Not for publication or presentation

MINUTES AND OVERVIEW PLAN
CIBMTR WORKING COMMITTEE FOR ACUTE LEUKEMIA
Salt Lake City, UT
Monday, April 25, 2022, 6:30 AM - 8:15 AM MDT

Co-Chair:	**Partow Kebriaei, MD; M.D. Anderson Cancer Center, Houston, TX; Telephone: 713- 792-8750; E-mail: pkebriae@mdanderson.org**
Co-Chair:	**Mark R. Litzow, MD; Mayo Clinic, Rochester, MN; Telephone: 206-667-4961; E-mail: litzow.mark@mayo.edu**
Co-Chair:	**Christopher Hourigan, MD, Dphil; National Heart Blood and Lung Institute; E-mail: hourigan@nih.gov**
Scientific Director:	**Kristin Page, MD, CIBMTR Statistical Center, Milwaukee, WI; E-mail: kpage@mcw.edu**
Statistical Director:	**Mei-Jie Zhang, PhD, CIBMTR Statistical Center, Milwaukee, WI; Telephone: 414-456-8375; E-mail: meijie@mcw.edu**
Statistician:	**Karen Chen, MS, CIBMTR Statistical Center, Milwaukee, WI; Telephone: 414-805-0834; E-mail: kachen@mcw.edu**

1. Introduction

Dr. Partow Kebriaei called the meeting to order and introduced the current LKWC leadership members. Dr. Christopher Hourigan discussed the goals, expectations, and limitations of the LKWC and criteria that must be met to be considered for authorship on a manuscript. Details on publicly available datasets on the CIBMTR website were discussed. Dr. Hourigan explained the proposal scoring process and guidelines.

2. Accrual summary

The accrual summary was not presented due to time constraints but was made available to attendees as an attachment.

3. Presentations, published or submitted papers

Details regarding presentations and publications were not presented due to time constraints but were made available to attendees as an attachment.

4. Studies in progress

Details regarding the studies in progress were not presented due to time constraints but were made available to attendees as an attachment.

5. Future/proposed studies

Drs. Kebriaei and Hourigan led this session.

a. **PROP 2110-21/2110-168:** Impact of *IDH1* and *IDH2* mutations on outcomes of acute myeloid leukemia patients undergoing allogeneic hematopoietic cell transplantation (S Iyer/E Chen/A Jimenez/Y-B Chen)

Dr. Sunil Iyer presented the proposal. The main objective of the proposed study is to compare post-transplant outcomes between patients with mutations in IDH1 or IDH2 and patients with wild type IDH1 and IDH2. A total of 2058 patients aged 18 years or older underwent allo-HCT for AML in 2013-2020 and had IDH1 and IDH2 molecular testing completed. In this cohort, 150 had mutated IDH1, 273 had mutated IDH2, 42 had both mutated IDH1 and IDH2, and 1593 had wild type IDH1 and IDH2.

Attendees questioned how patients who received maintenance therapy or those who only test positive for mutation at diagnosis and not after treatment will be handled. A comment was received noting the higher frequency of MRD positivity in the groups with IDH mutations.

b. **PROP 2110-29/2110-120/2110-128/2110-153/2110-204/2110-220/2110-294/2110-307/2110-326:** Outcomes of allogeneic hematopoietic cell transplantation following low intensity versus high intensity therapy for AML and MDS in first complete morphologic remission (A Jimenez/T Wang/J Reagan/A Pelcovits/M Salas/A Mussetti/H Murthy/J Foran/K Sahasrabudhe/S Wall/ J Esteve/N Ali/B Sandmaier/J Ignatz-Hoover/B Tomlinson/B Wirk)

Dr. Naveed Ali presented the proposal. The main objective of the proposed study is to compare post-transplant outcomes between AML and MDS patients who received low intensity induction therapies with those who received high intensity induction therapies. A total of 2592 patients aged 18 years or older underwent first allo-HCT for AML in first complete remission in the years 2015-2020, with 2352 receiving high intensity induction and 240 receiving low intensity induction. A total of 246 patients aged 18 years or older underwent first allo-HCT for MDS in complete remission in the years 2015-2020, with 55 receiving high intensity induction and 191 receiving low intensity induction.

