1. Alter BP. Diagnosis, genetics, and management of inherited bone marrow failure syndromes.Hematology Am Soc Hematol Educ Program. 2007:29-39.
2. Gluckman E, Devergie A, Schaison G, Bussel A, Berger R, Sohier J, Bernard J. Bone marrow transplantation in Fanconi anaemia. Br J Haematol. 1980 Aug;45(4):557-64.
3. Gluckman E, Devergie A, Dutreix J. Radiosensitivity in Fanconi anaemia: application to the conditioning regimen for bone marrow transplantation. Br J Haematol. 1983 Jul;54(3):431-40.
4. MacMillan ML, Auerbach AD, Davies SM, Defor TE, Gillio A, Giller R, Harris R, Cairo M, Dusenbery K, Hirsch B, Ramsay NK, Weisdorf DJ, Wagner JE. Haematopoietic cell transplantation in patients with

Fanconi anaemia using alternate donors: results of a total body irradiation dose escalation trial. Br J Haematol. 2000 Apr;109(1):121-9.

5. Wagner JE, Eapen M, MacMillan ML, Harris RE, Pasquini R, Boulad F, Zhang MJ, Auerbach AD. Unrelated donor bone marrow transplantation for the treatment of Fanconi anemia. Blood. 2007 Mar 1;109(5):2256-62.
6. Farzin A, Davies SM, Smith FO, Filipovich A, Hansen M, Auerbach AD, Harris RE. Matched sibling donor haematopoietic stem cell transplantation in Fanconi anaemia: an update of the Cincinnati Children's experience. Br J Haematol. 2007 Feb;136(4):633-40.
7. Chaudhury S, Auerbach AD, Kernan NA, Small TN, Prockop SE, Scaradavou A, Heller G, Wolden S, O'Reilly RJ, Boulad F. Fludarabine-based cytoreductive regimen and T-cell-depleted grafts from alternative donors for the treatment of high-risk patients with Fanconi anaemia. Br J Haematol. 2008 Mar;140(6):644-55.
8. MacMillan ML, DeFor TE, Young JA, Dusenbery KE, Blazar BR, Slungaard A, Zierhut H, Weisdorf DJ, Wagner JE. Alternative donor hematopoietic cell transplantation for Fanconi anemia. Blood. 2015 Jun 11;125(24):3798-804. doi: 10.1182/blood-2015-02-626002.
9. Mehta PA, Davies SM, Leemhuis T, Myers K, Kernan NA, Prockop SE, Scaradavou A, O'Reilly RJ, Williams DA, Lehmann L, Guinan E, Margolis D, Baker KS, Lane A, Boulad F. Radiation-free, alternative-donor HCT for Fanconi anemia patients: results from a prospective multi-institutional study. Blood. 2017 Apr 20;129(16):2308-2315.
10. Ebens CL, DeFor TE, Tryon R, Wagner JE, MacMillan ML. Comparable Outcomes after HLA-Matched Sibling and Alternative Donor Hematopoietic Cell Transplantation for Children with Fanconi Anemia and Severe Aplastic Anemia. Biol Blood Marrow Transplant. 2018 Apr;24(4):765-771.
11. Dietz AC, Savage SA, Vlachos A, Mehta PA, Bresters D, Tolar J, Bonfim C, Dalle JH, de la Fuente J, Skinner R, Boulad F, Duncan CN, Baker KS, Pulsipher MA, Lipton JM, Wagner JE, Alter BP. Late Effects Screening Guidelines after Hematopoietic Cell Transplantation for Inherited Bone Marrow Failure Syndromes: Consensus Statement From the Second Pediatric Blood and Marrow Transplant Consortium International Conference on Late Effects After Pediatric HCT. Biol Blood Marrow Transplant. 2017 Sep;23(9):1422-1428.
12. Dietz AC, Mehta PA, Vlachos A, Savage SA, Bresters D, Tolar J, Boulad F, Dalle JH, Bonfim C, de la Fuente J, Duncan CN, Baker KS, Pulsipher MA, Lipton JM, Wagner JE, Alter BP. Current Knowledge and Priorities for Future Research in Late Effects after Hematopoietic Cell Transplantation for Inherited Bone Marrow Failure Syndromes: Consensus Statement from the Second Pediatric Blood and Marrow Transplant Consortium International Conference on Late Effects after Pediatric Hematopoietic Cell Transplantation. Biol Blood Marrow Transplant. 2017 May;23(5):726-735

