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**MINUTES AND OVERVIEW PLAN**
**CIBMTR WORKING COMMITTEE FOR CHRONIC LEUKEMIA**
**Orlando, FL**
**Thursday, February 16, 2023, 12:45 p.m. – 2:15 p.m. (EST)**


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1. **Introduction**

   The Chronic Leukemia Working Committee (CKWC) met on **Thursday**, **February 16, 2023,** at 12:45 p.m. The chairs, scientific director and statisticians were all presented at the meeting. Attendees were asked to have their name badges scanned at the front gate for attendance purpose and to maintain the committee membership roster.

   As the scientific director of the CKWC, Dr. Wael Saber welcomed the attendees on behalf of the working committee leadership. Dr. Saber presented and thanked Dr. Bart Scott for his participation as a chair for the past years and welcomed the upcoming CKWC chair Dr. Mark Juckett from University of Minnesota. Dr. Scott emphasized the availability of research datasets for secondary analysis, explained the working committee membership process. Discussed the goals, expectations, and limitations of the committee, pointing out the limitations of the molecular data in our database. Explained the proposal scoring process and rules of authorship. Lastly, explained the new CIBMTR Patient Reported Outcomes protocol and data available.

2. **Accrual summary**

   Dr. Scott referenced the accrual summary, but not formally presented due to a full agenda. The full accrual summary was available online as part of the attachments.

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

   The following publications or submitted papers from 2022 were referenced, as well as abstracts that were presented at various conferences. Dr. Scott mentioned that it was a very productive year and emphasized the high metrics of the committee. He mentioned that CK18-02 was the most recent publication. At the time, four studies were published in scientific journals recently and four abstracts were presented or accepted for presentations. These include:

a. **CK16-01** Simone Feurstein, Amy M. Trottier, Noel Estrada-Merly, Matthew Pozsgai, Kelsey McNeely, Michael W. Drazer, Brian Ruhle, Katharine Sadera, Ashwin L. Koppayi, Bart L. Scott, Betul Oran, Taiga Nishihori, Vaibhav Agrawal, Ayman Saad, R. Coleman Lindsley, Ryotaro Nakamura, Soyoung Kim, Zhenhuan Hu, Ronald Sobecks, Stephen Spellman, Wael Saber, Lucy A. Godley; Germ line predisposition variants occur in myelodysplastic syndrome patients of all ages. ***Blood. 2022 Dec 15; 140(24):2533-2548. doi:10.1182/blood.2022015790. Epub 2022 Aug 19.***

b. **CK18-02** Mei M, Pillai R, Kim S, Estrada-Merly N, Afkhami M, Yang L, Meng Z, Bilal Abid M, Aljurf M, Bacher VU, Beitinjaneh A, Bredeson C, Cahn JY, Cerny J, Copelan E, Cutler C, DeFilipp Z, Diaz Perez MA, Farhadfar N, Freytes C, Gadalla S, Ganguly S, Gale RP, Gergis U, Grunwald M, Hamilton B, Hashmi S, Hildebrandt G, Lazarus H, Litzow M, Munker R, Murthy H, Nathan S, Nishihori T, Rizzieri D, Seo S, Shah M, Solh M, Verdonck L, Vij R, Sobecks R, Oran B, Scott B, Saber W, Nakamura R. The mutational landscape in chronic myelomonocytic leukemia and its impact on allogeneic hematopoietic cell transplantation outcomes: a Center for Blood and Marrow Transplantation Research (CIBMTR) analysis. ***Haematologica. doi:10.3324/haematol. 2021.280203.Epub 2022 Apr 21.***

