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MINUTES AND OVERVIEW PLAN
CIBMTR WORKING COMMITTEE FOR PEDIATRIC CANCER
Salt Lake City, UT
Sunday, April 24, 2022, 12:15 p.m. – 2:00 p.m. MDT

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1. **Introduction**
   The Pediatric Cancer Working Committee (PCWC) met on Sunday, April 24, 2022, at 12:18 p.m. The chairs, scientific director, and statistical team were all presented at the meeting. Dr. Greg Yanik attended the meeting virtually. Attendees were asked to have their name badges scanned at the front gate for attendance purposes and to maintain the committee membership roster.
   Dr. Larisa Broglie introduced herself as the new Scientific director and the PCWC leadership, then she introduced the new master's level statistician Rasha Atshan.
   Dr. Broglie proceeded to take the attendees through the committee's goals, expectations, and limitations. Dr. Broglie announced that the WC leadership is looking forward to WC members' engagement in all stages of a study's process. Dr. Broglie provided an overview of the CIBMTR, the data sources available for future study proposals, and public datasets that are available on the CIBMTR website. Dr. Broglie informed the attendees of the Information Request service that is available on the CIBMTR website. Then, she informed the attendees that the WC leadership is going to provide updates on ongoing studies and present the new studies proposals. Finally, Dr. Broglie introduced Dr. Yanik to the attendees as the next speaker to provide an overview of the Pediatric Cancer Accruals report summary.

2. **Accrual summary**
   Dr. Yanik introduced himself to the attendees then he directed the attendees' attention to the accrual summaries included in the meeting materials. Dr. Yanik provided a concise summary of the numbers of pediatric patients available in the CIBMTR database.

3. **Presentations, Published or Submitted Papers**
   Dr. Broglie introduced Dr. Schultz to the attendees. Dr. Schultz directed the attendee's attention to the working committee materials for information regarding the abstract presentation and to presentation that are accepted at various conferences:

Dr. Schultz introduced Dr. Tristan Knight to attendees and requested Dr. Knight to present the progress of his study. Dr. Knight introduced himself and thanked the WC chairs and statistical team for their leadership and work to complete the following study. Then, Dr. Knight provided an overview of the study and the corresponding findings. Dr. Broglie announced Dr. Knight's poster presentation date, time, and location.

a. **PC20-01** Autologous graft cell dose and post-transplant granulocyte colony stimulating factor in post-transplant outcomes among pediatric patients undergoing Autologous Hematopoietic Stem Cell Transplantation. (Tristan Knight; Donna A. Wall; Kanhatai Chiengthong). Manuscript in preparation**.** ***Poster Presentations at 2022 Tandem meeting.***

4. Studies in Progress

Dr. Schultz provided a brief overview of the committee's portfolio of active studies. He began with PC19-03, a collaboration study between CIBMTR and EBMT, this study requires merging North America and European databases. Dr. Schultz emphasized the difficulties of merging two databases that are collected differently. Dr. Schultz also emphasized that PC19-03 will be used as template for future collaboration between CIBMTR and EBMT to study uncommon diseases and answer uncommon scientific questions.

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

b. **PC19-03** The impact of pre-transplant extramedullary disease on the outcome of Allogeneic Hematopoietic Cell Transplantation for Acute Myeloid Leukemia in Children. (H Rangarajan/P Satwani/K Rao/D Chellapandian/Juliana Silva), ***Data file preparation.***

c. **PC20-01** Autologous graft cell dose and post-transplant granulocyte colony stimulating factor in post-transplant outcomes among pediatric patients undergoing Autologous Hematopoietic Stem Cell Transplantation. (Tristan Knight; Donna A. Wall; Kanhatai Chiengthong), ***Manuscript in preparation.***

d. **PC20-02** Germline genetics of pediatric Myelodysplastic Syndromes (MDS). (Jenny Poynter; Logan Spector), ***Sample Typing.***

5. PCWC Logistics

Dr. Schultz provided an overview of WC membership then he encouraged young investigators to engage in research with CIBMTR. He also encouraged senior investigators to collaborate and develop future study proposals with young investigators. Then, Dr. Schultz reminded the attendees of PCWC goals, expectations, and limitations. Dr. Schultz provided an overview of the rules of authorship at CIBMTR, and he reminded the attendees of the proposals' voting process.