Characteristics of patients undergoing first allogeneic HCT for Fanconi anemia in the United States, Canada, South America, or Saudi Arabia

	CRF		TED	
Characteristic	**Marrow failure**	**AML/MDS**	**Marrow failure**	**AML/MDS**
No. of patients	**610**	**17**	**1047**	**44**
Age at transplant, years - no. (%)				
Median (min-max)	9.12	18.04	8.97	20.66
	(0.74-46.07)	(1.55-40.75)	(0.74-52.68)	(1.55-44.59)
<1 to 17	555 (91)	8 (47.1)	957 (91.4)	16 (36.4)
18 to 29	47 (7.7)	7 (41.2)	71 (6.8)	20 (45.5)
30 to 49	8 (1.3)	2 (11.8)	19 (1.8)	8 (18.2)
Donor type - no. (%)				
HLA-identical sibling	184 (30.2)	2 (11.8)	335 (32)	11 (25)
Other relative	90 (14.8)	3 (17.6)	157 (15)	4 (9.1)
Unrelated donor	336 (55.1)	12 (70.6)	555 (53)	29 (65.9)
Graft (Product) type - no. (%)				
Bone marrow	363 (59.5)	3 (17.6)	619 (59.1)	17 (38.6)
Peripheral blood	125 (20.5)	6 (35.3)	249 (23.8)	19 (43.2)
Umbilical cord blood	122 (20)	8 (47.1)	179 (17.1)	8 (18.2)
Year of transplant - no. (%)				
2000-2004	217 (35.6)	0	270 (25.8)	0
2005-2009	175 (28.7)	0	261 (24.9)	0
2010-2014	71 (11.6)	6 (35.3)	291 (27.8)	15 (34.1)
2015-2018	147 (24.1)	11 (64.7)	225 (21.5)	29 (65.9)
Follow-up - median (min-max)	82.66	35.66	65.1	24.38
	(2.34-216.35)	(6.32-56.97)	(2.14-216.35)	(5.82-60.36)

Proposal: 1911-150

Title:
Clinical Outcome and Health Care Utilization of Children with Hemophagocytic Lymphohistiocytosis who received Hematopoietic Stem Cell Transplantation

Ram Kalpatthi, MD, ram.kalpatthi@chp.edu, UPMC Children's Hospital of Pittsburgh
Meghan Mccormick, MD, Meghan.mccormick3@chp.edu, UPMC Children's Hospital of Pittsburgh
Archana Ramgopal, DO, rampgopala@upmc.edu, UPMC Children's Hospital of Pittsburgh
Matt Hall, PhD, Matt.Hall@childrenshospitals.org, Children's Hospital Association
Jignesh Dalal, MD, Jignesh.Dalal@uhhospitals.org, Case Western Reserve University

Research hypothesis:
We hypothesize that in children with hemophagocytic lymphohistiocytosis undergoing hematopoeitic stem cell transplantation that post-transplant survival is improved with early transplant (as opposed to late transplant), disease remission at the time of transplantation (as opposed to active disease) and transplantation at the time of initial disease remission (as opposed to in second remission or later).

Specific aims:
The primary aim of this paper will be to describe the management of patients with hemophagocytic lymphohistiocytosis proceeding to hematopoietic stem cell transplantation to identify factors related to overall survival.