A question was raised about how patients who received both low and high intensity induction will be handled. It was suggested to include post-transplant maintenance treatment and TP53 mutation status in the analysis and to consider grouping patients based on characteristics other than induction intensity, as treatment choice is influenced by disease related factors.

c. **PROP 2110-104/2110-216:** Development of pre-transplant risk scores for patients undergoing allogeneic HCT for acute leukemia transplanted in complete remission or with relapsed/refractory disease (I Novitzky-Basso/M Walji/F Michelis/B Gyurkocza)

Dr. Moneeza Walji presented the proposal. The main objective of the proposed study is to evaluate the influence of pre-transplant factors on post-transplant outcomes of acute leukemia patients and to develop separate risk scores for patients transplanted in complete remission and patients transplanted with relapsed or refractory disease. A total of 5614 patients aged 18 years or older received first allo-HCT for acute leukemia in 2009-2019, with 4606 in complete remission and 1008 with relapsed/refractory disease prior to transplant.

A question was raised about whether MRD positive patients will be grouped with CR patients.

d. **PROP 2110-121:** Impact of Pretransplant Mutation Topography on Cumulative Incidence of Relapse after Allogeneic Haematopoietic Cell Transplants for T-Cell Acute Lymphoblastic Leukemia (Y Liang/ P Gale)

Dr. Yang Liang presented the proposal. The main objective of the proposed study is to perform mutational genetic analysis on pre-transplant blood samples from patients who received HCT for T-cell ALL and to evaluate the impact of these mutations on the incidence of relapse. A total of 1269 patients who underwent first allo-HCT for T-cell ALL in 2000-2020 were identified as having blood samples available through the NMDP biorepository.

Attendee comments included concerns about whether the sample quality will be sufficient for RNA-seq and the possible overlap between this study and existing work done on mutation classifiers for T-cell ALL. Questions were raised about the correlation between mutation topography during diagnosis and immediately before transplant and if early T-cell precursor ALL will be analyzed separately.

e. **PROP 2110-206:** Comparison of transplant outcomes using fludarabine, cyclophosphamide and total body irradiation (TBI) vs. fludarabine, melphalan and TBI based reduced-intensity conditioning regimens in patients undergoing haploidentical stem cell transplant (H Alkhateeb/A Baranwal)

Dr. Anmol Baranwal presented the proposal. The main objective of the proposed study is to compare post-transplant outcomes of AML patients who received haploidentical HCT with fludarabine, melphalan and TBI (Flu/Mel/TBI) to those of patients who received fludarabine, cyclophosphamide and TBI (Flu/Cy/TBI) conditioning. A total of 1423 patients aged 18 years or older underwent first allo-HCT from a haploidentical donor for AML in 2008-2020, with 208 receiving 208 Flu/Mel/TBI and 1423 receiving Flu/Cy/TBI.

Several suggestions were made including adding Flu/Mel/Thio as a third group, stratifying the study population by melphalan dose, and adding TBI dose as an analysis variable. A concern was raised regarding the increase in post-transplant cyclophosphamide use in the last few years and whether this would bias the results.

f. **PROP 2110-260:** Outcomes of allogeneic hematopoietic cell transplantation for relapsed acute myeloid leukemia based on minimal residual disease status: CIBMTR analysis (G Murthy/W Saber)

Dr. Guru Murthy presented the proposal. The main objective of the proposed study is to compare post-transplant outcomes for relapsed AML patients based on MRD status. A total of 1842 patients aged 18 years or older underwent first allo-HCT for AML in second or greater complete remission in 2008-2019, with 1186 testing MRD negative, 473 testing MRD positive, and 183 with unknown status prior to HCT.

Attendees suggested including data on the MRD testing methods used and adding time from diagnosis to achieving CR2 and time between CR2 and transplant as variables in the analysis.

g. **PROP 2110-293/2110-319:** Impact of Clonal Evolution in Post-Transplantation Relapsed Myeloid Neoplasms (L Williams/A-S Mirza/L Gowda/C Lai)

Dr. Lacey Williams presented the proposal. The main objective of the proposed study is to evaluate outcomes for AML and MDS patients after allo-HCT in the modern era and characterize molecular and cytogenetic mutations in relapsed patients. 2184 patients received first allo-HCT for AML and 2155 patients received first allo-HCT for MDS in 2011-2020 who relapsed after transplant.