6. Future/Proposed Studies

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

a. **Prop 2110-19:** Transplantation and Cellular Therapy for children and young adults with Down's Syndrome and Acute Leukemia. (Seth Rotz; Rabi Hanna), (Attachment 4).

Dr. Rotz presented the proposal on behalf of the group. The proposal hypothesizes that children and adolescents & young adults (AYA) with Down's syndrome (DS) and acute leukemia will have improved hematopoietic cell transplantation (HCT) outcomes in the more recent era. Further, the proposal hypothesizes that children and AYA with DS and relapsed/refractory Acute Lymphoblastic Leukemia (ALL) undergoing CAR T-cell therapies will have improved outcomes compared to those who underwent HCT. The objectives of the study are to determine if outcomes for children and AYA with DS and acute leukemia (ALL and AML) undergoing HCT have improved in more recent eras. And to Compare outcomes of CAR T-cell therapy for children and AYA with DS and relapsed/refractory ALL to HCT.

<u>Comments from discussion:</u>

i. *A comment regarding the outcomes of the study. Will there be a fundamental difference between the patients who are receiving CAR-T therapy compared to patients who receive HCT (in demographics, biology, outcomes, etc). Dr. Rotz replied that he doesn't know if the characteristics of CAR-T and HCT patients will be an exact match, and this could be a limitation of the study regarding relapse risk. However, he noted that focusing on the overall survival will not have such a limitation. Dr. Yanik added that a recent world data show that there is an increase in the number of patients with Down's syndrome and ALL who have received CART with an outstanding overall survival.*

ii. *A couple of attendees expressed enthusiasm for the study and express that the study presents a good question by looking at Down's syndrome and HCT outcomes, while comparing CAR-T and HCT can be complicated since there are confounding factors in deciding between CAR-T and HCT such as parental or legal guardian preferences.*

iii. *Another comment was made regarding the study years between 2000-2020, it is a large time span for the study and the field had changed in the past ten years. The attendee asked if Dr. Rotz considered focusing on comparing CAR-T and HCT between 2010-2020?*

iv. *An attendee noted that the Down's syndrome with AML is interesting, but children with Down's syndrome are more likely to develop M7 AML and asked how many cases have M7 AML. M7 may be*

difficult to combine with other AML subtypes. Dr. Rotz replied that the data collection forms need to be reviewed to see what type of data are collected for the different AML subtypes. Dr. Rotz added that considering the different subtypes of AML is a good point but there is different way to view the data for examples age and therapy type.

v. *A question was asked whether if biological samples are considered as a part of the study analysis since recent Down's syndrome and Chromosome 21 data showed that there are four of six interferon receptors. Dr. Rotz replied that he wasn't aware of these factors and Dr. Qayed added that CIBMT needs to investigate the biological samples inventory for patients with Down's syndrome before answering the question.*

b. **Prop 2110-43:** Evaluation of Allogeneic Hematopoietic Cell Transplantation outcomes and prognostic factors in Acute Megakaryoblastic Leukemia. (Akshay Sharma; Neel S. Bhatt), (Attachment 5).

Dr. Sharma presented the proposal on behalf of the group. The proposal hypothesizes that Allogeneic Hematopoietic Cell Transplantation (Allo-HCT) provides curative therapy for patients with Acute Megakaryoblastic Leukemia (AMKL), with improved outcomes in those who are transplanted in first complete remission. The objectives of this proposal are: to determine the outcomes (OS, DFS, NRM, Relapse) of Allo-HCT in AMKL patients and identify prognostic factors associated with improved outcomes, to determine the effect of remission status (first remission, second remission, progressive/refractory disease) on outcomes (OS, DFS, NRM, Relapse) in patients receiving Allo-HSCT for AMKL, and to determine the outcomes in AMKL utilizing alternative donor sources and compare them to traditional matched-related donor transplants.

<u>Comments from discussion:</u>

An attendee suggested combining Dr. Rotz proposal 2110-19 with Dr. Sharma proposal 2110-43. Dr. Sharma agreed with the suggestion, and he acknowledge the positive impact of combining the two proposals.

c. **PROP 2110-45/2110-81:** <u>Combined proposal:</u> Outcomes after post-transplant Cyclophosphamide based haploidentical Hematopoietic Cell Transplantation in pediatric patients with Acute Leukemia and Myelodysplastic Syndrome. (Akshay Sharma; Neel S. Bhatt; Hemalatha Rangarajan; Prakash Satwani), (Attachment 6).