Scientific impact:
- Due to the rarity of HLH, and the need for multi-country patient analysis, we propose a collaboration between CIBMTR and the PHIS databases in order to conduct a large-scale analysis of HLH patients who undergo HSCT. CIBMTR will be able to provide information regarding pre-transplant conditioning regiments, and important transplant complications that PHIS database does not include, and PHIS will provide a large pediatric population and economic burden for treating HLH patients with and without transplant, which CIBMTR currently does not include. For example, Emapalumab has been recently approved for relapsed/refractory HLH however is a costly therapy, and the economic burden of treating HLH patients with and without transplant is an area where there is much analysis to be done, which is why we are proposing a collaborative approach between PHIS and CIBMTR.
- By merging the CIBMTR database with the pediatric health information system (PHIS) database we obtain access to clinical information as well as administrative data. This will allow us to publish a comprehensive evaluation of the factors which are associated with survival.
- In particular we will plan on describing outcomes by stem cell source, conditioning regimens and graft-versus-host disease (GVHD) prophylaxis regimens. Administrative data will allow us to identify procedural interventions, medication and imaging utilization, cost of care and impact of therapy-related complications.

Scientific justification:
- Hemophagocytic Lymphohistiocytosis (HLH) is a life-threatening disease characterized by uncontrolled activation of the immune system. Five-year survival results range between 50-60% (1,2).
- Disease reactivation commonly occurs during later phases of therapy as treatment intensity is reduced. Due to the risk of recurrence, hematopoietic stem cell transplantation is recommended in

all patients with primary HLH (familial or genetic form) as well as in patients with severe disease or relapsed disease. In patients with primary HLH who underwent HSCT on HLH-04 (the most recently completed trial of HLH directed therapy), the 5 year survival was as high as 70%.

- The Histiocyte Society has put forward consensus guidelines for the treatment of HLH based on current available evidence. In reference to hematopoietic stem cell transplantation (HSCT) these guidelines state that allogeneic HSCT is the only option for long-term cure in primary HLH, prompting early discussion among physicians caring for these patients. Due to the very high risk of developing later disease, HSCT is also recommended for consideration among patients who are currently asymptomatic but carry two HLH-associated gene mutations (3).
- Prior studies have demonstrated that patients who relapse after achieving remission are at especially high risk of a mortality event (2). In addition, risk of mortality is much higher in patients who undergo HSCT with continued active disease rather than with disease in remission. These factors indicate that the decision to pursue transplantation is time-sensitive (4).
- Although there are clear recommendations for the front-line therapy of HLH and for indications to pursue HSCT, there is less guidance for the optimal management of patients in the peri-transplant period, including the ideal stem cell source, conditioning regimen and graft-versus-host prophylaxis. Although HLH-94 gave suggestions for a conditioning regimen and GVHD prophylaxis, composed of busulphan, cyclophosphamide and etoposide, one study of 86 patients found that as few as 48% of patients received all three medications, highlighting variability in provider practice (4).Allen et al also published recently prospective study of 47 patients accured by multiple pediatric institutions. Probability of intervention free engraftment was 40% inspite of Flu-Mel Intermediate timed Campath(6)
- Given the severity of disease and the importance of HSCT as the only means to achieve life-long cure, this project is needed to identify the optimal recommendations for HSCT in this vulnerable population.

Patient eligibility population:

- Our inclusion criteria will be pediatric patients (age <22 years old), undergoing HSCT for a diagnosis of HLH.
- We will include patients transplanted over the last 15 year period (2002-2017) to allow for adequate follow-up of the most recently transplanted patients.
- We will include all graft and donor types, prior treatments and transplant regimens.

Data Requirements:

- We will require access to the “Hemophagocytic Lymphohistiocytosis Pre-HCT Data” collection form and the “Hemophagocytic Lymphohistiocytosis Post-HCT Data” collection form.
- We will collect supplemental data regarding health care utilization and long-term follow-up through the PHIs database. We will not require collection of supplemental data through the CIBMTR database.

Sample requirements:

No biologic samples will be required.

Study design:

We will use data from CIBMTR and the PHIS database to determine the length of elapsed time between initial diagnosis with HLH and HSCT. We will use logistic regression to determine the impact on length of time from diagnosis to transplantation on survival. CIBMTR data on clinical and laboratory features at the time of transplantation will be used to establish disease remission, which will be similarly analyzed

by regression models to determine the impact on survival. Survival will be determined through data on post-HCT data collection forms maintained by CIBMTR as well as through mortality data obtained from PHIS database. We will complete univariate and multivariate models to determine the effect of adjustment for confounding variables on outcome.