c. **CK19-01** Murthy HS, Ahn KW, Estrada-Merly N, Alkhateeb HB, Bal S, Kharfan-Dabaja MA, Dholaria B, Foss F, Gowda L, Jagadeesh D, Sauter C, Abid MB, Aljurf M, Awan FT, Bacher U, Badawy SM, Battiwalla M, Bredeson C, Cerny J, Chhabra S, Deol A, Diaz MA, Farhadfar N, Freytes C, Gajewski J, Gandhi MJ, Ganguly S, Grunwald MR, Halter J, Hashmi S, Hildebrandt GC, Inamoto Y, Jimenez-Jimenez AM, Kalaycio M, Kamble R, Krem MM, Lazarus HM, Lazaryan A, Maakaron J, Munshi PN, Munker R, Nazha A, Nishihori T, Oluwole OO, Ortí G, Pan DC, Patel SS, Pawarode A, Rizzieri D, Saba NS, Savani B, Seo S, Ustun C, van der Poel M, Verdonck LF, Wagner JL, Wirk B, Oran B, Nakamura R, Scott B, Saber W. Outcomes of allogeneic hematopoietic cell transplantation in T cell prolymphocytic leukemia: A contemporary analysis from the Center for International Blood and Marrow Transplant Research. ***Transplantation and Cellular Therapy. 2022 Apr 1; 28(4):187.e1-187.e10. doi:10.1016/j.jtct.2022.01.017. Epub 2022 Jan 23. PMC8977261.***

d. **CK19-01b** Dholaria B, Radujkovic A, Estrada-Merly N, Sirait T, Kim S, Hernández-Boluda JC, Czerw T, Hayden PJ, Kansagra A, Ho VT, Nishihori T, Shaughnessy P, Scott B, Nakamura R, Oran B, Kharfan-Dabaja M, Savani BN, McLornan D, Yakoub-Agha I, Saber W. Outcomes of allogeneic haematopoietic cell transplantation for chronic neutrophilic leukaemia: A combined CIBMTR/CMWP of EBMT analysis. ***British Journal of Haematology. 2022 Aug 1; 198(4):785-789. doi:10.1111/bjh.18297. Epub 2022 Jun 3. PMC9750039.***

e. **CK21-01** Jain T, Estrada-Merly N, Kim S, Queralt Salas M, Andrade Campos M, Elmariah H, Kumar R, Bejanyan N, Jones RJ, Nishihori T, Oran B, Nakamura R, Scott B, Gupta V, Saber W. PTCy-based Transplantation from Haplo-identical Donors have Similar Outcomes as Unrelated Donor Blood or Marrow Transplantation (BMT) in Myelofibrosis: A Center For International BMT Research (CIBMTR) Study. ***Oral presentation at Tandem 2023***

**4. Studies in Progress**

Due to the full agenda, studies in progress were referenced but not presented at the meeting. Dr. Nakamura mentioned that the summary of the progress of the ongoing studies was available online as part of the attachments.

a. **CK17-01** Development of a prognostic scoring system predictive of outcomes in patients with myelofibrosis after allogeneic hematopoietic cell transplantation. (T Roni/SA Giralt/J Palmer) **Submitted.**

b. **CK20-01** Outcomes of allogeneic hematopoietic cell transplantation for myelofibrosis based on the conditioning regimen. (G Murthy/ W Saber) **Submitted.**

c. **CK21-01** Outcomes of allogeneic hematopoietic cell transplantation for myelofibrosis based on the conditioning regimen. (Tania Jain/ M Queralt Sala/V Gupta/ T Nishihori) **Manuscript Preparation.**
d. **CK22-01** Impact of somatic mutations on outcomes after allogeneic hematopoietic cell transplantation in patients with myelodysplastic syndrome with ring sideroblasts (MDS-RS) and MDS/myeloproliferative neoplasm with RS and thrombocytosis (MDS/MPN-RS-T). (S Arslan/ R Nakamura) **Protocol Development.**
e. **CK22-02** Toxicity and survival of AML/MDS patients receiving allogeneic stem cell transplantation using reduced-intensity conditioning: A propensity score analysis. (P Kongtim/ A Portuguese/ S Ciurea/ B Scott) **Protocol Development.**

**5. Future/Proposed Studies**

Dr. Saber thanked the investigators whose proposals were submitted, but not selected for presentation, emphasizing that proposals were dropped due to overlaps with current studies. He also reminded the audience of the voting process.