Dr. Sharma presented this proposal on behalf of the group. The proposal hypothesizes that haploidentical Hematopoietic Cell Transplantation (haplo HCT) using post-transplant Cyclophosphamide (PT-Cy) in pediatric patients (≤ 21 years) with Acute Leukemia and Myelodysplastic Syndrome (MDS) is associated with a disease-free survival (DFS) that is comparable to HLA matched donor HCT and better than mismatched unrelated donor HCT. Further, haplo HCT with PT-Cy is associated with a comparable incidence of acute and chronic graft versus host disease (GVHD) to HLA matched donor HCT and the incidence is lower than mismatched unrelated donor HCT. Further, the proposal hypothesizes that through the CIBMTR database, risk factors for GVHD in pediatric patients receiving haploidentical transplantation using PT-Cy can be identified. The objectives of the proposal are: to compare the DFS among pediatric patients (≤ 21 years) with acute Leukemia and MDS who have undergone haplo HCT with PT-Cy and those undergoing HLA matched sibling donor HCT, matched unrelated donor HCT, or mismatched unrelated donor HCT, and to describe the incidence, characteristics, and risk factors for

acute and chronic GVHD in children and adolescents undergoing PT-Cy based haploidentical HCT.

Comments from discussion:

i. *A question was raised regarding excluding mismatch Cord Blood as comparative group, Dr. Sharma replied that including Mismatch CB is great suggestion and if the proposal is selected to move forward as PCWC study, he will consider looking into mismatch CB group.*

ii. *The next comment addressed using PT-Cy for matched unrelated and mismatched unrelated donors in adult patients, which had good results in preventing GVHD. Since the pediatric data is outdated in comparison to the adult data regarding PT-Cy, Dr. Sharma agreed with the attendee, and he added that there is enough adults data that compares the matched unrelated and mismatched unrelated donors, while not the same volume of data is available for pediatrics data.*

iii. *Another comment suggested investigating the possible outcomes from using PT-Cy such as overall survival, relapse free survival, and non-relapse mortality; and investigating the connection between viral infections and HCT when using a haploidentical donor.*

d. **Prop 2110-165:** Evaluating predictors of access and outcomes with Hematopoietic Cell Transplantation (HCT) in pediatric and adolescent patients with relapsed/refractory classical Hodgkin Lymphoma (cHL) after treatment on an initial cooperative group clinical trial. (Sharon M. Castellino; Justine Kahn), (Attachment 7).

Dr. Kahn presented the proposal virtually on behalf of the group. This proposal hypothesizes that outcomes following relapse of Hodgkin Lymphoma, including receipt of Hematopoietic Cell Transplantation HCT, will differ by age and race/ethnicity among patients receiving up-front response-based therapy or salvage therapy for classical Hodgkin Lymphoma (cHL) on Children's Oncology Group (COG) trials. The objectives of this proposal are: to compare outcomes by histologic category, to compare outcomes by donor platform and conditioning intensity and finally to develop a predictive model for survival post-AlloHCT for MDS/MPN's.

Comments from discussion:

i. *Dr. Schultz added a comment that this will be the first study merge the CIBMTR and COG data. Dr. Broglie added that the CIBMTR and COG data has been linked to complete clinical trials but combining the two datasets to complete a study has not been done previously. Dr. Qayed asked if the patient's population will based on patient enrolled in COG trials, linking the patient's data to the follow up data from CIBMTR database. Dr. Kahn replied that the study will use patients' data whose disease relapsed from the COG trials adding transplant and outcome data from CIBMTR database.*

ii. *A Question was asked about the difficulties of linking the COG trials and CIBMTR databases? Dr. Broglie replied that linking the databases can be performed but will require time and collaboration. Dr. Kahn added that linking the databases has not been done previously, and she added that cHL is a rare disease and the population consist of pediatric patients. Dr. Broglie added that the logistic of data sharing & combining are time consuming but linking the two databases is feasible.*

e. **Prop 2110-211:** Outcomes of children and adolescents undergoing Autologous or Allogeneic Hematopoietic Stem Cell Transplantation for first relapse or refractory non-Hodgkin Lymphoma. (Jennifer Belsky; Sarah Alexander), (Attachment 8).