A question was asked about the availability of post-transplant maintenance therapy date and dosing data. A comment was made that there may be multiple mechanisms aside from clonal evolution that lead to relapse.

h. **PROP 2110-298:** Impact of Pre-Transplant Extramedullary Disease on Allogeneic Transplant Outcomes in Acute Lymphoblastic Leukemia (ALL) (R Ramlal)

Dr. Reshma Ramlal presented the proposal. The main objective of the proposed study is to compare post-transplant outcomes between ALL patients with and without extramedullary disease (EMD) prior to transplant. A total of 2312 patients aged 18 years or older underwent first allo-HCT for ALL in 2008-2018, including 387 with extramedullary disease and 1925 without extramedullary disease before transplant.

Attendees asked questions about availability of treatment data for EMD and documentation of remission status for patient with non-CNS EMD. It was suggested to analyze patients with CNS and non-CNS EMD separately.

i. **PROP 2110-323:** Allogeneic transplant for Relapsed Refractory ALL in Modern Era (L Gowda/A Zeidan)

Dr. Lohith Gowda presented the proposal. The main objective of the proposed study is to compare post-transplant outcomes of relapsed or refractory B-cell ALL patients who received novel therapies with those who received conventional chemotherapy. A total of 1040 patients underwent first allo-HCT for relapsed or refractory B-cell ALL in 2011-2020, with 289 receiving novel therapies and 751 receiving standard therapies.

Comments were received on appropriately accounting for a patient who received multiple therapies and limitations in available data on treatments used before transplant.

j. **PROP 2110-347:** Role of Post Remission Consolidation Therapy Prior to Haploidentical Transplantation for Patients with Acute Myeloid Leukemia (L Gowda/A-S Mirza)

Dr. Sayeef Mirza presented the proposal. The main objective of the proposed study is to evaluate the impact of the number of consolidation cycles on post-transplant outcomes of AML patients transplanted in first complete remission. A total of 468 patients underwent first allo-HCT from a haploidentical donor for AML in first complete remission in 2013-2018, with 193 receiving no consolidation and 275 receiving one or more cycles of consolidation prior to transplant.

Attendees suggested including time from diagnosis to transplant for patients who did not receive consolidation therapy and MRD status in the analysis. A comment was made that donor availability may be a confounding factor since more cycles of consolidation may be given to patients with difficulty finding donors.

Proposed studies; not accepted for consideration at this time

k. **PROP 2109-22:** Utilization and outcomes of second allogeneic hematopoietic stem cell transplantation for adult for acute lymphoblastic leukemia

l. **PROP 2110-01:** Outcomes of Hematopoietic Cell transplantation (HCT) for T cell Large Granular Lymphocytic Leukemia

m. **PROP 2110-10:** Haploidentical SCT in pre-transplant MRD positive AML patients

n. **PROP 2110-14:** Outcomes of patients with extramedullary disease with or without marrow involvement and patterns of relapse after allogeneic hematopoietic cell transplantation

o. **PROP 2110-40:** Analysis of hypomethylating agent plus venetoclax and CPX-351 as a bridge to allogeneic hematopoietic stem cell transplantation in patients with secondary acute myeloid leukemia (sAML)/ AML with myelodysplastic syndrome related changes (MRC)

p. **PROP 2110-42:** Developing a Super Learner Machine Learning Model and Clinical Decision Support System for Prediction of Overall Survival and Non-relapse Mortality in Patients with Acute Leukemias Undergoing Allogeneic Hematopoietic Cell Transplantation

q. **PROP 2110-78:** Donor Lymphocyte infusion vs second allogeneic hematopoietic cell transplantation for relapse after transplantation for AML/MDS

r. **PROP 2110-95:** Comparison of outcomes of patients with secondary, therapy-related, and antecedent-malignancy acute lymphoblastic leukemia to de novo acute lymphoblastic leukemia after allogeneic hematopoietic cell transplantation