Dr. Ryotaro Nakamura then announced the presenters for the first proposal and asked the audience to stand up to the microphones and present themselves before asking the presenter about their proposed studies. Also welcomed the virtual attendees and invited them to post their questions through chat.

a. **PROP 2210-95/2210-137/ 2210-237/ 2210-285** Combined proposal: Developing a Molecular Risk Score for Patients with Myelodysplastic Syndrome undergoing Allogeneic Hematopoietic Cell Transplantation (MRS-MDS-HCT) (A Kelkar/ C Cutler/ T Badar/ M Kharfan-Dabaja/ G Murthy/ W Saber/ S Sanikommu) (Attachment 4)

Dr. Kelkar presented the proposal on behalf of the group. The proposal hypothesizes that molecular data can be used in conjunction with clinical, cytogenetic, and routine laboratory data can be used to develop a clinical prediction rule for risk stratification and allogeneic hematopoietic cell transplantation (HCT) decision-making in patients with myelodysplastic syndrome (MDS). The study will look to develop and validate an accessible clinical prediction rule for outcomes in patients with MDS undergoing allogeneic HCT outcomes that utilizes available mutation data in addition to clinical, cytogenetic, and routine laboratory data and validate this new clinical prediction rule compared with the revised international prognostic scoring system (IPSS-R) in prognosticating clinical outcomes. It will look to determine mutation-specific outcomes and evaluate prognostic value of molecular international prognostic scoring system (IPSS-M) predicting clinical outcomes of patients with MDS undergoing allogeneic hematopoietic cell transplantation, if the mutation data for calculating IPSS-M are available in the dataset. A total of 1,673 MDS patients reported to CIBMTR between the period 2017 to 2019 met the selection criteria for this concept. About 72-75% of patients did not report molecular markers testing performed. We identified 4,264 TED level patients with Samples and 1, 468 CRF level cases with samples.

The proposal was open for discussion. The audience asked if we could supplement the study dataset with the sequenced data used in Dr. Coleman's published manuscript. Another member suggested to colleagues from EBMT for collaboration. The leadership believed EBMT has the same issues in data availability for cytogenetics and molecular markers. A member of the audience asked in which timepoint is the data presented is from, leadership confirmed that before transplant. The audience liked the idea of using the repository samples for sequencing and based on results complete this project as done by Dr. Nakamura's publication recently.

b. **PROP 2210-119:** Identifying the Optimal Graft-versus-Host Disease Regimen in Allogeneic Transplantation for Myelofibrosis (S Patel/ D Couriel) (Attachment 5)

Dr. Nakamura welcomed Dr. Sagar Patel, presenter of the proposal. The study hypothesizes that a graft-versus-host disease (GVHD) prophylaxis strategy in allogeneic hematopoietic cell transplantation (allo-HCT) for primary and secondary myelofibrosis (MF) will utilize a combination of tacrolimus, mycophenolate mofetil, and post-transplant cyclophosphamide. Such a combination will be the optimal approach regarding graft-versus-host disease-free/relapse-free survival (GFRS) as well as acute and chronic GVHD incidence and severity. The study will primarily focus on identifying the optimal GVHD prophylaxis strategy in allo-HCT for primary and secondary myelofibrosis as assessed by GFRS, acute and chronic GVHD incidence and severity. The secondary aim of the study will evaluate the risk factors engraftment failure after allo-HCT in those receiving ATG vs PTCY. The study seeks to assess the impact of pre-transplant ruxolitinib use on engraftment and GFRS. Will also evaluate the impact of renal function on GFRS and GVHD incidence. A total of 1535 cases with Myelofibrosis receiving 1$^{st}$ allo-HCT between 2008 and 2019 met the criteria for this study. Vast majority receiving a TAC-Based (without PTCy) GVHD prophylaxis regimen.