Dr. Belsky presented this proposal virtually on behalf of the group. This proposal hypothesizes that pediatric patients with first relapse or refractory (R/R) non-Hodgkin lymphoma (NHL), excluding Lymphoblastic Lymphoma (LL), who have undergone Allogeneic Hematopoietic Stem Cell Transplantation (Allo-HSCT) had a superior event free survival (EFS) than those who received Autologous Hematopoietic Stem Cell Transplantation (Auto-HSCT), when accounting for disease subtype, time in first remission and disease status at time of transplant. The objectives of this proposal are: 1) to compare event free survival (EFS) at one year for children and adolescents who have undergone Allo-HSCT or Auto-HSCT for R/R NHL, excluding LL and accounting for disease subtype, time in first remission and disease status at the time of transplant; 2) to compare overall survival (OS) at 5 years for those who have undergone Allo-HSCT or Auto-HSCT for R/R NHL, time in first remission and disease status at the time of transplant, and 3) to compare treatment related mortality at 100 days for children and adolescents who have undergone Allo-HSCT or Auto-HSCT.

<u>Comments from discussion:</u>

A question was asked about whether patients who receive both Allo and Auto transplant will be considered in the study population. Dr. Belsky replied that the study team is considering including the patients who received multiple transplants in the study population. Dr. Alexander added that the number of patients who received multiple transplants is small, and those patients will not be included in the primary analysis, but the descriptive analysis results could potentially be examined.

f. **Prop 2110-272:** Hematopoietic Stem Cell Transplant outcomes for Infant Acute Lymphoblastic Leukemia. (Nahal Rose Lalefar), (Attachment 9).

Dr. Lalefar presented this proposal. This proposal hypothesizes that Disease free survival and overall survival for infant B-cell ALL will be higher for infants who undergo Hematopoietic Stem Cell Transplant (HSCT) in complete remission (CR1) compared to historical controls if they received their transplant within the last decade. The objectives of this proposal are: to determine the Leukemia free survival and overall survival at 1yr and 3yr for infants with Acute B-Lymphoblastic Leukemia (CR1 vs other) who received HSCT between 2008-2018.

<u>Comments from discussion:</u>

i. *An attendee made a comment about expanding the year of transplant up to 2020 or 2021 to increase the number of cases in the study. Dr. Schultz added that some investigators debate that transplant don't improve the outcomes of two types of ALL, and AMKL is one of them. Dr. Schultz added that if this study can answer the scientific question that will be an important contribution to this debate.*

ii. *An attendee added this is a good scientific question specially if the MRD are included in the study's population.*

iii. *A virtual attendee asked since in the past ten years only very high-risk patients had BMT, how is the study team going to consider them in the population? Dr. Lalefar replied that after*

investigating the AMKL patients who had transplant, and she found that not only high-risk patients had a transplant.

g. **Prop 2110-274:** Developing a pediatric Hematopoietic Cell Transplantation-Composite Risk (pHCT-CR) Score to predict outcomes in children with Acute Leukemia undergoing Hematopoietic Cell Transplantation. (Madhavi Lakkaraja; Brian Friend), (Attachment 10).

Dr. Lakkaraja presented this proposal on behalf of the group. This proposal hypothesizes that a novel prognostic tool termed the pediatric hematopoietic cell transplantation-composite risk (pHCT-CR) score will be able to predict overall survival in children undergoing first Allogeneic HCT with Acute Myeloid Leukemia (AML) and Acute Lymphoid Leukemia (ALL). The objectives of this proposal are: to develop and validate a pHCT-CR score in children with ALL and AML who underwent their first allogeneic HCT, and to compare performance of pHCT-CR score to previously described risk scores including pediatric DRI and original HCT-CI.

<u>Comments from discussion:</u>

An attendee asked how is MRD will be defined? Dr. Lakkaraja clarified that the MRD will be defined according to the CIBMTR definition of MRD to stay consistent with CIBMTR database.