- For estimates of healthcare utilization we will use Wilcoxon rank-sum tests or chi-squared tests based on continuous versus categorical outcomes.

Data source

- CIBMTR Research Database
- Pediatric Health Information System (PHIS) Database.
- Linkage of the datasets will be required in order to access information on the use of medications administered, procedures, blood bank resources, imaging studies and cost of hospitalization and medical care. Although the CIBMTR collects data on HLH-directed therapies prior to transplantation, the use of conditioning regimens and the use of GVHD prophylaxis, the PHIS database will allow for the collection of additional information such as the use of prophylactic and treatment antibiotics and other medications administered for supportive care practices. Other data elements listed are not available in the CIBMTR database.
- We will link databases through the use of indirect patient identifiers, which will allow all data to remain de-identified. The process of using indirect identifiers to merge the PHIS database with other database sources has been previously described with over 90% concordant matches (5). The exact variables to be used for linkage have yet to be determined but will likely include treatment site, gender, month and year of birth and year of HSCT. We will develop a stepwise merge algorithm with assistance from analysts at the PHIS database

Conflicts of interest:

No

References:

1. Henter J-I, Samuelsson-Horne A, Aricò M, Egeler RM, Elinder G, Filipovich AH, et al. Treatment of hemophagocytic lymphohistiocytosis with HLH-94 immunochemotherapy and bone marrow transplantation. Blood. 2002 Oct 1;100(7):2367–2373.
2. Bergsten E, Horne A, Aricó M, Astigarraga I, Egeler RM, Filipovich AH, et al. Confirmed efficacy of etoposide and dexamethasone in HLH treatment: long-term results of the cooperative HLH-2004 study. Blood. 2017 Dec 21;130(25):2728–2738.
3. Ehl S, Astigarraga I, von Bahr Greenwood T, Hines M, Horne A, Ishii E, et al. Recommendations for the Use of Etoposide-Based Therapy and Bone Marrow Transplantation for the Treatment of HLH: Consensus Statements by the HLH Steering Committee of the Histiocyte Society. J Allergy Clin Immunol Pract. 2018 Jul 4;6(5):1508–1517.
4. Horne A, Janka G, Maarten Egeler R, Gadner H, Imashuku S, Ladisch S, et al. Haematopoietic stem cell transplantation in haemophagocytic lymphohistiocytosis. Br J Haematol. 2005 Jun;129(5):622–630.
5. Li Y, Hall M, Fisher BT, Seif AE, Huang Y-S, Bagatell R, et al. Merging Children's Oncology Group Data with an External Administrative Database Using Indirect Patient Identifiers: A Report from the Children's Oncology Group. PLoS One. 2015 Nov 25;10(11):e0143480.
6. Carl E. Allen, Rebecca Marsh, Peter Dawson**,** et al Reduced-intensity conditioning for hematopoietic cell transplant for HLH and primary immune deficiencies**,** Blood**.** 2018 Sep 27; 132(13): 1438–1451

Characteristics of pediatric patients undergoing first allogeneic HCT for HLH in the United States, CRF track only

Characteristic	
No. of patients	**295**
Age at transplant, years - no. (%)	
Median (min-max)	1.33 (0.18-17.79)
< 1	134 (45.4)
1 to 5	110 (37.3)
6 to 10	26 (8.8)
11 to 18	25 (8.5)
Interval from diagnosis to transplant, months - no. (%)	
Median (min-max)	5.1 (1.15-162.53)
Less than or equal to 3 months	38 (12.9)
3 to 6 months	138 (46.8)
6 to 12 months	62 (21)
Greater than 12 months	57 (19.3)
Donor type - no. (%)	
HLA-identical sibling	17 (5.8)
Other relative	18 (6.1)
Unrelated donor	260 (88.1)
Year of transplant - no. (%)	
2000-2004	67 (22.7)
2005-2009	121 (41)
2010-2014	64 (21.7)
2015-2018	43 (14.6)
Follow-up - median (min-max)	86.91 (6.18-216.41)