The proposal was open for questions and comments. A member of the audience asked how different this concept to Dr. Tania Jain's study would be presented in the oral abstract session at the Tandem meetings. Dr. Jain study restricted to Haploidentical donor with PTCy, other donors containing PTCy. A member commented on restricting the population to more contemporary years. Another member suggested looking at the use of ruxolitinib in this cohort. A member via the chat added that there are multiple completed studies looking into the effect of peri-transplant use of ruxolitinib. Lastly, a member asked about how to address the possible center effects and the variety of regimens by centers.

c. **PROP 2210-169; 2210-225; 2210-238** Combined proposal: Allogeneic Stem Cell Transplant Outcomes for Patients with TP53-Mutant Myelodysplastic Syndrome and Myeloproliferative Neoplasm: A CIBMTR Analysis (S Patel/ J Cerny/ G Murthy/ W Saber/ H Bhatt/ M De Lima) (Attachment 6)

Dr. Betul Oran welcomed Dr. Shyam Patel, who presented this proposal on behalf of the group. The study hypothesizes that that transplant outcomes for patients with TP53-mutant MDS and MPN are heterogeneous with respect to conditioning regimen, stem cell donor source, and GvHD prophylaxis regimen. The study hypothesizes that a tailored approach to selection of transplant factors should be considered, given the heterogeneity within this genetically defined subset. The study will examine as subgroup analyses for conditioning regimen, stem cell donor source and GVHD prophylaxis. Additionally, will focus on evaluating the DFS and OS at 30 days, 100 days, 6 months, 1 year, and 5 years. Lastly, will evaluate NRM and incidence of GvHD at 30 days, 100 days, 6 months, 1 year, and 5 years.

A total of 301 cases of MDS/ MPN patients undergoing 1$^{st}$ allo-HCT with TP53 mutation at any timepoint between diagnosis and transplant between 2008-2019 were identified. Dr. Patel addressed the comments and suggestions made by the committee on the Tandem 2022 meetings.
The proposal was opened for comments and questions. A member mentioned a publication in which they looked at conditioning regimen and intensity for these diseases and suggested they should also look at this in this subset of patients and commented on assessing treatment-failure and relapse as outcomes of this study.

d. **PROP 2210-259:** The mutational landscape in Myelodysplastic Syndrome arising from Aplastic Anemia and its impact on Allogeneic Stem Cell Transplantation Outcomes. (B Ball/ R Nakamura) (Attachment 7)

Dr. Betul Oran welcomed Dr. Ball, presenter of this proposal. This study hypothesizes that somatic gene mutations detected in patients with MDS arising from aplastic anemia prior to allogeneic stem cell transplantation impact post-transplant outcomes. The study will determine the impact of IPSS, IPSS-R, and IPSS-M assessed prior to conditioning on overall survival among patients with post-AA MDS undergoing allo-HCT. It will evaluate the impact of IPSS, IPSS-R, and IPSS-M assessed prior to conditioning on Disease-free survival, relapse/progression, non-relapse mortality.
Will seek to determine the mutational landscape of mutations among patients with post-AA MDS undergoing allo-HCT and the mutational burden (allele fraction) of myeloid mutations among patients MDS arising from aplastic anemia. Lastly, to determine correlation between mutations and disease phenotype. A total of 272 patients with MDS cases arising from Aplastic Anemia were reported to CIBMTR between 2001-2019 met the study criteria. About half of the cases have CRF-level information. Additionally, 135 (50%) of the cases have recipient samples available for research.

The floor was opened from questions and comments from the audience. A member of the audience pointed out that the ability to assess the impact of therapies given before HCT and the effect on mutation status is limited in the dataset and suggested looking at how many patients progressing from Aplastic Anemia to MDS received therapeutic interventions. Another member asked how many recipients you have samples for in this cohort, and how reliable are the peripheral blood samples for this analysis. It was commented that this same analysis has been done in in previous CIBTMR studies. A member of the audience asked about the context of HLA-expression on this type of this study. Dr. Nakamura, co-PI of this study added that they are looking for funding on this study is it is accepted by the committee. Lastly, a question was asked on the telomere length analysis.