s. **PROP 2110-105:** Haploidentical transplant versus mismatched unrelated donor transplant with post-transplant cyclophosphamide for acute myeloid leukemia and myelodysplastic syndromes

t. **PROP 2110-114:** Comparison Of Outcomes Between Busulfan-Based Myeloablative Conditioning Regimens With Cyclophosphamide (Bu/Cy) Or Fludarabine (Bu/Flu) For Acute Myeloid Leukemia

u. **PROP 2110-132:** Thiotepa-based conditioning in pre-transplant MRD+ AML patients may improve survival outcomes due to decreased post-transplant relapse risk

v. **PROP 2110-155:** Evaluating Outcomes of Allogeneic Hematopoietic Cell Transplantation in Therapy related Acute Lymphoblastic Leukemia (tr-ALL)

w. **PROP 2110-167:** Hematopoietic Cell Transplant Outcomes in Adult Patients with Philadelphia Chromosome like Acute Lymphoblastic Leukemia

x. **PROP 2110-192:** Impact of Minimal Residual Disease in Acute Lymphoblastic Leukemia patients undergoing Allogeneic Stem cell Transplant in first complete remission

y. **PROP 2110-212:** Impact of MRD status < alloHCT on D+30, D+100, and D+180 post-transplant infectious complications in adults with AML, ALL, and MDS

z. **PROP 2110-221:** Comparison of allogeneic hematopoietic cell transplantation following antigen-targeted salvage strategies for relapsed/refractory B-cell acute lymphoblastic leukemia

aa. **PROP 2110-235:** CD19+CAR-T therapy vs allogeneic HCT for poor-risk B-cell ALL with post-induction MRD positivity

ab. **PROP 2110-236:** Evaluating the Significance of Blast Maturation State as a Novel Approach to Further Risk Stratify High Risk Patients with Acute Myeloid Leukemia who are Referred for Allogeneic Hematopoietic Cell Transplantation in CR1

ac. **PROP 2110-304:** The effect of the prophylactic donor lymphocyte infusion on allogeneic hematopoietic cell transplantation outcomes in patients with acute myeloid leukemia

ad. **PROP 2110-346:** Role of Measurable Residual Disease in AML and MDS with reduced Intensity Allografting

6. Other business

After the proposals were presented, meeting participants had the opportunity to rate each proposal via the Tandem mobile app. Based on the voting results, current scientific merit, available number of relevant cases, and the impact of the study on the field, the following study will move forward in the committee's research portfolio for the upcoming year:

- **PROP 2110-29/2110-120/2110-128/2110-153/2110-204/2110-220/2110-294/2110-307/2110-326:** Outcomes of allogeneic hematopoietic cell transplantation following low intensity versus high intensity therapy for AML and MDS in first complete morphologic remission

Not for publication or presentation

Working Committee Overview Plan for 2022-2023

Study Number and Title	Current Status	Chairs Priority
LK19-01: Evaluating outcomes of hematopoietic cell transplantation in blastic plasmacytoid dendritic cell neoplasm	Manuscript Preparation	1
LK19-02: Evolving significance of Philadelphia chromosome status on acute lymphoblastic leukemia prognosis in the TKI era	Manuscript Preparation	1
LK19-03: Outcomes of allogeneic transplants in acute myeloid leukemia patients who achieved first complete remission after two or more cycles of induction chemotherapy	Submitted	1
LK20-01: Acute myeloid leukemia with chromosome 17 abnormalities with or without TP53 abnormalities and outcomes after hematopoietic stem cell transplantation	Data File Preparation	2
LK20-02: Outcomes of allogeneic hematopoietic cell transplantation among germline RUNX1 mutation carriers with acute myeloid leukemia	Data File Preparation	3
LK20-03: Evaluating outcomes of allogeneic hematopoietic cell transplantation in T-cell acute lymphoblastic leukemia	Protocol Development	2
LK21-01: Impact of measurable residual disease status on outcomes of acute myeloid leukemia and patients 18-65 years old in first complete remission undergoing allogeneic hematopoietic cell transplantation	Analysis	1
LK22-01: Intensive induction chemotherapy vs. hypomethylating agent therapy for older AML patients undergoing allogeneic hematopoietic cell transplantation	Protocol Pending	2