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

*Dr. Larisa reminded the attendees that proposal "**Prop 2110-38:** Impact of Graft Versus Host Disease following Allogeneic Hematopoietic Cell Transplantation on Leukemia free survival in Hematologic Malignancies within the pediatric disease Risk Index Risk Stratification." was selected to be presented at the Collaborative Session.*

7. Dropped proposed studies

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

a. **Prop 2109-16:** Use of Thiotepa in Stem Cell Transplantation for pediatric Acute Lymphoblastic Leukemia. ***Dropped due to limited availability of resources.***

b. **Prop 2110-67:** Impact of Non-HLA donor characteristics in pediatric patients receiving haploidentical Stem Cell Transplantation for Malignant and Non-Malignant diseases. ***Dropped due to overlapping with current study/publication.***

c. **Prop 2110-77:** Outcomes of Allogeneic Hematopoietic Cell Transplantation in pediatric patients with non-remission Acute Leukemia. ***Dropped due to small sample size.***

d. **Prop 2110-170 / 2110-330:** Post-transplant Cyclophosphamide vs. TCR αβ depletion approaches for Haploidentical Transplant in pediatric patients with Acute Leukemias and Myelodysplastic Syndromes. ***Dropped due to small sample size.***

e. **Prop 2110-183:** Comparison of relapse incidence following Allogeneic Hematopoietic Cell Transplantation among children with Philadelphia Positive like versus non-Philadelphia Positive like Acute Lymphoblastic Leukemia. ***Dropped due to the need for supplemental data.***

f. **Prop 2110-261:** Outcomes of Myeloablative Chemotherapy with Autologous Hematopoietic Cell rescue in pediatric patients with Choroid Plexus Carcinoma. ***Dropped due to small sample size.***

g. **Prop 2110-282:** The burden of intermediate infections in children, adolescents, and young adults with Hematologic Malignancies undergoing Allogeneic Hematopoietic Cell Transplantation. ***Dropped due to the need for supplemental data.***

h. **Prop 2110-305:** Outcomes of Allogenic Hematopoietic Cell Transplantation in children and young adults with Advance Stage Chronic Myeloid Leukemia. ***Dropped due to small sample size.***

8. Concluding Notes

*The meeting was adjourned at **2:00** p.m. After the new proposals were presented, each attendee had the opportunity to vote using the Tandem mobile application or Tandem website. Based on the voting results, current scientific merit, and impact of the studies on the field, the PCWC leadership will determine which studies will move forward as the committee's research portfolio for the upcoming year.*

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Working Committee Overview Plan 2022-2023

Study Number and Title	Current Status	Chairs Priority
PC19-02: Does mixed peripheral blood T cell chimerism predict relapse?	Protocol development	2
PC19-03: The impact of pre-transplant extramedullary disease on the outcome of allogeneic hematopoietic cell transplantation for Acute Myeloid Leukemia in Children- A combined CIBMTR and EBMT analysis	Datafile preparation	2
PC20-01: Autologous graft cell dose and post-transplant granulocyte colony stimulating factor in post-transplant outcomes among pediatric patients undergoing autologous hematopoietic stem cell transplantation	Manuscript preparation	3
PC20-02: Germline genetics of pediatric myelodysplastic syndromes.	Sample Typing	3
PC22-01: Impact of Graft Versus Host Disease following Allogeneic Hematopoietic Cell Transplantation on Leukemia free survival in Hematologic Malignancies within the pediatric disease Risk Index Risk Stratification	Protocol Pending	2
PC22-02: Evaluating predictors of access and outcomes with Hematopoietic Cell Transplantation (HCT) in pediatric and adolescent patients with relapsed/refractory classical Hodgkin Lymphoma (cHL) after treatment on an initial cooperative group clinical trial.	Protocol Pending	3

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Working Assignments for Working Committee Leadership (May 2022)

Muna Qayed	**PC19-02:** Does mixed peripheral blood T cell chimerism predict relapse?
	PC22-01: Impact of Graft Versus Host Disease following Allogeneic Hematopoietic Cell Transplantation on Leukemia free survival in Hematologic Malignancies within the pediatric disease Risk Index Risk Stratification.
Gregory Yanik	**PC20-01:** Autologous graft cell dose and post-transplant granulocyte colony stimulating factor in post-transplant outcomes among pediatric patients undergoing autologous hematopoietic stem cell transplantation.
	PC22-02: Evaluating predictors of access and outcomes with Hematopoietic Cell Transplantation (HCT) in pediatric and adolescent patients with relapsed/refractory classical Hodgkin Lymphoma (cHL) after treatment on an initial cooperative group clinical trial.
Kirk Schultz	**PC19-03:** The impact of pre-transplant extramedullary disease on the outcome of allogeneic hematopoietic cell transplantation for Acute Myeloid Leukemia in Children- A combined CIBMTR and EBMT analysis.
	PC20-02: Germline genetics of pediatric myelodysplastic syndromes.