*22 additional proposals were submitted but not presented as listed below:*

a. **PROP 2205-05**: Validation of HLA-genotype associations with allogeneic hematopoietic stem cell transplantation outcomes in MDS. *Dropped- overlap*
b. **PROP 2210-12**: Allogeneic Hematopoietic Cell Transplantation (HCT) for the Treatment of Myelodysplastic Syndromes (MDS) in Younger Adults. *Dropped-low scientific impact*
c. **PROP 2210-17**: Outcomes after Hematopoietic Stem Cell Transplant for Chronic Myeloid Leukemia in Blast Crisis when using Busulfan-based versus Total Body Irradiation-based Conditioning Regimens. *Dropped-low scientific impact*
d. **PROP 2210-40**: Allogeneic stem cell transplant for chronic myelogenous leukemia (CML) using post-transplant cyclophosphamide (PT-Cy) as GVHD prophylaxis: An analysis from the CIBMTR database. *Dropped-low scientific impact*
e. **PROP 2210-74**: Hematopoietic Cell Transplantation Risk Assessment Tool for older patients with Myelodysplastic Syndrome Undergoing Allogeneic Cell Transplantation using Reduced Intensity Conditioning Regimens. *Dropped-low scientific impact*
f. **PROP 2210-92**: Comparison of FluMel and FluCy as Reduced Intensity Conditioning Regimens for Haploidentical Hematopoietic Cell Transplant with Post-Transplant Cyclophosphamide in Older Patients with Acute Myeloid Leukemia and Myelodysplastic Syndrome. *Dropped- overlap*
g. **PROP 2210-112**: Predicting outcomes of Allogenic stem cell transplant in patients with CMML using Machine learning. *Dropped-small sample for Machine Learning (n <=2000 cases)*
h. **PROP 2210-137**: Validation of Molecular International Prognostic Scoring System for Myelodysplastic Syndrome Patients receiving Allogeneic Hematopoietic Cell. C*ombined with other proposals*
i. **PROP 2210-159**: The impact of donor germline variants in genes linked to hereditary hematopoietic diseases on outcomes after allogeneic hematopoietic cell transplantation. *Dropped- overlap*
j. **PROP 2210-207**: Post-Transplant Maintenance Treatment in MDS Patients. *Dropped-supplemental data needed*
k. **PROP 2210-211**: Effect of Ruxolitinib prior to allogeneic hematopoietic stem cell transplantations in patients with myelofibrosis in the post-transplant cyclophosphamide era. *Dropped- overlap*
l. **PROP 2210-214**: Effect of Venetoclax-based therapies for high-risk myelodysplastic syndrome prior to allogeneic hematopoietic stem cell transplant in the post-transplant cyclophosphamide (PTCy) era. *Dropped-overlap*
m. **PROP 2210-225**: Characteristics and outcomes of MDS with TP53 mutation undergoing allogeneic hematopoietic cell transplantation: CIBMTR analysis. C*ombined with other proposals*
n. **PROP 2210-237**: Assessing the applicability of the molecular IPSS (IPSS-M) and development of CIBMTR molecular risk stratification system for predicting the outcomes of allogeneic hematopoietic cell transplantation in myelodysplastic syndrome. *Combined with other proposals*
o. **PROP 2210-238**: Outcomes of allogeneic hematopoietic stem cell transplantation for patients with TP53-mutated acute myeloid leukemia and myelodysplastic syndrome. *Dropped-low scientific impact*
p. **PROP 2210-245**: Clinical outcomes and therapeutic strategies for myeloid/lymphoid neoplasm associated with FGFR1 rearrangement. *Dropped-small sample size (n <= 15 cases)*
q. **PROP 2210-255**: Comparison of higher vs. lower dose of melphalan (140 mg/m2 vs. 100 mg/m2) for elderly patients undergoing reduced-intensity conditioning (RIC) transplant for myelodysplastic syndrome (MDS). *Dropped- overlap*

r. **PROP 2210-256**: Comparison of Haploidentical Donor Allogeneic Hematopoietic Cell Transplant (HCT) with Post-Transplant Cyclophosphamide to Matched Donor HCT for Myelodysplastic Syndrome/Myeloproliferative Neoplasm Overlap Syndromes. *Dropped-low scientific impact*
s. **PROP 2210-257**: Role of ruxolitinib use after allogeneic hematopoietic stem cell transplant. *Dropped-low scientific impact*
t. **PROP 2210-285**: Pretransplant Molecular International Prognostic System (IPSS-M) score on transplant outcomes in Myelodysplastic Syndromes. *Combined with other proposals*
u. **PROP 2210-287**: Characteristics Associated with Improved Survival Following Allogeneic Hematopoietic Cell Transplant (HCT) for Myelodysplastic Syndrome/Myeloproliferative Neoplasm Overlap Syndromes. *Dropped-low scientific impact*
v. **PROP 2210-299**: DDX41 mutated myeloid Neoplasm: Impact of allogeneic stem cell transplant. *Dropped-small sample (n <= 15 cases)*

**6. Other Business**

The meeting was adjourned at **2:15** p.m. The chairs of the working committee, scientific director and statisticians had a post-WC meeting afterwards. After the new proposals were presented, attendees had the opportunity to vote on the proposals using the Tandem app until March 3. Based on the voting results, current scientific merit, and impact of the studies on the field, the following studies were decided to move forward as the committee's research portfolio for the upcoming year:

***Not for publication or presentation***

| Working Committee Overview Plan for 2023-2024 | | |
|---|---|---|
| **Study number and title** | **Current status** | **Chairs priority** |
| CK17-01 Development of a prognostic scoring system predictive of outcomes in patients with myelofibrosis after allogeneic hematopoietic cell transplantation | Manuscript Preparation | 3 |
| CK20-01 Outcomes of allogeneic hematopoietic cell transplantation for myelofibrosis based on the conditioning regimen. | Submitted | 4 |
| CK21-01 Haploidentical donor transplantation versus matched donor allogeneic hematopoietic cell transplantation outcomes in patients with myelofibrosis. | Datafile Preparation | 3 |
| CK22-01 Impact of somatic mutations on outcomes after allogeneic hematopoietic cell transplantation in patients with myelodysplastic syndrome with ring sideroblasts (MDS-RS) and MDS/myeloproliferative neoplasm with RS and thrombocytosis (MDS/MPN-RS-T). | Protocol Development | 1 |
| CK22-02 Toxicity and survival of AML/MDS patients receiving allogeneic stem cell transplantation using reduced-intensity conditioning: A propensity score analysis. | Protocol Development | 2 |
| CK23-01 Identifying the Optimal Graft-versus-Host Disease Regimen in Allogeneic Transplantation for Myelofibrosis. | Protocol Pending | 3 |
| CK23-02 The mutational landscape in Myelodysplastic Syndrome arising from Aplastic Anemia and its impact on Allogeneic Stem Cell Transplantation Outcomes. | Protocol Pending | 3 |

**Working Assignments for Working Committee Leadership (March 2023)**

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| Mark Juckett | **CK22-02** Toxicity and survival of AML/MDS patients receiving allogeneic stem cell transplantation using reduced-intensity conditioning: A propensity score analysis. |
| | **CK23-01** Identifying the Optimal Graft-versus-Host Disease Regimen in Allogeneic Transplantation for Myelofibrosis. |
| Ryotaro Nakamura | **CK17-01** Development of a prognostic scoring system predictive of outcomes in patients with myelofibrosis after allogeneic hematopoietic cell transplantation. |
| | **CK23-02** The mutational landscape in Myelodysplastic Syndrome arising from Aplastic Anemia and its impact on Allogeneic Stem Cell Transplantation Outcomes. |
| Betul Oran | **CK21-01** Haploidentical allogeneic stem cell transplantation in patients with myelofibrosis. |
| | **CK22-01** Impact of somatic mutations on outcomes after allogeneic hematopoietic cell transplantation in patients with myelodysplastic syndrome with ring sideroblasts (MDS-RS) and MDS/myeloproliferative neoplasm with RS and thrombocytosis (MDS/MPN-RS-T). |